http://www.eurekalert.org/pub_releases/2013-10/uoc - usu101613.php

UCLA scientist uncovers biological clock able to measure age of most human tissues

Study finds women's breast tissue ages faster than rest of body

Everyone grows older, but scientists don't really understand why. Now a UCLA study has uncovered a biological clock embedded in our genomes that may shed light on why our bodies age and how we can slow the process.

Published in the Oct. 21 edition of Genome Biology, the findings could offer valuable insights into cancer and stem cell research.

While earlier clocks have been linked to saliva, hormones and telomeres, the new research is the first to identify an internal timepiece able to accurately gauge the age of diverse human organs, tissues and cell types.

Unexpectedly, the clock also found that some parts of the anatomy, like a woman's breast tissue, age faster than the rest of the body.

"To fight aging, we first need an objective way of measuring it. Pinpointing a set of biomarkers that keeps time throughout the body has been a four-year challenge," explained Steve Horvath, a professor of human genetics at the David Geffen School of Medicine at UCLA and of biostatistics at the UCLA Fielding School of Public Health.

"My goal in inventing this clock is to help scientists improve their understanding of what speeds up and slows down the human aging process."

To create the clock, Horvath focused on methylation, a naturally occurring process that chemically alters DNA. Horvath sifted through 121 sets of data collected previously by researchers who had studied methylation in both healthy and cancerous human tissue.

Gleaning information from nearly 8,000 samples of 51 types of tissue and cells taken from throughout the body, Horvath charted how age affects DNA methylation levels from pre-birth through 101 years.

To create the clock, he zeroed in on 353 markers that change with age and are present throughout the body.

Horvath tested the clock's effectiveness by comparing a tissue's biological age to its chronological age. When the clock repeatedly proved accurate, he was thrilled—and a little stunned.

"It's surprising that one could develop a clock that reliably keeps time across the human anatomy," he admitted. "My approach really compared apples and oranges, or in this case, very different parts of the body: the brain, heart, lungs, liver, kidney and cartilage."

While most samples' biological ages matched their chronological ages, others diverged significantly. For example, Horvath discovered that a woman's breast tissue ages faster than the rest of her body.

"Healthy breast tissue is about two to three years older than the rest of a woman's body," said Horvath. "If a woman has breast cancer, the healthy tissue next to the tumor is an average of 12 years older than the rest of her body."

The results may explain why breast cancer is the most common cancer in women. Given that the clock ranked tumor tissue an average of 36 years older than healthy tissue, it could also explain why age is a major risk factor for many cancers in both genders.

Horvath next looked at pluripotent stem cells, adult cells that have been reprogrammed to an embryonic stem cell–like state, enabling them to form any type of cell in the body and continue dividing indefinitely.

"My research shows that all stem cells are newborns," he said. "More importantly, the process of transforming a person's cells into pluripotent stem cells resets the cells' clock to zero."

In principle, the discovery proves that scientists can rewind the body's biological clock and restore it to zero.

"The big question is whether the biological clock controls a process that leads to aging," Horvath said. "If so, the clock will become an important biomarker for studying new therapeutic approaches to keeping us young."

Finally, Horvath discovered that the clock's rate speeds up or slows down depending on a person's age.

"The clock's ticking rate isn't constant," he explained. "It ticks much faster when we're born and growing from children into teenagers, then slows to a constant rate when we reach 20."

In an unexpected finding, the cells of children with progeria, a genetic disorder that causes premature aging, appeared normal and reflected their true chronological age.

UCLA has filed a provisional patent on Horvath's clock.

His next studies will examine whether stopping the body's aging clock halts the aging process - or increases cancer risk. He'll also explore whether a similar clock exists in mice.

http://www.eurekalert.org/pub_releases/2013-10/sumc-srd101813.php

Stanford researchers demonstrate efficient method for converting fat cells to liver cells

In a feat of modern-day alchemy with huge potential for regenerative medicine, Stanford University School of Medicine scientists have developed a fast, efficient way to turn cells extracted from routine liposuction into liver cells.

STANFORD, Calif. - The scientists performed their experiments in mice, but the adipose stem cells they used came from human liposuction aspirates and became human, liver-like cells that flourished inside the mice's bodies. This method is distinct from those producing liver cells from embryonic stem cells or induced pluripotent stem cells. Although iPS and embryonic stem cells are pluripotent - they can, in principle, differentiate into every cell type - they carry a palpable risk of forming tumors. However, the cells produced using this new technique, which involves no intermediate pluripotent phase, show no signs of being tumorogenic. The advance is described in a study to be published Oct. 21 in Cell Transplantation.

The liver is the body's chemistry set. It builds complex biomolecules we need, and it filters and breaks down waste products and toxic substances that might otherwise accumulate to dangerous levels. Unlike most other organs, a healthy liver can regenerate itself to a significant extent. But this capacity cannot overcome acute liver poisoning or damage from chronic alcoholism or viral hepatitis.

Acute liver failure from acetaminophen alone takes about 500 lives annually and accounts for close to 60,000 emergency-room visits and more than 25,000 hospitalizations annually. Other environmental toxins, including poisonous mushrooms, contribute still more cases.

All aspects of the new fat-to-liver technique are adaptable for human use, said Gary Peltz, MD, PhD, professor of anesthesia and the study's senior author. Creating iPS cells requires introducing foreign and potentially carcinogenic genes. But adipose stem cells merely have to be harvested from fat tissue. The process takes nine days from start to finish — fast enough to regenerate liver tissue in acute liver poisoning victims, who would otherwise die within a few weeks, barring liver transplantation.

Some 6,300 liver transplants are performed annually in the United States, with another 16,000 patients on the waiting list. Every year, more than 1,400 people die before a suitable liver can be found for them. While it can save lives, liver transplantation is complicated, risky and, even when successful, fraught with aftereffects. Typically, the recipient is consigned to a lifetime of taking immunosuppressant drugs to prevent organ rejection.

"We believe our method will be transferable to the clinic," Peltz said. "And because the new liver tissue is derived from a person's own cells, we do not expect that immunosuppressants will be needed."

Liver cells are not something an adipose stem cell normally wants to turn into, Peltz said.

The Stanford team knew it was possible, though. Another way of converting liposuction-derived adipose stem cells to liver-like cells (called i-Heps, for induced hepatocytes) had been developed in 2006 by Japanese researchers. But that method, which relies on chemical stimulation, requires 30 days or longer and is inefficient; it could not produce enough material for liver reconstitution. (Working with iPS cells takes even longer; they must first be generated from adult cells before they can be converted to i-Heps.)

Using a different technique — Peltz refers to it as spherical culture - he and his associates were able to achieve the conversion within nine days with an efficiency of 37 percent, as opposed to the vastly lower yield obtained with the prior method (12 percent) or using iPS cells. (Peltz said improvements since the study's publication now enable yields exceeding 50 percent within seven to eight days.)

Dan Xu, PhD, a postdoctoral scholar and the study's lead author, adapted the spherical culture methodology from early embryonic-stem-cell literature. Instead of growing on flat surfaces in a laboratory dish, the harvested adipose stem cells are cultured in a liquid suspension in which they form spheroids. "This seems to make them happier," Peltz said.

When they had enough cells, the investigators tested them by injecting them into immune-deficient laboratory mice that accept human grafts. These mice were bioengineered in 2007, in a collaboration between Peltz's lab and study co-author Toshihiko Nishimura, MD, PhD, and other scientists at the Tokyo-based Central Institute for Experimental Animals. Only the livers of these mice contained an extra gene that would convert the antiviral compound gancyclovir into a potent toxin. When these mice were treated with gancyclovir, their liver cells died off quickly.

At this point the investigators injected 5 million i-Heps into the mice's livers. To do that - no mean feat, as these tiny organs weigh a scant 1.8 grams - they used an ultrasound-guided injection procedure that is routinely employed in gastroenterological clinics for biopsies.

Four weeks later, the investigators examined the mice's blood and found the presence of a protein (human serum albumin) that is only produced by human liver cells and was shown to be an accurate proxy for the

number of new human liver cells in these experimental mice's livers. The mice's blood had substantial human serum albumin levels, which nearly tripled in the following four weeks. These blood levels correspond with the repopulation of roughly 10-20 percent of the mice's pre-destroyed livers by new human liver tissue. (Past studies have shown only miniscule human serum albumin production, at best, in mice given similar amounts of chemically induced i-Heps.)

Blood tests also revealed that the mice's new liver tissue was discharging its waste-filtration responsibility. Examination of the livers themselves showed that the transplanted cells had integrated into the liver, expressed surface markers unique to mature human hepatocytes and produced multi-cell structures required for human bile duct formation. Other tests indicated that the spherically cultured i-Heps resembled natural human hepatocytes more closely than did i-Heps produced from iPS cells.

Importantly, two months after injection of i-Heps produced by spherical culture, there was no evidence of tumor formation. But mice in which IPS-cell-originated i-Heps were introduced developed multiple tumors, which could be felt through the body surface within three weeks.

At 1,500 grams, a healthy human liver is more than 800 times the size of a mouse's and contains about 200 billion cells. "To be successful, we must regenerate about half of the damaged liver's original cell count," said Peltz. With spherical culture, he said, close to a billion injectable iHeps can be produced from 1 liter of liposuction aspirate, readily obtained from a single liposuction procedure. The cell replication that takes place after injection expands that number further, to over 100 billion i-Heps.

That could be enough to substitute for a human liver transplant, Peltz said. Stanford's Office of Technology Licensing has filed a patent on the use of spherical culture for hepatocyte induction. Peltz's group is optimizing the culture and injection techniques, talking to the U.S. Food and Drug Administration, and gearing up for safety tests on large animals. Barring setbacks, the new method could be ready for clinical trials within two to three years, he estimated.

Additional Stanford co-authors were Jeffrey Glenn, MD, PhD, associate professor of medicine; Sara Michie, MD, professor of pathology; Gordon Lee, MD, associate professor of plastic surgery; and research associates Ming Zheng, PhD, and Manhong Wu, PhD.

The study was funded by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (grant 1R01DK0909921).

http://www.eurekalert.org/pub_releases/2013-10/dumc-bmp101613.php

Breast milk protein may be key to protecting babies from HIV infection

A substance in breast milk that neutralizes HIV and may protect babies from acquiring HIV from their infected mothers has been identified for the first time by researchers at Duke Medicine.

DURHAM, N.C. – The protein, called Tenascin-C or TNC, had previously been recognized as playing a role in wound healing, but had not been known to have antimicrobial properties. The discovery could lead to potential new HIV-prevention strategies.

Reporting in the journal Proceedings of the National Academy of Sciences during the week of Oct. 21, 2013, the researchers describe how the TNC protein in breast milk binds to and neutralizes the HIV virus, potentially protecting exposed infants who might otherwise become infected from repeated exposures to the virus.

"Even though we have antiretroviral drugs that can work to prevent mother-to-child transmission, not every pregnant woman is being tested for HIV, and less than 60 percent are receiving the prevention drugs, particularly in countries with few resources," said senior author Sallie Permar, M.D., Ph.D., assistant professor of pediatrics, immunology and molecular genetics and microbiology at Duke. "So there is still a need for alternative strategies to prevent mother-to-child transmission, which is why this work is important."

Worldwide in 2011, an estimated 330,000 children acquired HIV from their mothers during pregnancy or birth, or through breastfeeding according to UNICEF. As international health organizations have set a goal of eliminating mother-to-child infections, researchers have worked to develop safe and affordable alternatives to antiretroviral therapy that can be used to block HIV transmission to infants.

Permar and colleagues focused on breast milk, which has long been recognized as having some protective quality that inhibits mother-to-child transmission despite multiple daily exposures over months and even years of nursing. Earlier studies had identified some antiviral properties in breast milk, but the majority of the HIV-neutralizing activity of breast milk remained unexplained. More recent studies pointed to a large protein that had yet to be identified.

In their study, the Duke team screened mature milk samples from uninfected women for neutralizing activity against a panel of HIV strains, confirming that all of the detectable HIV-neutralization activity was contained in the high molecular weight portion. Using a multi-step protein separation process, the researchers narrowed the detectable HIV-neutralization activity to a single protein, and identified it as TNC.

"TNC is a component of the extracellular matrix that is integral to how tissues hold themselves together," Permar said, noting that co-author Harold Erickson, Ph.D., professor of cell biology at Duke, was among the first to identify and describe TNC in the 1980s. "This is a protein involved during wound healing, playing a role in tissue repair. It is also known to be important in fetal development, but its reason for being a component of breast milk or its antiviral properties had never been described."

Further analysis described how TNC works against HIV by blocking virus entry. The protein is uniquely effective in capturing virus particles and neutralizes the virus, specifically binding to the HIV envelope. These properties provide widespread protection against infection.

"It's likely that TNC is acting in concert with other anti-HIV factors in breast milk, and further research should explore this," Permar said. "But given TNC's broad-spectrum HIV-1-binding and neutralizing activity, it could be developed as an HIV-prevention therapy, given orally to infants prior to breastfeeding, similar to the way oral rehydration salts are routinely administered to infants in developing regions."

Permar said TNC would also appear to be inherently safe, since it is a naturally occurring component of breast milk, and it may avoid the problem of HIV resistance to antiretroviral regimens that complicate maternal/infant applications.

"The discovery of the HIV inhibiting effect of this common protein in breast milk provides a potential explanation for why nursing infants born to HIV-infected mothers do not become infected more often than they do," said Barton F. Haynes, M.D., director of the Duke Human Vaccine Institute. "It also provides support for inducing inhibitory factors in breast milk that might be even more protective, such as antibodies, that would completely protect babies from HIV infection in this setting."

In addition to Permar, co-senior author was S. Munir Alam. Other authors include Genevieve G. Fouda, Frederick H. Jaeger, Joshua D. Amos, Carrie Ho, Erika L. Kunz, Kara Anasti, Lisa W. Stamper, Brooke E. Liebl; Kimberly H. Barbas, Tomoo Ohashi, M. Arthur Moseley, Hua-Xin Liao and Harold P. Erickson.

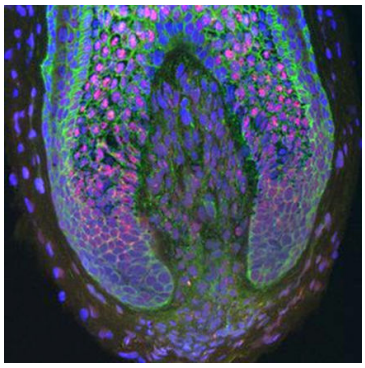
The study was funded by the Doris Duke Charitable Foundation Clinical Scientist Development Award; Duke University School of Medicine; Center for HIV/AIDS Vaccine Immunology; and the National Institute of Allergic and Immunologic Diseases (U19 AI067854) (K08AI087992) (CA047056).

http://www.bbc.co.uk/news/health-24607696

Baldness treatment a 'step closer'

Scientists say they have moved a step closer to banishing bald spots and reversing receding hairlines after human hair was grown in the laboratory.

By James Gallagher Health and science reporter, BBC News



Cells were taken from the base of a follicle and used to grow new hairs

A joint UK and US team was able to create new hairs from tissue samples. Far more research is needed, but the group said its technique had the "potential to transform" the treatment of hair loss. The study results were published in the journal Proceedings of the National Academy of Sciences.

There are baldness therapies including drugs to slow the loss of hairs, and transplants, which move hair from the back of the head to cover bald spots. The scientists at the University of Durham, in the UK, and Columbia University Medical Centre, in the US, were trying to actually grow new hairs. Their plan was to start with material taken from the base of a hair and use it to grow many new hairs.

Tricky feat

But human hair has been tricky to grow despite successes in animal studies. Whenever human tissue was taken from the dermal papillae, the cells which form the base of each hair follicle, the cells would transform into skin instead of growing new hairs. However, the group found that by clumping the cells together in "3D spheroids" they would keep their hairy identity.

Tissue was taken from seven people and grown in 3D spheroids. These were then transplanted into human skin which had been grafted on to the backs of mice. After six weeks, new hair follicles formed in five out of the seven cases and some new tiny hairs began to form.

Prof Colin Jahoda, from Durham University, told the BBC a cure for baldness was possible but it was too soon for men to be hanging up the toupee. "It's closer, but it's still some way away because in terms of what people want cosmetically they're looking for re-growth of hair that's the same shape, the same size, as long as before, the same angle. Some of these are almost engineering solutions. "Yeah I think it [baldness] will eventually be treatable, absolutely." He added: "It's hard to say exactly how long that would take, but the fact that we've done it now should reawaken interest."

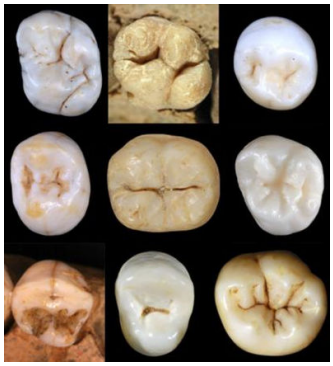
Any future therapy would involve transplanting cells which have been grown in the laboratory so safety is a concern. There would be a risk of infection and the cells could become abnormal, or even cancerous, while being grown. Baldness cures may not be the first application of the research. Prof Jahoda believes the findings will be used to improve the quality of skin grafts used after severe burns.
Prof Angela Christiano, from Columbia University, said: "This approach has the potential to transform the medical treatment of hair loss. "Current hair-loss medications tend to slow the loss of hair follicles or potentially stimulate the growth of existing hairs, but they do not create new hair follicles. "Our method, in contrast, has the potential to actually grow new follicles using a patient's own cells."

http://www.eurekalert.org/pub_releases/2013-10/iu-snk101713.php

Study: No known hominin is ancestor of Neanderthals and modern humans

The search for a common ancestor linking modern humans with the Neanderthals who lived in Europe thousands of years ago has been a compelling subject for research.

But a new study suggests the quest isn't nearly complete.
The researchers, using quantitative methods focused on the shape of dental fossils, find that none of the usual suspects fits the expected profile of an ancestor of Neanderthals and modern humans. They also present evidence that the lines that led to Neanderthals and modern humans diverged nearly 1 million years ago, much earlier than studies based on molecular evidence have suggested.
The study, which will be published online this week by the Proceedings of the National Academy of Sciences, was carried out by an international team of scholars from The George Washington University, Konrad Lorenz Institute for Evolution and Cognition Research in Austria, Indiana University and Atapuerca Research Team in Spain.



This image shows diversity in premolar and molar morphology in Neanderthals, modern humans and potential ancestral species. **Aida Gómez-Robles**

"Our results call attention to the strong discrepancies between molecular and paleontological estimates of the divergence time between Neanderthals and modern humans," said Aida Gómez-Robles, lead author of the paper and a postdoctoral scientist at the Center for the Advanced Study of Hominid Paleobiology of The George Washington University. "These discrepancies cannot be simply ignored, but they have to be somehow reconciled."
P. David Polly, professor in the Department of Geological Sciences in the IU Bloomington College of Arts and Sciences, is a co-author of the study. Other co-authors are Spanish researchers José María Bermúdez de Castro, Juan-Luis Arsuaga and Eudald Carbonell, co-directors of the excavations at Atapuerca sites. The study resulted from a collaboration that developed when Gómez-Robles spent a semester at IU studying with Polly while she was a graduate student at the National Research Centre for Human Evolution and at the University of Granada, both in Spain. It also makes use of statistical methods developed by IU Bloomington biologist Emilia Martins.
The article, "No known hominin species matches the expected dental morphology of the last common ancestor of Neanderthals and modern humans," relies on fossils of approximately 1,200 molars and premolars from 13 species or types of hominins - humans and human relatives and ancestors. Fossils from the well-known Atapuerca sites have a crucial role in this research, accounting for more than 15 percent of the complete studied fossil collection.
The researchers use techniques of morphometric analysis and phylogenetic statistics to reconstruct the dental morphology of the last common ancestor of Neanderthals and modern humans. They conclude with high statistical confidence that none of the hominins usually proposed as a common ancestor, such as Homo heidelbergensis, H. erectus and H. antecessor, is a satisfactory match. "None of the species that have been previously suggested as the last common ancestor of Neanderthals and modern humans has a dental morphology that is fully compatible with the expected morphology of this ancestor," Gómez-Robles said.
The study also finds that the potential human ancestors discovered in Europe are morphologically closer to Neanderthals than to modern humans. This suggests the line leading to Neanderthals arose around 1 million years ago and the divergence of humans took place much earlier than previously thought. Other studies have placed the divergence around 350,000 years ago.
The researchers argue that quantitative and statistical methods provide a better way to settle debates about human origins than the descriptive analyses that have been used in the past. "Our primary aim," they write, "is to put questions about human evolution into a testable, quantitative framework and to offer an objective means to sort out apparently unsolvable debates about hominin phylogeny." They also suggest applying their methodology to study other body parts represented in the hominin fossil record.

What comes next? Answers to the ancestry question could come from studying hominin fossils from Africa, the researchers say. But the African fossil record from the era of interest is sparse.
"The study tells us that there are still new hominin finds waiting to be made," Polly said. "Fossil finds from about 1 million years ago in Africa deserve close scrutiny as the possible ancestor of Neanderthals and modern humans."

http://www.eurekalert.org/pub_releases/2013-10/uow-hvc102113.php

Hitchhiking virus confirms saga of ancient human migration

A study of the full genetic code of a common human virus offers a dramatic confirmation of the "out-of-Africa" pattern of human migration, which had previously been documented by anthropologists and studies of the human genome.

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MADISON, Wis. — The virus under study, herpes simplex virus type 1 (HSV-1), usually causes nothing more severe than cold sores around the mouth, says Curtis Brandt, a professor of medical microbiology and ophthalmology at the University of Wisconsin-Madison. Brandt is senior author of the study, now online in the journal PLOS ONE.
When Brandt and co-authors Aaron Kolb and Cécile Ané compared 31 strains of HSV-1 collected in North America, Europe, Africa and Asia, "the result was fairly stunning," says Brandt.
"The viral strains sort exactly as you would predict based on sequencing of human genomes. We found that all of the African isolates cluster together, all the virus from the Far East, Korea, Japan, China clustered together, all the viruses in Europe and America, with one exception, clustered together," he says.
"What we found follows exactly what the anthropologists have told us, and the molecular geneticists who have analyzed the human genome have told us, about where humans originated and how they spread across the planet."
Geneticists explore how organisms are related by studying changes in the sequence of bases, or "letters" on their genes. From knowledge of how quickly a particular genome changes, they can construct a "family tree" that shows when particular variants had their last common ancestor.
Studies of human genomes have shown that our ancestors emerged from Africa roughly 150,000 to 200,000 years ago, and then spread eastward toward Asia, and westward toward Europe.
Scientists have previously studied herpes simplex virus type 1 by looking at a single gene, or a small cluster of genes, but Brandt notes that this approach can be misleading. "Scientists have come to realize that the relationships you get back from a single gene, or a small set of genes, are not very accurate."
The PLOS ONE study used high-capacity genetic sequencing and advanced bioinformatics to analyze the massive amount of data from the 31 genomes.
The technology of simultaneously comparing the entire genomes of related viruses could also be useful in exploring why certain strains of a virus are so much more lethal than others. In a tiny percentage of cases, for example, HSV-1 can cause a deadly brain infection, Brandt notes.
"We'd like to understand why these few viruses are so dangerous, when the predominant course of herpes is so mild. We believe that a difference in the gene sequence is determining the outcome, and we are interested in sorting this out," he says.
For studies of influenza virus in particular, Brandt says, "people are trying to come up with virulence markers that will enable us to predict what a particular strain of virus will do."
The researchers broke the HSV-1 genome into 26 pieces, made family trees for each piece and then combined each of the trees into one network tree of the whole genome, Brandt says. "Cécile Ané did a great job in coming up with a new way to look at these trees, and identifying the most probable grouping." It was this grouping that paralleled existing analyses of human migration.
The new analysis could even detect some intricacies of migration. Every HSV-1 sample from the United States except one matched the European strains, but one strain that was isolated in Texas looked Asian. "How did we get an Asian-related virus in Texas?" Kolb asks. Either the sample had come from someone who had travelled from the Far East, or it came from a native American whose ancestors had crossed the "land bridge" across the Bering Strait roughly 15,000 years ago.
"We found support for the land bridge hypothesis because the date of divergence from its most recent Asian ancestor was about 15,000 years ago. Brandt says. "The dates match, so we postulate that this was an Amerindian virus."
Herpes simplex virus type 1 was an ideal virus for the study because it is easy to collect, usually not lethal, and able to form lifelong latent infections. Because HSV-1 is spread by close contact, kissing or saliva, it tends to run in families. "You can think of this as a kind of external genome," Brandt says.

Furthermore, HSV-1 is much simpler than the human genome, which cuts the cost of sequencing, yet its genome is much larger than another virus that also has been used for this type of study. Genetics often comes down to a numbers game; larger numbers produce stronger evidence, so a larger genome produces much more detail.
But what really jumped out of the study, Brandt says, "was clear support for the out-of-Africa hypothesis. Our results clearly support the anthropological data, and other genetic data, that explain how humans came from Africa into the Middle East and started to spread from there."
The correspondence with anthropology even extends, as before, to the details. In the virus, as in human genomes, a small human population entered the Middle East from Africa. "There is a population bottleneck between Africa and the rest of the world; very few people were involved in the initial migration from Africa," Brandt says. "When you look at the phylogenetic tree from the virus, it's exactly the same as what the anthropologists have told us."
The PLOS ONE paper is available at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0076267.
These studies were supported by grants from the National Institutes of Health: R01EY07336 and R01EY018597.

http://www.bbc.co.uk/news/health-24607136

Polio outbreak fears in war-ravaged Syria

Experts are concerned that polio may have made a return to war-torn Syria.

The World Health Organization says it has received reports of the first suspected outbreak in the country in 14 years. Syrian's Ministry of Public Health is launching an urgent response, but experts fear the disease will be hard to control amid civil unrest.
Immunisation is almost impossible to carry out in regions under intense shellfire. As a result, vaccination rates have been waning - from 95% in 2010 to an estimated 45% in 2013. At least a third of the country's public hospitals are out of service, and in some areas, up to 70% of the health workforce has fled.
Outbreak risks have also increased due to overcrowding, poor sanitation and deterioration in water supply. More than four million Syrians who have relocated to less volatile areas of the country are mostly living in overcrowded, unsanitary conditions.
The WHO says it is already seeing increased cases of measles, typhoid and hepatitis A in Syria.
Dr Jaouad Mahjour, director of the department for communicable diseases at WHO's regional office for the Eastern Mediterranean, said: "Given the scale of population movement both inside Syria and across borders, together with deteriorating environmental health conditions, outbreaks are inevitable."
The cluster of suspected polio cases was detected in early October 2013 in Deir al-Zour province.
Initial results from a laboratory in Damascus indicate that at least two of the cases could indeed be polio.
A surveillance alert has been issued for the region to actively search for additional potential cases.
Supplementary immunisation activities in neighbouring countries are currently being planned.
WHO's International Travel and Health recommends that all travellers to and from polio-infected areas be fully vaccinated against polio.
Most people infected with the poliovirus have no signs of illness and are never aware they have been infected. These symptomless people carry the virus in their intestines and can "silently" spread the infection to thousands of others before the first case of polio paralysis emerges.
Polio is spread by eating food or drink contaminated with faeces or, more rarely, directly from person-to-person via saliva.

http://www.medscape.com/viewarticle/812875?src=rss

Measles Vaccine: First Dose at 12 Months May Erode Potency Later

Quebec schoolchildren were 6.2 times more likely to contract measles during a 2011 outbreak if they had received the first of a 2-dose vaccination at 12 to 13 months of age than if they received it at 15 months of age, according to a case-control study.

Diedtra Henderson

Fannie Defay, MSc, from the Unité de Recherche en Santé Publique, Centre hospitalier universitaire de Quéébec, Canada, and colleagues published the results of their study online October 21 in Pediatrics.
An initial investigation of the 2011measles outbreak, centered at a Quebec high school, revealed a sobering vulnerability among schoolchildren who had received a second dose of the measles vaccine. Rather than boosting their protection, vaccine effectiveness at that high school dipped among twice-vaccinated students (94.2% vaccine efficacy) vs once-vaccinated students (95.9%).
Defay and coauthors sought to shed light on how the age of students' first vaccination affected their measles risk. Although the recommended age for the first measles shot for American infants is 12 to 15 months, in Canada, the recommended age for the first dose has been 12 months since 1970. The research team looked at all

measles cases reported in Quebec in 2011 among twice-vaccinated school-age patients attending 17 schools, matching 102 students with confirmed measles with 510 control students. All of the students had received their first vaccine dose at age 12 months or older.

"In participants outside the outbreak school, when the first dose was administered at 12 to 13 versus ≥15 months of age, measles risk was 6.2 times higher (95% [confidence interval] CI, 1.33–29.3; P = .02), and in pooled analysis it was 5.2 times higher (95% CI, 1.91–14.26; P = .0013)," Defay and coauthors write.

"A pooled fivefold greater risk of measles among those whose first [measles, mumps, and rubella] dose was administered at 12 to 13 vs ≥15 months is concerning, especially in the context of measles elimination efforts that require high levels of immunity."

The vaccine efficacy results come on the heels of a study published last week in JAMA Pediatrics that found compelling safety reasons for not delaying the first measles dose beyond 12 to 15 months.

The lead author of a commentary published in concert with that study told Medscape Medical News that both articles underscore the importance of optimally timing measles vaccination.

"The most important thing is to ensure protection when children are most at risk, and to do so safely," Kristen A. Feemster, MD, MPH, MSHPR, from the Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and Division of Infectious Diseases and the Vaccine Education Center, The Children's Hospital of Philadelphia, Pennsylvania, told Medscape Medical News. "The paper [by Defay and colleagues] raises some issues about different efficacy when vaccinated at 12 vs 15 months, but for a pediatrician, I think it's still important to focus upon the currently recommended window," Dr. Feemster said.

The authors of the Quebec study caution that the erosion of vaccine protection in certain children should trigger additional studies.

"Although unvaccinated people should remain the prime target for measles vaccination, the unexpected vulnerability we have identified in twice-vaccinated people could ultimately lead to failed measles elimination efforts," Defay and colleagues conclude. "If the effect of early vaccination permanently alters the ability to respond to subsequent doses, even adding a third or fourth dose may not provide long-lasting protection."

Support for the study was provided by the Ministère de la Santé et des Services Sociaux du Québec. One author disclosed receiving research funds from GlaxoSmithKline (GSK) and Sanofi Pasteur and travel reimbursement from GSK. A second author disclosed receiving research funds from GSK. Another study author disclosed employment by Medicago Inc; receiving research funds from GSK, Sanofi Pasteur, and Pfizer; and being an advisory board member for GSK, Merck, Novartis, Pfizer, and Sanofi Pasteur. The remaining authors and the commentator have disclosed no relevant financial relationships.

Pediatrics. Published online October 21, 2013. ***Abstract***

http://arstechnica.com/science/2013/10/an-insecticide-infection-connection-in-bee-colony-collapses/

An insecticide-infection connection in bee colony collapses

Researchers discover a common insecticide shuts down a key immune protein in bees.

by John Timmer - Oct 22 2013, 8:00am TST

Colony collapse disorder has been decimating bees for several years, but explanations have been hard to come by. After some spurious claims about cell phones causing the problem, researchers began identifying factors that did create problems for the health of bees, including infections, insecticides, and agricultural practices. The problem is that all of these seemed connected to colony collapse, which suggested the cause was likely to be complex.

Now, some researchers may have cut through the complexity. They've found that a common insecticide causes changes in the immune system of insects, which in turn leaves them more vulnerable to infection. And they've begun the process of determining how those immune changes come about on the molecular level.

The Italian researchers behind this current work previously analyzed an infection present in bees. But the concerns being raised about insecticides motivated them to look into whether there might be a connection between the two. Rather than focusing on bee mortality, they decided to look at the pathways that mediate immune responses in insects.

Bees lack that adaptive immune system that generates pathogen-specific antibodies and T cells in mammals. But they share an innate immune system, which is able to generally recognize infectious agents like bacteria. In fact, this innate immune system is evolutionarily ancient, as the same genes are used to control the response in animals as distantly related as bees and humans.

Previous toxicology work in mammals indicated that a specific class of insecticides, the neonicotinoids, could influence the activity of genes involved in the innate immune system. These genes were activated by the presence of neonicotinoids, and they shut down a key regulator of the innate immune system (a protein called

NF-κb). Thus, the more of these insecticides, the less effective the innate immune system is likely to be—at least in mammals.
The researchers started by showing that the same is true in insects. Initially, they worked with everyone's favorite fruit fly, Drosophila, showing that the equivalent genes responded in the same ways in the flies. They then showed that the innate immune response isn't activated when these same flies are exposed to an infection. A different class of insecticide (an organophosphate) had a much weaker effect on the fly's innate immunity. With the molecular activity well characterized, they went on to demonstrate that the same effects could be seen in bees.
To show that the changes in gene activity had an impact on the bees' immune function, the authors turned to the deformed wing virus. Animals that were not given a dose of a neonicotinoid were able to largely keep the viral infection in check. But two different neonicotinoid insecticides showed a dose response: the more you gave the bees, the more likely the infection was to flourish.
If this result holds up, it neatly ties together a number of observations. Various infections may still be doing the ultimate job of killing the bees, but their virulence could be explained by compromised immune function, caused by a combination of insecticide use and agricultural practices. The results will also provide further support for the European Union's attempt to ban the use of neonicotinoid pesticides, a decision that was made earlier this year. Several chemical companies have announced that they will sue to block the ban.
PNAS, 2013. DOI: 10.1073/pnas.1314923110 (About DOIs).

http://www.eurekalert.org/pub_releases/2013-10/aga-ccr102213.php

Coffee consumption reduces risk of liver cancer

Coffee consumption reduces risk of hepatocellular carcinoma

Bethesda, MD - Coffee consumption reduces risk of hepatocellular carcinoma (HCC), the most common type of liver cancer, by about 40 percent, according to an up-to-date meta-analysis published in Clinical Gastroenterology and Hepatology, the official clinical practice journal of the American Gastroenterological Association. Further, some data indicate that three cups of coffee per day reduce liver cancer risk by more than 50 percent.
"Our research confirms past claims that coffee is good for your health, and particularly the liver," said Carlo La Vecchia, MD, study author from the department of epidemiology, Istituto di Ricerche Farmacologiche "Mario Negri," and department of clinical sciences and community health, Università degli Studi di Milan, Italy. "The favorable effect of coffee on liver cancer might be mediated by coffee's proven prevention of diabetes, a known risk factor for the disease, or for its beneficial effects on cirrhosis and liver enzymes."
Researchers performed a meta-analysis of articles published from 1996 through September 2012, ultimately studying 16 high-quality studies and a total of 3,153 cases. This research fills an important gap as the last meta-analysis was published in 2007, and since then there has been data published on more than 900 cases of HCC. Despite the consistency of results across studies, time periods and populations, it is difficult to establish whether the association between coffee drinking and HCC is causal, or if this relationship may be partially attributable to the fact that patients with liver and digestive diseases often voluntarily reduce their coffee intake. "It remains unclear whether coffee drinking has an additional role in liver cancer prevention," added Dr. La Vecchia. "But, in any case, such a role would be limited as compared to what is achievable through the current measures."
Primary liver cancers are largely avoidable through hepatitis B virus vaccination, control of hepatitis C virus transmission and reduction of alcohol drinking. These three measures can, in principle, avoid more than 90 percent of primary liver cancer worldwide.
Liver cancer is the sixth most common cancer in the world, and the third most common cause of cancer death. HCC is the main type of liver cancer, accounting for more than 90 percent of cases worldwide. Chronic infections with hepatitis B and C viruses are the main causes of liver cancer; other relevant risk factors include alcohol, tobacco, obesity and diabetes.

http://phys.org/news/2013-10-veterinary-scientists-track-deadly-emerging.html

Veterinary scientists track the origin of a deadly emerging pig virus in the United States

The sudden emergence of porcine epidemic diarrhea virus, which belongs to the coronavirus family has caused economic and public health concerns in the United States.

Veterinary researchers at the Virginia-Maryland Regional College of Veterinary Medicine at Virginia Tech have helped identify the origin and possible evolution of an emerging swine virus with high mortality rates that has already spread to at least 17 states. A team of researchers led by Dr. X.J. Meng, University Distinguished Professor of Molecular Virology, has used virus strains isolated from the ongoing outbreaks in Minnesota and

Iowa to trace the likely origin of the emergent porcine epidemic diarrhea virus (PEDV) to a strain from the Anhui province in China. The virus, which causes a high mortality rate in piglets, was first recognized in the United States in May of this year.

"The virus typically only affects nursery pigs and has many similarities with transmissible gastroenteritis virus of swine," said Meng, who is a faculty member in the Department of Biomedical Sciences and Pathobiology. "There is currently no vaccine against porcine epidemic diarrhea virus in the United States. Although some vaccines are in use in Asia, we do not know whether they would work against the U.S. strains of the virus."

The researchers determined not only that the three U.S. strains of the porcine epidemic diarrhea virus are most closely related to the Chinese strains of the virus, but also that the U.S. strains likely diverged two or three years ago following an outbreak of a particularly virulent strain in China. They published their findings on the "Origin, Evolution, and Genotyping of Emergent Porcine Epidemic Diarrhea Virus Strains in the United States" in the Oct. 15 issue of the American Academy of Microbiology's journal, mBio.

According to the study, the U.S. strains of the virus share 99.5 percent of their genetic code with their Chinese counterpart. Allan Dickerman, a co-author of the paper and research assistant professor at the Virginia Bioinformatics Institute, performed the molecular clock analysis to determine that the divergence of the U.S. and Chinese virus strains coincides with a porcine epidemic diarrhea virus outbreak in China back in December of 2010. Meng said it is unclear whether the U.S. strains of the virus diverged in China or in the United States.

The sudden emergence of porcine epidemic diarrhea virus, which belongs to the coronavirus family, has caused economic and public health concerns in the United States.

"The ongoing outbreaks of Middle East respiratory syndrome coronavirus in humans from countries in or near the Arabian Peninsula and the historical deadly nature of the 2002 outbreaks of severe acute respiratory syndrome coronavirus create further anxiety about the emergency of PEDV in the United States due to the lack of scientific information about the origin and evolution of this emerging coronavirus," wrote Dr. Yao-Wei Huang, the first author of the paper and a former research assistant professor at the veterinary college who is now a professor at Zhejiang University in Hangzhou, China.

Researchers have found no evidence that the virus can spread to humans or pose a threat to food safety. They did, however, come across additional evidence that the U.S. strains share several genetic features with a bat coronavirus—findings which point to an evolutionary origin from bats and the potential for cross-species transmission.

Though commonly accepted that the virus spreads through the fecal-oral route, Meng said that scientists have not yet ruled out the possibility of other transmission routes. Symptoms include acute vomiting, anorexia, and watery diarrhea with high mortality rates in pigs less than 10 days old.

"Veterinarians need to recognize the symptoms of the disease, and with the lack of a vaccine in the United States, practicing strict biosecurity and good sanitation procedures on the farm are important for prevention and control of this deadly disease," Meng added.

More information: mbio.asm.org/content/4/5/e00737-13.abstract

http://www.eurekalert.org/pub_releases/2013-10/plos-hei101613.php

HIV elimination in South Africa could be achieved by current treatment policy

Universal test and treat (UTT) approach could achieve elimination by 2027

The current antiretroviral treatment policy in South Africa could lead to elimination of HIV within the country over the next 24 to 34 years, but a universal test and treat (UTT) approach could achieve elimination 10 years earlier according to new research published this week in PLOS Medicine.

The research, which is an international collaboration led by Jan Hontelez from Erasmus MC, University Medical Center Rotterdam, Netherlands, used nine increasingly sophisticated mathematical models aimed to test the time frames in which expanded access to antiretroviral viral therapy could lead to HIV elimination in South Africa..

Antiretroviral therapy is usually started when a person's CD4 count (a type of white blood cell) falls below 350 cells/µl blood, but evidence exists that treatment of all HIV-positive individuals, regardless of their CD4 count, could reduce HIV transmission by reducing the infectiousness of HIV-positive individuals ("treatment as prevention"). Previous studies have suggested that scale up of HIV treatment could lead to elimination of HIV although within differing time scales.

In their study Hontelez and colleagues systematically assessed a UTT intervention (defined as annual screening of individuals age 15+ years and immediate initiation of antiretroviral therapy (ART) for all HIV-infected adults starting in 2012 and scaled up to 90% coverage by 2019) by simulating the HIV epidemic in South Africa with increasing degrees of complexity and realism—including sexual networks, HIV stages with

different degrees of infectiousness, and updated treatment effectiveness assumptions to explore the timeframes to elimination.

All the models replicated the prevalence of HIV in South Africa (the proportion of the population that was HIV-positive) between 1990 and 2010, and all predicted that UTT would result in HIV elimination (less than one new infection per 1,000 person-years). However, whereas the simplest model predicted that UTT would eliminate HIV after seven years, the more complex, realistic models predicted elimination at much later time points. Importantly, the most comprehensive model predicted that, although elimination would be reached after about 17 years of UTT, the current strategy of ART initiation for HIV-positive individuals at a CD4 cell count at or below 350 cells/μl would also lead to HIV elimination, albeit ten years later than UTT.

In a related Perspective article Nathan Ford and Gottfried Hirnschall (uninvolved in the study) from the World Health Organization reflect on the research noting, "[t]he case for ART impact on HIV transmission is proven. The priority now is to help translate this concept into benefits for patients and communities by identifying and implementing approaches that work to maximize early HIV testing and ART uptake and long-term retention in care."

Funding: This work is supported by the HIV Modelling Consortium. The HIV Modelling Consortium is supported by a grant from the Bill & Melinda Gates Foundation to Imperial College London. This work is also supported by the US National Institutes of Health (1R01MH083539) and (1R01-HD058482). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: TBH and MLN are members of the PLOS Medicine Editorial Board. TBH is the director of the HIV Modelling Consortium, a project funded by the Bill & Melinda Gates Foundation, which contributed funding toward this study. TBH did not have a role in deciding that funding should be awarded to this team. All other authors have declared that no competing interests exist.

Citation: Hontelez JAC, Lurie MN, Bärnighausen T, Bakker R, Baltussen R, et al. (2013) Elimination of HIV in South Africa through Expanded Access to Antiretroviral Therapy: A Model Comparison Study. PLoS Med 10(10): e1001534. doi:10.1371/journal.pmed.1001534

http://www.eurekalert.org/pub_releases/2013-10/wch-fsh102213.php

Flu shot halves risk of heart attack or stroke in people with history of heart attack, study finds

Flu vaccine may not only ward off serious complications from influenza, it may also reduce the risk of heart attack or stroke by more than 50 per cent

TORONTO, ON - The flu vaccine may not only ward off serious complications from influenza, it may also reduce the risk of heart attack or stroke by more than 50 per cent among those who have had a heart attack, according to new research led by Dr. Jacob Udell, a cardiologist at Women's College Hospital and clinician-scientist at the University of Toronto. What's more, the vaccine's heart protective effects may be even greater among those who receive a more potent vaccine.

"Our study provides solid evidence that the flu shot helps prevent heart disease in vulnerable patients —with the best protection in the highest risk patients," Dr. Udell said. "These findings are extraordinary given the potential for this vaccine to serve as yearly preventative therapy for patients with heart disease, the leading cause of death among men and women in North America."

Published today in the Journal of the American Medical Association, the study reviewed six clinical trials on heart health in people who received the flu vaccine. The studies included more than 6,700 patients with a history of heart disease. The researchers found people who received the flu shot:

Had a 36 percent lower risk of a major cardiac event (heart attack, stroke, heart failure, or death from cardiac–related causes) one year later

Had a 55 percent lower risk of a major cardiac event if they had a recent heart attack

Were less likely to die from cardiac-related and other causes, and

Were less likely to have a major cardiac event with a more potent vaccine compared with the standard seasonal vaccine

Dr. Udell carried out this research in collaboration with Dr. Michael Farkouh, senior co-author of the study and Chair of the Peter Munk Centre of Excellence in Multinational Clinical Trials, which is within the Peter Munk Cardiac Centre at the University Health Network.

"If the flu vaccine can reduce the risk of cardiac events, these shots could have considerable impact on cardiac health," said Dr. Udell. However, Drs. Udell and Farkouh caution that a large prospective clinical trial is necessary to confirm the effectiveness and safety of the influenza vaccine as a therapy that will reduce the risk of heart attack or stroke in people with heart disease. The researchers are now organizing this type of clinical trial to follow heart disease patients for up to 12 months after receiving the flu shot.

"These findings are all the ammunition we need to move forward," said Dr. Farkouh, who is also director of the Heart and Stroke Richard Lewar Centre at the University of Toronto. "We'll build on this research with a definitive, international trial to conclusively determine whether the flu shot prevents heart attack."
If proven to be a safe and simple prevention method, the impact could be significant for people with or at risk of heart disease and stroke.
"Hundreds of thousands of people die each year from cardiac causes in North America," Dr. Udell said. "While preventative care involves lifestyle changes and taking your pills, now, we may also be able to tell patients by getting your flu shot, it might save your life – what a simple and significant way to reduce deaths and the burden on our healthcare system."

http://www.eurekalert.org/pub_releases/2013-10/ca-tgi102213.php

There's gold in them thar trees

Eucalyptus trees - or gum trees as they are know - are drawing up gold particles from the earth via their root system and depositing it their leaves and branches.

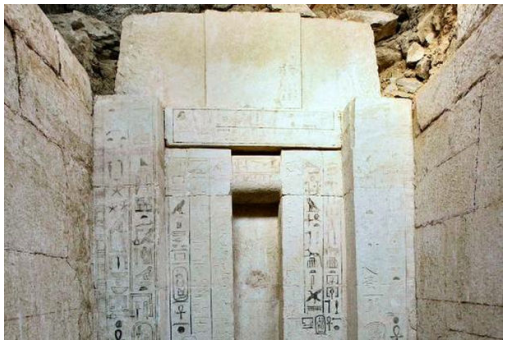
Scientists from CSIRO made the discovery and have published their findings in the journal Nature Communications. "The eucalypt acts as a hydraulic pump – its roots extend tens of metres into the ground and draw up water containing the gold. As the gold is likely to be toxic to the plant, it's moved to the leaves and branches where it can be released or shed to the ground," CSIRO geochemist Dr Mel Lintern said.
The discovery is unlikely to start an old-time gold rush – the "nuggets" are about one-fifth the diameter of a human hair. However, it could provide a golden opportunity for mineral exploration, as the leaves or soil underneath the trees could indicate gold ore deposits buried up to tens of metres underground and under sediments that are up to 60 million years old.
"The leaves could be used in combination with other tools as a more cost effective and environmentally friendly exploration technique," Dr Lintern said. "By sampling and analysing vegetation for traces of minerals, we may get an idea of what's happening below the surface without the need to drill. It's a more targeted way of searching for minerals that reduces costs and impact on the environment. "Eucalyptus trees are so common that this technique could be widely applied across Australia. It could also be used to find other metals such as zinc and copper."
Using CSIRO's Maia detector for x-ray elemental imaging at the Australian Synchrotron, the research team was able to locate and see the gold in the leaves. The Synchrotron produced images depicting the gold, which would otherwise have been untraceable.
"Our advanced x-ray imaging enabled the researchers to examine the leaves and produce clear images of the traces of gold and other metals, nestled within their structure," principal scientist at the Australian Synchrotron Dr David Paterson said. "Before enthusiasts rush to prospect this gold from the trees or even the leaf litter, you need to know that these are tiny nuggets, which are about one-fifth the diameter of a human hair and generally invisible by other techniques and equipment." CSIRO research using natural materials, such as calcrete and laterite in soils, for mineral exploration has led to many successful ore deposit discoveries in regional Australia. The outcomes of the research provide a direct boost to the national economy.

http://phys.org/news/2013-10-unearths-year-tomb-doctor-pharaohs.html

Dig unearths 4,000 year old tomb of doctor to pharaohs

Archaeologists have unearthed a 4,000 year old tomb outside the Egyptian capital containing what they believe are the remains of a prominent doctor to the pharaohs, officials said on Tuesday.

The tomb, part of a 21 metre (70 foot) by 14 metre (46 foot) plot, with four-metre (13 feet) high walls, was discovered at Abusir, southwest of Cairo, senior antiquities ministry official Ali al-Asfar said. "This discovery is important because this is the tomb of one of the greatest doctors from the time of the pyramid builders, one of the doctors closely tied to the king," Antiquities Minister Ibrahim Ali said in a statement.
Asfar said the area in which the grave was found appeared to be a family plot and the Czech team of archaeologists was now looking for mummies of relatives. Abusir, a vast necropolis dating back to Egypt's Old Kingdom, houses the pyramids of several pharaohs of the Fifth Dynasty, which began its rule shortly after 2,500 BC.



A picture taken on October 22, 2013 shows Egyptian hieroglyphics on a 4,000 year old tomb which was discovered by archaeologists in Abusir on the outskirts of the Egyptian capital, Cairo

http://www.medscape.com/viewarticle/812677?src=rss

Can Watermelon Relieve Muscle Soreness?

Watermelon is a rare food source of citrulline, which may reduce muscle fatigue

Gayle Nicholas Scott, PharmD

True to its name, watermelon (*Citrullus lanatus*) is made up of greater than 90% water.[1] Watermelon is low in calories (a 2-cup serving contains about 90 calories) and is regarded as a healthy food. Watermelon contains a high concentration of lycopene,[1,2] a carotenoid that may have beneficial effects on cancer and cardiovascular disease risk.[2] Watermelon is also high in vitamins A and C.[1]

In addition, watermelon is a rare food source of citrulline, an amino acid that was first isolated in 1930 from watermelon.[3-5] Citrulline is an antioxidant and is thought to allow watermelon to survive drought-related oxidative stress.[6]

Citrulline is a precursor for arginine, which is involved in the formation of nitric oxide and creatine, and is a key constituent of the urea cycle, which detoxifies ammonia.[7] Nitric oxide is involved in many physiologic processes, such as mediating noradrenergic and noncholinergic neurotransmission, learning, memory, and neuroprotection.[7,8] Nitric oxide also appears to modulate blood flow and mitochondrial respiration during physical exercise.[7]

Interest in watermelon to enhance exercise centers around its ability to increase plasma citrulline and arginine levels.[3,4] In theory, citrulline via arginine and nitric oxide could augment detoxification of ammonia generated during exercise and improve recovery.[7] Citrulline has been shown to increase renal reabsorption of bicarbonate, which could lessen the effects of exercise-induced acidosis.[9] Research in rats suggests that citrulline may reduce muscle fatigue.[10]

Studies of citrulline supplements in humans have shown mixed results. One group of researchers found that a single 8-g dose of citrulline malate enhanced aerobic exercise performance and ameliorated muscle soreness; however, the researchers did not measure any serum metabolites that would indicate enhanced buffering of lactic acid or hyperammonemia.[11]

Another group of researchers found that citrulline supplementation decreased time to exhaustion on a treadmill test.[12] Interest in citrulline supplementation to enhance physical performance was sufficient to induce the Air Force to conduct a randomized, double-blind, cross-over study of citrulline malate (6 g/day).[13] The researchers found no differences between citrulline and placebo in measures of respiration, lactate production, or time to exhaustion during incremental cycle ergometry.

Watermelon juice was tested in 7 athletes using cycle ergometry. Researchers compared the effect of watermelon juice (containing 1.17 g of citrulline), enriched watermelon juice (4.83 g of citrulline plus 1.17 g from watermelon), and placebo. Watermelon juice and watermelon juice enriched with citrulline similarly reduced perceived muscle soreness better than placebo, but no significant differences among any of the 3 treatments were observed in terms of lactate levels.[6]

More research is required to clarify the effect of watermelon or citrulline on exercise in general and muscle soreness in particular. Until such research is available, watermelon can be recommended as a healthy, low-calorie food for everyone except patients with rare inborn disorders involving citrulline or arginine metabolism.[3] For patients interested in trying watermelon to lessen muscle soreness after exercise, suggest exercising with and without eating watermelon and comparing the results. Tell patients that research on citrulline supplements has shown conflicting results, and watermelon enhanced with additional citrulline does not appear to offer any benefit.

References

1. *Agricultural Research Service, US Department of Agriculture, National Nutrient Database for Standard Reference. Basic Report: 09326. Watermelon, raw. http://archive.is/MJ8Td Accessed October 16, 2013.*
2. *Edwards AJ, Vinyard BT, Wiley ER, et al. Consumption of watermelon juice increases plasma concentrations of lycopene and beta-carotene in humans. J Nutr. 2003;133:1043-1050. Abstract*
3. *Mandel H, Levy N, Izkovitch S, Korman SH. Elevated plasma citrulline and arginine due to consumption of Citrullus vulgaris (watermelon). J Inherit Metab Dis. 2005;28:467-472. Abstract*
4. *Collins JK, Wu G, Perkins-Veazie P, et al. Watermelon consumption increases plasma arginine concentrations in adults. Nutrition. 2007;23:261-266. Abstract*
5. *Fearon WR. The carbamido diacetyl reaction: a test for citrulline. Biochem J. 1939;33:902-907. Abstract*
6. *Tarazona-Díaz MP, Alacid F, Carrasco M, Martinez I, Aguayo E. Watermelon juice: potential functional drink for sore muscle relief in athletes. J Agric Food Chem. 2013 Jul 29. [Epub ahead of print]*
7. *Sureda A, Pons A. Arginine and citrulline supplementation in sports and exercise: ergogenic nutrients? Med Sport Sci. 2012;59:18-28.*
8. *Moncada S, Higgs A. The L-arginine-nitric oxide pathway. N Engl J Med. 1993;329:2002-2012. Abstract*

9. Callis A, Magnan de Bornier B, Serrano JJ, Bellet H, Saumade R. Activity of citrulline malate on acid-base balance and blood ammonia and amino acid levels. Study in the animal and in man. Arzneimittelforschung. 1991;41:660-663. Abstract
10. Goubel F, Vanhoutte C, Allaf O, Verleye M, Gillardin JM. Citrulline malate limits increase in muscle fatigue induced by bacterial endotoxins. Can J Physiol Pharmacol. 1997;75:205-207. Abstract
11. Pérez-Guisado J, Jakeman PM. Citrulline malate enhances athletic anaerobic performance and relieves muscle soreness. J Strength Cond Res. 2010;24:1215-1222. Abstract
12. Hickner RC, Tanner CJ, Evans CA, et al. L-citrulline reduces time to exhaustion and insulin response to a graded exercise test. Med Sci Sports Exerc. 2006; 38:660-666. Abstract
13. Walker TB, Zupan MF, Rutter MJ, Vojta CN. AFRL-RH-BR-TR-2010-0068. Does citrulline malate enhance physical performance? Air Force Research Laboratory, Human Effectiveness Directorate. October 2010. http://www.dtic.mil/dtic/tr/fulltext/u2/a532948.pdf Accessed September 29, 2013.

http://www.bbc.co.uk/news/health-24625808

Saturated fat heart disease 'myth'

The risk from saturated fat in foods such as butter, cakes and fatty meat is being overstated and demonised, according to a cardiologist.

Dr Aseem Malhotra said there was too much focus on the fat with other factors such as sugar often overlooked.
It is time to "bust the myth of the role of saturated fat in heart disease", he writes in an opinion piece in the British Medical Journal. But the British Heart Foundation said there was conflicting evidence. It added reducing cholesterol through drugs or other means does lower heart risk.
Studies on the link between diet and disease have led to dietary advice and guidelines on how much saturated fat, particularly cholesterol, it is healthy to eat. Millions of people in the UK have been prescribed statins to reduce cholesterol levels.
Dr Malhotra, a cardiology registrar at Croydon University Hospital, London, says the "mantra that saturated fat must be removed to reduce the risk of cardiovascular disease has dominated dietary advice and guidelines for almost four decades". He says saturated fat has been "demonised" and any link with heart disease is not fully supported by scientific evidence.
The food industry has compensated for lowering saturated fat levels in food by replacing it with sugar, he says, which also contributes to heart disease. Adopting a Mediterranean diet - olive oil, nuts, oily fish, plenty of fruit and vegetables and a moderate amount of red wine - after a heart attack is almost three times as powerful in reducing mortality as taking a statin, writes Dr Malhotra.
However, Prof Peter Weissberg, medical director at the British Heart Foundation, says studies on the link between diet and disease frequently produce conflicting results. Unlike drug trials, it is difficult to carry out a controlled, randomised study, he says. "However, people with highest cholesterol levels are at highest risk of a heart attack and it's also clear that lowering cholesterol, by whatever means, lowers risk."
Cholesterol levels can be influenced by many factors including diet, exercise and drugs, in particular statins, he adds. "There is clear evidence that patients who have had a heart attack, or who are at high risk of having one, can benefit from taking a statin. "But this needs to be combined with other essential measures, such as eating a balanced diet, not smoking and taking regular exercise."
Statins are a group of medicines that can help lower rates of cholesterol in the blood. Cholesterol can also be reduced by eating a healthy, balanced diet, maintaining a healthy weight and doing regular physical activity.

http://www.wired.com/design/2013/10/can-these-houseplants-prevent-cancer/

Do-Gooder Turns Ferns Into Arsenic-Filtering Super System

More than 70 million people in Bangladesh drink polluted water every day and one in five water wells have dangerous levels of arsenic, a metalloid that leads to high rates of infant mortality and cancer.

By Joseph Flaherty

3.4 million people, almost the entire population of Los Angeles, die from water-related diseases every year. One of the chief polluters is arsenic, a metalloid that is vital to the fabrication of semiconductors, and by extension, everything from solar panels to iPads. Unfortunately, a single drop of liquified arsenic could render an entire swimming pool's worth of water unsafe for human consumption. Over time, that amount would lead to increased infant mortality and cancer.
Well-meaning designers have tried to solve the clean water problem with design thinking in the past. Their solutions are often clever and beautiful, but are often too expensive to deploy at scale and end up winning design awards without solving the problem at hand.
Stephen Goodwin Honan, a 24-year-old U.S. Navy officer, decided to address the problem using ferns. He discovered a species called Pteris cretica that could thrive near arsenic mines. He set up a hydroponic rig in his basement to see if the plant would leach arsenic from the water. After a rough start where his lack of a green

thumb nearly killed plants that can subsist on one of the world's most toxic carcinogens, the experiment succeeded.

Honan's system, dubbed Clean Water, isn't pretty in any conventional sense, but the elegance of the design can't be overstated. No specialized equipment is needed—any watertight bin filled with $10 dollars worth of starter plants and placed on a makeshift bamboo table will work. Tainted water is poured into the vessel and the plants immediately start absorbing the toxin through their roots, cleaning a half-gallon of arsenic tainted water every minute. Newly filtered water is tested to ensure the plants have done their job and is then poured into another vessel for household use. After many cycles, the plants become saturated with arsenic, are harvested, and taken to a lab where they're transformed into a substance that looks a bit like green Jell-O. This gross gelatin is heated releasing arsenic vapor into an enclosed chamber here it's captured and sold to manufacturers, leaving harmless biomass behind.

"Phytoremediation, using plants to rapidly extract toxins from the environment, has existed for decades, but few plants have been adapted for small scale drinking water filters," says Honan. "Most people in western countries are unwilling to trade-off long remediation periods for lower cost filtration systems; however, in developing countries, such as Bangladesh, this trade-off proves critical for technology adoption."

Proof of concept in hand, Honan took his plants and blue plastic bins to Bangladesh, the most densely populated country in the world, where more than 70 million people are essentially forced to drink poison on a daily basis. His process worked in the field, but there were surprising side effects. As demand for testing and filtration services exploded, Honan started training villagers to analyze water sources and set up new purification systems, allowing them to pocket some extra money in the process.

Honan's smart design choices could help Clean Water succeed where so many projects have failed before it. Training is minimal and leverages skills the agrarian population already has in spades. The arsenic captured in a single system's plants is worth about $85 to manufacturers, a life changing sum in a country where most of the citizens subsist on just a dollar a day. Honan has managed to turn a destructive chemical into a potentially lucrative crop that could lead to a thriving social enterprise.

Now the challenge is effectively handling the poisonous plants come harvest time. "We are currently working to upcycle or recycle all of the components of the filter: arsenic for semiconductors, green biomass for plant fertilizers, and plastic containers for future filters," says Honan. "In order to scale our project, we are looking to partner with a semiconductor manufacturer and deliver the world's first socially responsible arsenic."

http://www.eurekalert.org/pub_releases/2013-10/uom-osc102313.php

Older siblings' cells can be passed from female dogs to their puppies in the womb, MU researchers find

Discovery will help further research into health effects of microchimerism

COLUMBIA, Mo. – Some people possess a small number of cells in their bodies that are not genetically their own; this condition is known as microchimerism. In prior studies, researchers from the University of Missouri College of Veterinary Medicine found that this condition also exists in dogs. Now, the researchers have found evidence that this condition can be passed from a female dog to her offspring while they are still in the womb. Jeffrey Bryan, an associate professor of oncology at the MU College of Veterinary Medicine and director of Comparative Oncology and Epigenetics Laboratory, says this discovery will help further study into the health effects of microchimerism in dogs and in humans.

"We already have some evidence that microchimerism may increase risk of thyroid disease while lowering the risk of breast cancer in women," Bryan said. "The pet dog represents an excellent model of many ailments in people, and the presence of fetal microchimerism in dogs will allow studies which further clarify its role in health and disease. Knowing that the condition can be passed on through birth will help us track the condition and its effects through several generations of animals."

Microchimerism most often occurs when a mother gives birth to a child. In some cases, cells from that child are left in the mothers' body and continue to live, despite being of a different genetic makeup than surrounding cells. The MU researchers have identified evidence that those cells can then be passed on to other children the mother may give birth to at a later time.

In their study, Senthil Kumar, a co-investigator in this study and assistant research professor and assistant director of the Comparative Oncology and Epigenetics Laboratory and Bryan, along with MU researchers Sandra Axiak-Bechtel, assistant professor of oncology, and Sara Hansen, a comparative medicine resident at MU,found microchimerism in a female dog that had given birth to male and female puppies. The researchers found cells with Y-chromosomes in the mother after these births, meaning the mother had male cells present in her female body. The researchers also found genetically similar male cells in the mother's female puppies from

a later litter. Those puppies were newborn and had never been pregnant, strongly suggesting that they acquired the cells that were left behind by their older brothers while in the womb.
"These new findings are significant because they suggest that the movement, or trafficking, of fetal cells is quite extensive in dogs, as has been suggested in people," Bryan said. "This degree of cell trafficking can have an impact on health, disease, and therapy, including in transplantation. The identification of this phenomenon strongly suggests that companion dogs will help us more rapidly understand the real impact of microchimerism in human medicine."
Kumar, Hansen, Axiak-Bechtel, and Bryan plan on continuing their research to follow the lifespans of dogs with microchimerism to determine to what diseases those dogs may be susceptible.

http://www.eurekalert.org/pub_releases/2013-10/jhm-cl102313.php

'Common courtesy' lacking among doctors-in-training

Johns Hopkins researchers say 'etiquette-based' communications needed to improve medical outcomes

Johns Hopkins investigators have found that doctors-in-training are unlikely to introduce themselves fully to hospitalized patients or sit down to talk to them eye-to-eye, despite research suggesting that courteous bedside manners improve medical recovery along with patient satisfaction.
A report on the research, published online this month in the Journal of Hospital Medicine, calls for some simple adjustments to intern communications to make the whole experience of a hospital stay better.
"Basic things make a difference in patient outcomes and they're not being done to the extent they should be," says study leader Leonard S. Feldman, M.D., an assistant professor of medicine at the Johns Hopkins University School of Medicine and one of the associate program directors of the internal medicine residency program at The Johns Hopkins Hospital. "These are things that matter to patients and are relatively easy to do."
For the study, trained observers followed 29 internal medicine interns — physicians in their first year out of medical school — at The Johns Hopkins Hospital and the University of Maryland Medical Center for three weeks during January 2012. They witnessed 732 inpatient "encounters" during 118 intern work shifts. The observers used an iPod Touch app to record whether the interns employed five key strategies known as etiquette-based communication: introducing oneself, explaining one's role in the patient's care, touching the patient, asking open-ended questions such as "How are you feeling today?" and sitting down with the patient.
Interns touched their patients (which could be either a physical exam or just a handshake or a gentle, caring touch) during 65 percent of visits and asked open-ended questions 75 percent of the time. But they introduced themselves only 40 percent of the time, explained their role only 37 percent of the time and sat down during only 9 percent of visits.
Worse, interns performed all five of the recommended behaviors during just 4 percent of all patient encounters, and were only slightly more likely to introduce themselves to patients during their first encounter than a later one, the researchers say.
"Many times when I sit down," Feldman says, "patients say 'Oh my God, is something wrong?' because I actually bothered to take a seat. People should expect their physicians to sit down with them, to introduce themselves. They shouldn't be taken aback when they actually do. It's part of being a doctor."
Feldman and co-author Lauren Block, M.D., M.P.H., a former general internal medicine fellow at Johns Hopkins, say one of the reasons internal medicine trainees may not be following such basic social protocols is that hospitalists, the senior doctors they often learn from, fail to use them. Previous studies have shown that to be the case.
In a follow-up study six months after the observational research was completed, the Johns Hopkins researchers surveyed nine of the 10 Johns Hopkins interns, asking how often they believe they used the five communication strategies. The interns estimated they introduced themselves to their patients and explained their role 80 percent of the time and that they sat down with patients 58 percent of the time — far more often than they actually did.
"Our perception of ourselves is off a lot of the time and that's why it is so important to have data," Block noted.
Block says follow-up care also suffers because of the lack of good doctor-patient communications. "It's no wonder patients don't feel connected to what we are telling them because many times we are not doing as much as we could to make that connection," she says. Other research, she says, has shown that only 10 percent of patients can name a doctor who cared for them in the hospital. The researchers say hospitals and training program officials can take simple steps to improve things, such as providing chairs and photos of the care team in patient rooms and adding lessons on etiquette-based communication to the curriculum.
Feldman says that when he brings trainees into a patient room on rounds, he has everyone introduce themselves. Even if it's unlikely the patient will remember everyone, it creates a better relationship, he says, adding that modeling appropriate behavior for interns is a good place to start.

"The hospital is a dizzying place," he says. "It's a new crew all the time — in the emergency room, on the unit, the day team, the night team, the nurses, the respiratory therapist, the pharmacist. By introducing ourselves, we can go a long way toward making the entire hospital experience a little less daunting."

The Osler Center for Clinical Excellence at Johns Hopkins and the Johns Hopkins Hospitalist Scholars Program provided stipends for the observers and covered the transportation and logistical costs of the study.

Other Johns Hopkins researchers involved in the study include Lindsey Hutzler, B.A.; Albert W. Wu, M.D., M.P.H.; Sanjay V. Desai, M.D.; and Timothy Niessen, M.D., M.P.H.

http://www.eurekalert.org/pub_releases/2013-10/uonh-urb102113.php

UNH researcher: Bees underwent massive extinction when dinosaurs did

For the first time ever, scientists have documented a widespread extinction of bees that occurred 65 million years ago, concurrent with the massive event that wiped out land dinosaurs and many flowering plants.

DURHAM, N.H. - Their findings, published this week in the journal PLOS ONE, could shed light on the current decline in bee species.

Lead author Sandra Rehan, an assistant professor of biological sciences at UNH, worked with colleagues Michael Schwarz at Australia's Flinders University and Remko Leys at the South Australia Museum to model a mass extinction in bee group Xylocopinae, or carpenter bees, at the end of the Cretaceous and beginning of the Paleogene eras, known as the K-T boundary.

Previous studies have suggested a widespread extinction among flowering plants at the K-T boundary, and it's long been assumed that the bees who depended upon those plants would have met the same fate. Yet unlike the dinosaurs, "there is a relatively poor fossil record of bees," says Rehan, making the confirmation of such an extinction difficult.

Rehan and colleagues overcame the lack of fossil evidence for bees with a technique called molecular phylogenetics. Analyzing DNA sequences of four "tribes" of 230 species of carpenter bees from every continent except Antarctica for insight into evolutionary relationships, the researchers began to see patterns consistent with a mass extinction. Combining fossil records with the DNA analysis, the researchers could introduce time into the equation, learning not only how the bees are related but also how old they are.

"The data told us something major was happening in four different groups of bees at the same time," says Rehan, of UNH's College of Life Sciences and Agriculture. "And it happened to be the same time as the dinosaurs went extinct."

While much of Rehan's work involves behavioral observation of bees native to the northeast of North America, this research taps the computer-heavy bioinformatics side of her research, assembling genomic data to elucidate similarities and differences among the various species over time. Marrying observations from the field with genomic data, she says, paints a fuller picture of these bees' behaviors over time.

"If you could tell their whole story, maybe people would care more about protecting them," she says. Indeed, the findings of this study have important implications for today's concern about the loss in diversity of bees, a pivotal species for agriculture and biodiversity. "Understanding extinctions and the effects of declines in the past can help us understand the pollinator decline and the global crisis in pollinators today," Rehan says.

The article, "First evidence for a massive extinction event affecting bees close to the K-T boundary," is published in the Oct. 23, 2013 edition of PLOS ONE (link will become active once the embargo lifts). Funding for the research was provided by Endeavour Research Fellowships (Rehan) and Australian Research Council Discovery Grants (Schwarz).

http://bit.ly/16Ca9cv

Bid to Use Common Anesthetic for Executions Threatens U.S. Patients

The politics of capital punishment is affecting drug manufacturing decisions and forcing doctors to worry about sources of anesthesia, such as propofol

By Chris Woolston and Nature magazine | Wednesday, October 23, 2013 | 21

Allen Nicklasson has had a temporary reprieve. Scheduled to be executed by lethal injection in Missouri on 23 October, the convicted killer was given a stay of execution by the state's governor, Jay Nixon, on 11 October - but not because his guilt was in doubt. Nicklasson will live a while longer because one of the drugs that was supposed to be used in his execution - a widely used anesthetic called propofol — is at the center of an international controversy that threatens millions of US patients, and affects the way that US states execute inmates.

Shortages of anesthetic drugs usually used in lethal injection, the most common method of execution, are forcing states to find alternative sedatives. Propofol, used up to 50 million times a year in US surgical procedures, has never been used in an execution. If the execution had gone ahead, US hospitals could have lost access to the drug because 90% of the US supply is made and exported by a German company subject to European Union (EU) regulations that restrict the export of medicines and devices that could be used for capital

punishment or torture. Fearing a ban on propofol sales to the United States, in 2012 the drug's manufacturer, Fresenius Kabi in Bad Homburg, ordered its US distributors not to provide the drug to prisons.
This is not the first time that the EU's anti-death-penalty stance has affected the US supply of anesthetics. Since 2011, a popular sedative called sodium thiopental has been unavailable in the United States. The manufacturer, US company Hospira, abandoned plans to produce the drug at its plant in Italy after regulators in the country required that the thiopental never be used in executions. The drug, which is difficult and costly to make, was already in short supply because of manufacturing problems.
"There has been a collision of the politics of capital punishment in the United States and Europe, forcing us to hopscotch around looking for suitable methods for anesthesia," says Jerry Cohen, a former president of the American Society of Anesthesiology.
"The European Union is serious," says David Lubarsky, head of the anesthesiology department at the University of Miami Miller School of Medicine in Florida. "They've already shown that with thiopental. If we go down this road with propofol, a lot of good people who need anesthesia are going to be harmed."
The loss of thiopental from the anesthesia arsenal was a relatively minor inconvenience, says Cohen, because propofol provided an alternative. But if propofol is used for executions in Missouri or any other state, it could disappear too, leaving hospitals in a serious bind. "Propofol has a lot of uses for which there are no substitutes," says Cohen. It is the preferred way to sedate people who have breathing tubes because it acts quickly and does not cause vomiting. Federal regulations make propofol difficult to manufacture in the United States.
The 35 US states with prisoners on death row were already scrambling to find effective drugs for lethal injection, which was used for 43 executions last year. The procedure previously relied on a course of three injections: thiopental to sedate the prisoner, muscle relaxant pancuronium bromide to induce paralysis, and potassium chloride to stop the heart. As supplies of thiopental ran low in 2009 and 2010, many states started stockpiling pentobarbital, another sedative. But in 2011, Lundbeck, a drug company in Copenhagen and sole US supplier of pentobarbital, banned it from use in executions because of Danish and EU human-rights laws. Texas's supply of pentobarbital expired in September, but the state obtained more from unregulated compounding pharmacies, which tailor-make drugs. Pentobarbital is not "especially" useful as a surgical anesthetic, says Lubarsky, so its shortage has little impact on patient care.
On 15 October, after running out of pentobarbital, Florida executed William Happ using midazolam as the sedative. But midazolam, which is similar to diazepam (Valium), had never been used in an execution, and, according to media reports, Happ was still blinking and moving his head minutes after the injection.
Nobody knows whether midazolam is appropriate for lethal injections, says Lubarsky. "We've turned this into a circus of experimenting on prisoners," he says. "The state is playing doctor without any regard for efficacy. It changes protocols willy-nilly." The drug is not a good anesthetic, he says, and it may not shield prisoners from the pain of the final injection.
Although midazolam has now entered the realm of capital punishment, it is unlikely that surgical supplies will be affected. Hospira is one of many companies that makes midazolam and has no plans to stop, says Dan Rosenberg, a company spokesman. Rosenberg would not say where Hospira makes midazolam, but he says that European regulations "aren't an issue".
Meanwhile, Missouri has suspended another execution, scheduled for 20 November, while it tries to find an alternative to propofol. Lubarsky notes that although a single, large dose of propofol could work as a method of execution, its use in US prisons would be problematic because it could be complex to administer and physicians are generally not willing to participate in the process (see Nature 441, 8–9; 2006). "Putting together a foolproof protocol that could be carried out by prison guards with high-school educations is another matter entirely," he says.

http://www.sciencedaily.com/releases/2013/10/131023153742.htm

Cancer Wasting Due in Part to Tumor Factors That Block Muscle Repair, Study Shows

A new study reveals that tumors release factors into the bloodstream that inhibit the repair of damaged muscle fibers, and that this contributes to muscle loss during cancer wasting.

he condition, also called cancer cachexia, accompanies certain types of cancer, causes life-threatening loss of body weight and lean muscle mass, and is responsible for up to one-in-four cancer deaths. There is no treatment for the condition.
The study was led by researchers at The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James), and it points to new strategies and new drug targets for treating cancer cachexia. The findings were published in the Journal of Clinical Investigation.

The researchers looked at muscle stem cells, which are also called satellite cells. These cells are associated with muscle fibers and are essential for repairing damaged fibers. Normally, damage to muscle fibers causes these stem cells to proliferate and to differentiate into mature muscle cells. These muscle cells then fuse with damaged surrounding fibers to limit muscle wasting. This process is blocked during cancer cachexia, the researchers say.

"Our study showed that although muscle stem cells are activated during cachexia, factors released by the tumor block these cells from differentiating into muscle cells, which leaves them unable to repair cachectic muscle fibers," says principal investigator Denis Guttridge, PhD, professor of molecular virology, immunology and medical genetics and a member of the OSUCCC - James Molecular Biology and Cancer Genetics Program. "By identifying agents that overcome the block and allow muscle stem cells to differentiate, it might be possible to restore muscle mass and enhance the quality of life of cancer patients with cachexia," he says.

For this study, Guttridge and his colleagues used animal models and tissue from cachectic pancreatic-cancer patients to identify factors in the muscle microenvironment that contribute to cancer cachexia. Key findings include:

Cachexia is associated with tumor-induced damage to skeletal muscle cells and tumor-induced proliferation of muscle stem cells;

Overexpression of the muscle stem cell factor, Pax7, blocks the cells' ability to differentiate and promotes cancer-induced wasting;

The overexpression of Pax7 promotes cancer wasting by blocking the maturation of muscle cells and their fusion with surrounding fibers, which allows muscle to gain mass;

The overexpression of Pax7 is controlled by NF-kappa B (NF-kB), which has been shown to play multiple roles in cancer. In cachexia, NF-kB causes the deregulation of Pax7 expression, which in turn impairs differentiation of muscle progenitor cells and promotes muscle atrophy;

Because of its tissue specificity, Pax7 inhibition might offer an attractive therapy for cancer cachexia.

"For decades, studies in cachexia have focused on mechanisms that lead to muscle wasting from within skeletal muscle fibers," Guttridge says. "Our study is the first to show proof of concept that events occurring outside the muscle fiber and within the muscle microenvironment also play a part in driving muscle wasting in cancer."

Wei A. He, Emanuele Berardi, Veronica M. Cardillo, Swarnali Acharyya, Paola Aulino, Jennifer Thomas-Ahner, Jingxin Wang, Mark Bloomston, Peter Muscarella, Peter Nau, Nilay Shah, Matthew E.R. Butchbach, Katherine Ladner, Sergio Adamo, Michael A. Rudnicki, Charles Keller, Dario Coletti, Federica Montanaro, Denis C. Guttridge. NF-κB–mediated Pax7 dysregulation in the muscle microenvironment promotes cancer cachexia. Journal of Clinical Investigation, 2013; DOI: 10.1172/JCI68523

http://www.medscape.com/viewarticle/813084?src=rss

Misconceptions About Cause, Frequency of Miscarriage Common

Most Americans mistakenly believe that miscarriages are rare and do not understand the causes, according to the first national survey to assess attitudes and perceptions about miscarriage.

Larry Hand

BOSTON - We assume that patients understand that a miscarriage is a very common event, but they don't," Zev Williams, MD, director of the program for early and recurrent pregnancy loss at Montefiore and Einstein, told Medscape Medical News. "There's a disconnect between what we healthcare providers know and what patients believe. Unless you're aware of that discrepancy, it's hard to address it."

Researchers at the Montefiore Medical Center and the Albert Einstein College of Medicine of Yeshiva University in New York City surveyed almost 1100 women and men in 48 states. Just over half of the respondents were female, and 15% reported a history of miscarriage.

Among the respondents, 55% said that they believed miscarriages are rare, although researchers report that miscarriages occur in about 25% of pregnancies. An even larger number of respondents said they believe that a stressful event frequently causes a miscarriage (76%), and that a common cause was lifting a heavy object (64%). Most miscarriages are actually caused by chromosomal abnormalities. The survey also showed that 78% would want to know the cause of a miscarriage — even if they could not do anything about it.

Dr. Williams presented the survey results here at the American Society for Reproductive Medicine 69th Annual Meeting.

He also gave a related presentation on rescue karyotyping, a new technology that allows physicians to analyze archived tissue samples to obtain genetic information from a previous miscarriage. "Standard protocol calls for no testing after a first or second miscarriage," Dr. Williams said. "We're now able to go back and find out the cause of a previous miscarriage. It used to be that this information was lost."

The development of rescue karyotyping was a response to the amount of guilt he saw patients feeling, he explained.

"Almost without exception, after a miscarriage patients feel that they did something wrong," he said. "It's one of those things that is kept very quiet. As a result, there are a lot of people who feel very alone. I've even taken care of sisters who didn't realize that they were both being seen for miscarriages."

Guilt and Shame

Among the other survey results, 40% of the respondents who had had a miscarriage believed that they had done something wrong to cause it, 27% felt ashamed, 40% felt alone, and 47% felt guilty.

Dr. Williams said the results of the survey, in general, confirmed what he already thought, but he was surprised to find "that over half the people thought that miscarriages occurred in fewer than 5% of pregnancies." Also surprising to him was that people felt "less alone, less ashamed, and less guilty when celebrities and public figures disclosed that they had had miscarriages."

Getting this information about how patients think about miscarriage to clinicians could help educate both patients and clinicians and correct misperceptions, said Dr. Williams.

"Discovering that a genetic anomaly is the most common cause of miscarriage makes patients feel less guilty and have much less self-blame," he added.

The average number of miscarriages per patient at Dr. Williams' institution is 7.

"We have some patients who have had more than 30 miscarriages," he said. "It's a real challenge to find the cause, but when you do and you're able to fix the problem, it's very rewarding."

This study was supported by the Department of Obstetrics and Gynecology at Einstein and the National Institutes of Health. Dr. Williams is employed by Einstein and Montefiore.

American Society for Reproductive Medicine (ASRM) 69th Annual Meeting: Abstract 369. Presented October 16, 2013.

http://news.discovery.com/human/health/girl-still-cured-of-aids-13102.htm#mkcpgn=rssnws1

Girl Still 'Cured' of AIDS

New details in the case of a girl in Mississippi validate researchers' hope that she represents the first documented case of HIV remission in a child.

Oct 23, 2013 05:00 PM ET // by Sheila M. Eldred

Last March, early findings were presented that very early, aggressive treatment appeared to have prevented the virus from taking hold of the girl's immune cells. "Our findings suggest that this child's remission is not a mere fluke," Deborah Persaud, M.D., lead author of the NEJM report and a virologist and pediatric HIV expert at the Johns Hopkins Children's Center, said in a press release.

According to the updated report published today in the New England Journal of Medicine, the 3-year-old's HIV-specific antibodies remain negative. Tests for certain immune cells that would indicate an active infection are also negative. Trace amounts of the virus may remain, but it appears incapable of forming a new virus. The researchers have also ruled out the possibility that the girl has a revved-up immune system that is naturally able to suppress the virus.

"We're thrilled that the child remains off medication and has no detectable virus replicating," said pediatrician Hannah Gay, M.D., of the University of Mississippi Medical Center, who identified and treated the baby. "We've continued to follow the child, obviously, and she continues to do very well. There is no sign of the return of HIV, and we will continue to follow her for the long term."

The current treatment for high-risk newborns requires waiting until infection is confirmed to start the full treatment regimen. Researchers are hoping that the Mississippi case may help speed that process up to help babies already infected.

http://www.bbc.co.uk/news/health-24607698

Daily aspirin 'risky' for healthy

Healthy people should not take aspirin to ward off heart attacks and cancer, according to the most comprehensive review of the risks and benefits.

By James Gallagher Health and science reporter, BBC News

There has been growing debate about whether all people over 50 should take a daily, low dose aspirin.

But the review, conducted by the research arm of the NHS, said it was a "fine balance" due to the dangers of bleeding in the brain and stomach. Overall it warned against taking the drug, until there was more evidence.

Aspirin makes the blood less sticky so it reduces the odds of a blood clot forming inside the body, which could cause a heart attack or stroke. There are even studies suggesting it can cut the risk of some cancers.

However, as the drug makes it harder for the blood to clot it can cause problems inside the body.

The drug is given to people at high risk of a heart attack or stroke as the medical benefit is clear.

However, there have been calls to give aspirin to otherwise healthy people as well. A team at Warwick Medical School was asked to assess the evidence by the NHS National Institute for Health Research.

For heart attacks and strokes, they concluded giving everyone aspirin would cause "net harm due to increased potential for bleeding". This was in part due to better management of at-risk patients including prescribing drugs to lower blood pressure. On cancer, they concluded the evidence was not strong enough to base a decision on, but trials taking place would give clearer proof in the next five years.
Prof Aileen Clarke, who led the review, told the BBC: "The risks are finely balanced and for now there is not the evidence to advise people to take it. "It would be lovely to say over-50s should take an aspirin a day and have much less cancer, but the research hasn't yet been done and we should be cautious. "We need to be extremely careful about over-promoting aspirin."
Amy Thompson, senior cardiac nurse at the British Heart Foundation, said: "Aspirin is extremely important for many heart patients, but for people free of heart disease the jury is still out as the risks are likely to outweigh the benefits. "Further research is underway which will shed light on who else is likely to benefit the most from taking aspirin."

http://nyti.ms/1aIp8h3

Christening the Earliest Members of Our Genus

Around 1.8 million years ago, human evolution passed a milestone. Our ancestors before then were little more than bipedal apes.

By CARL ZIMMER

Those so-called hominids had chimpanzee-size bodies and brains, and they still had adaptations in their limbs for climbing trees. But the fossils of hominids from 1.8 to 1.5 million years ago are different. They had bigger brains, flatter faces and upright bodies better suited to walking.
Their geography changed, too. While earlier hominid fossils have only been found in Africa, the newer ones also turn up at sites stretching across Asia, from the Republic of Georgia all the way to Indonesia. These cosmopolitan hominids are so much like modern humans that paleoanthropologists consider them the earliest members of our own genus, Homo.
But they didn't belong to our species, Homo sapiens. After all, their brains were still no more than two-thirds the size of our own, and they could only make simple hand axes and other crude stone tools. But if not Homo sapiens, then Homo what? What species did these fossils belong to?
That turns out to be a remarkably hard question to answer — in part because it is difficult to settle on what it means to be a species.
The first early Homo fossils were discovered in 1891 in Indonesia by Eugene DuBois. They came to be known as Homo erectus, named for its erect stance. In later decades, scientists found other fossils in other places, and they often decided that the fossils were so different from anything found before that they must belong to a separate species. Species names exploded: Homo erectus was joined by Homo ergaster, Homo georgicus, Homo rudolfensis and others.
But all those species were established based on only a modest numbers of fossils. And so some uncertainty is inevitable. Imagine that paleontologists from the distant future learned everything they knew about our entire species from the skeleton of a single NBA player. If they then uncovered the skeleton of a five-foot gymnast, they would be right to wonder whether they had found a separate species.
Last week, a team of scientists offered a rare glimpse of the diversity of early Homo fossils. In the journal Science, they compared five gorgeously preserved, 1.8 million-year-old skulls from a site called Dmanisi in the Republic of Georgia. In just one spot, they found a stunning diversity of forms. One skull had a large jaw and a tiny brain less than half the size of a human one. But some of their brains were up to 25 percent bigger than that specimen, while their jaws were much smaller.
Nevertheless, the scientists found a lot of underlying similarities in the skulls' structures. Their variation is no greater than that found in living species, like chimpanzees and humans.
"They don't represent distinct species," said G. Philip Rightmire of Harvard University, a co-author on the study. "They're just one group."
Dr. Rightmire and his colleagues then compared the Dmanisi skulls to many of the early Homo skulls found across the Old World. All of those far-flung fossils fell within the same range of variation that the scientists found at Dmanisi.
Based on this analysis, the scientists declared that all those early Homo fossils belong to a single species — which they suggest should be called Homo erectus. If other researchers find evidence to support this view, said Dr. Rightmire, it would have a big impact on how we understand human evolution. "We'll have to go back to drawing boards and rethink the origins of Homo right from the start," he said.

If Homo erectus was indeed a single species, its range would have been tremendous compared with our closest living ape relatives. Chimpanzees, for example, live only across a narrow band of sub-Saharan Africa. What's more, ape species tend to split apart into new ones.
Two million years ago, for example, a bend of the Congo River cut off the chimpanzees in the southern part of the species's range. Those southern chimpanzees evolved into smaller, more slender apes that today are more peaceful than their warring cousins north of the river. Their DNA reveals little sign that they have interbred with other chimpanzees over the past two million years — despite living within a few miles of them. As a result, biologists have given them their own species name: Pan paniscus, commonly known as bonobos.
If Homo erectus was like chimpanzees, it would be remarkable for them to hang together across rivers and deserts and mountain ranges as a single species. But Todd R. Disotell, a biological anthropologist at New York University, suggests that early Homo might be more like another primate. "Baboons probably make a good analog," said Dr. Disotell.
Baboons live across much of Africa, as well as the Middle East. From place to place, the baboons look different — so different, in fact, that scientists have split them into some half a dozen species. And if you look at their DNA, you can find evidence that these so-called species have remained distinct from each other for up to four million years.
These baboons have overlapping ranges, and where they come into contact, they regularly interbreed. They have hybrid babies that are perfectly healthy. Some genes from one group of baboons can spread into another this way. And yet the groups remain distinct, never blurring together.
Each group of baboons has adapted to one particular way of life — some surviving in a desert, for example, and others in a woodland. For the most part, the genes that help a baboon in one range put it at a disadvantage somewhere else.
The baboon expert Clifford Jolly first proposed that our ancient relatives were joined together by a baboon-like web of connections. Distinct groups of hominids lived in distinct ranges. But in some places, at some times, they came into contact with other hominids, and their biology allowed them to interbreed. "Maybe Dmanisi was the equivalent of that," said Dr. Disotell.
While this explanation may turn out to be closer to the truth than the idea of a single species, it would leave us struggling to find the right name for our ancient relatives. Was each one a separate species, deserving of its own name? Dr. Disotell doubts we can answer that question, pointing to baboons. Despite a luxury of data, scientists continue to debate whether baboons belong to different species, or just one.
"What we need, practically, is labels for them," said Dr. Disotell. "We will never solve the species problem for fossils if we can't for living, breathing animals."

http://bit.ly/18YyBn5

English guidebook opens China's floral treasure chest

China's botanical riches are now open to the world, thanks to an ambitious 25-year-long effort to produce an English-language version of the country's botanical bible – itself a work that took 45 years.

17:59 23 October 2013 by Li Jiao

Among the 31,000 plants listed in the Flora of China (FOC) are some that offer the hope of treatments for malaria and HIV, and others that illuminate the evolutionary roots of the plant kingdom.
"The FOC is a key to open the treasure house of Chinese botany," says Hong De-Yuan of the Institute of Botany in Beijing, who co-chaired the project's editorial committee. "It will help us understand and use our wild resources."
About 8 per cent of the world's plant species are found in China, and half of these species – about 15,600 – occur nowhere else. In 1958, researchers at 80 Chinese scientific institutions began compiling a Chinese language botanical treatise to document all of them. The final book in the 80-volume series was published in 2003.

A growing project

Some 15 years earlier, in 1988, efforts began to produce a version in English, spearheaded by the Chinese Academy of Sciences and the Missouri Botanical Garden in St Louis. The final volume of this English-language version was published at the end of last month.
"It's not a simple translation but a comprehensive revision," says Hong. "It contains additions and amendments by Chinese and foreign experts."
Will McClatchey at the Botanical Research Institute of Texas in Fort Worth thinks the project is very important. China is the only country on Earth in which there are unbroken connections between tropical, subtropical, temperate and boreal forests – all of which are covered in the FOC.

"This is close to the natural ecosystem or biome scale where evolutionary action is happening," says McClatchey.

Living fossils

We already have hints of the evolutionary importance of China's forests. In the mid-twentieth century, the dawn redwood (Metasequoia glyptostroboides) was described from fossils that are over 65 million years old. A few years later the tree, which supposedly went extinct about 10 million years ago, was found thriving in Hubei and Sichuan provinces.

Another famous "living fossil", the Ginkgo tree (Ginkgo biloba), is also found in the wild only in China. Fossilised examples 270 million years old have been found, but it disappeared from most parts of the world 2.5 million years ago. It clung on through to modern times in Zhejiang province.

The FOC should help biologists understand the distribution of such species, shedding light on their evolution, says Yan Enrong at the East China Normal University in Shanghai.

Malaria tree-tment

"Many plants that were widespread throughout the temperate regions of the northern hemisphere over the past tens of millions of years now survive only in China," says Peter Raven of the Missouri Botanical Garden, who co-chaired the FOC editorial committee with Hong.

But it is not just evolutionary researchers who are keen to explore China's flora. The country's plants have long been a source of medicinal compounds, and researchers in the West as well as those in China are now beginning to explore their potential to tackle the modern world's ailments.

"Artemisinin is currently the most important medicine against malaria, a worldwide scourge," says Raven. "It is derived from a Chinese plant – sweet wormwood (Artemisia annua) – and based on Chinese use of that plant as a drug," he says.

And one of the fundamental plants used in Chinese medicine, Trichosanthes kirilowii, is now being investigated for its anti-HIV properties. Zheng Yongtang at the Kunming Institute of Zoology in China is involved in the work.

"The FOC is an important reference book," he says. "It's the foundation for research and development of traditional Chinese medicine – it provides references for our studies."

http://www.eurekalert.org/pub_releases/2013-10/sumc-bsa102113.php

Bee sting allergy could be a defense response gone haywire, Stanford scientists say

For most people, a bee sting causes temporary pain and discomfort, but for those with a bee venom allergy, the consequences can be devastating: They experience anaphylactic shock, including a drop in blood pressure, itchy hives and breathing problems, and may die if not promptly treated.

STANFORD, Calif. - New findings by Stanford University School of Medicine scientists may provide an evolutionary explanation for severe allergic reactions. In a paper to be published online Oct. 24 in Immunity, the researchers show that mice injected with a small dose of bee venom were later resistant to a potentially lethal dose of the same venom. The study is the first experimental evidence that the same immune response involved in allergies may have evolved to serve a protective role against toxins.

The study builds on earlier work by the researchers, characterizing the innate immune response to snake venom and honeybee venom. Innate immune responses occur in subjects exposed to a foreign substance, such as a pathogen or a toxic material like venom, for the first time. Immune cells called mast cells, which reside in most of the body's tissues, are poised to unleash signals that turn on defense responses when a pathogen or toxin intrudes. In a previous study, the researchers found that mast cells produce enzymes that can detoxify components of snake venom, and that mast cells can also enhance innate resistance to honeybee venom.

Such innate immune responses do not require prior immunization or the development of specific antibodies. By contrast, during an adaptive immune response, the immune system generates antibodies that recognize the invading pathogen or toxin; this process makes it possible to vaccinate against infectious diseases. Adaptive immunity is usually a faster, more specific and more effective form of defense than innate immunity.

In allergic reactions, a type of antibody called IgE binds to the surface of mast cells and prompts them to initiate an adaptive immune response when exposed to the antigen recognized by that IgE. "The functions of IgE and mast cells are mostly known in the context of allergies," said Thomas Marichal, DVM, PhD, a postdoctoral scholar and co-lead author of the study.

"It was kind of a dogma that most IgE-related responses are detrimental," said postdoctoral scholar Philipp Starkl, PhD, the other lead author. "We and others speculated that there should be some very positive evolutionary pressure to keep these cells and these antibodies, because if they were just bad and deleterious, they would have been eliminated."

The researchers hypothesized that IgE might be required for protection against a lethal sting, and that allergies are an extreme, and maladaptive, example of this type of defense. This idea, known as the toxin hypothesis of allergy, was first proposed by Margie Profet in 1991, but was largely ignored by immunologists until recently.
To find out whether adaptive immune responses could help mice resist bee venom, Marichal and Starkl first injected mice with a low dose of venom equivalent to one or two stings. The mice developed more venom-specific immune cells, and higher levels of IgE antibodies against the venom, than control mice injected with a salt solution.
Three weeks later, they injected both groups of mice with a potentially lethal dose of venom, similar to five bee stings. The immunized mice had less hypothermia and were three times more likely to survive than the control mice. Moreover, they did not develop the anaphylactic reactions characteristic of severe allergies.
To determine whether IgE antibodies were required for this protection, the team tested mice with three types of mutations: mice without IgE, mice without functional IgE receptors on their mast cells, and mice without mast cells. The IgE-deficient mutant mice were previously developed by Hans Oettgen, MD, PhD, associate professor of pediatric immunology at Harvard Medical School and a co-author of the study.
In all three groups of mutant mice, pre-immunization with a low dose of bee venom did not confer protection against a lethal dose, suggesting that the protection depends on IgE signaling and mast cell activation. "That was pretty exciting for us," said Marichal. "It was the first time we could see a beneficial function for these IgE antibodies."
Pre-immunization with a low dose of venom from the Russell's viper also protected mice from a higher dose of venom from this snake, which is one of the "big four" species responsible for most snakebite deaths in India. So the researchers believe the response could be generalized to different types of toxic venoms.
"Our findings support the hypothesis that this kind of venom-specific, IgE-associated, adaptive immune response developed, at least in evolutionary terms, to protect the host against potentially toxic amounts of venom, such as would happen if the animal encountered a whole nest of bees, or in the event of a snakebite," said Stephen Galli, MD, professor and chair of pathology and the co-senior author of the study. "Anaphylaxis probably represents the extreme end of a spectrum of IgE-associated reactivity, which in some unfortunate individuals is either poorly regulated or excessively robust, so the reaction itself can become dangerous to them."
Galli cautioned that it's not yet known whether IgE responses also protect humans from the toxic effects of arthropod or reptile venom, but it would be unthinkable to test lethal doses of venom in humans. Reptile and arthropod venoms are complex chemical cocktails. Some venom components have evolved to mimic chemicals made by the human body, such as endothelin-1, which causes blood vessels to constrict during bacterial infections. At the same time, mammals have evolved immune responses to venom, which in some cases escalate into maladaptive allergic reactions.
"We experience allergies in a much cleaner world, where we don't have the same threats of venomous creatures and potentially toxic food that existed for much of our evolutionary history," said Galli. "And so we're left with this residual type of reactivity that seems completely mysterious and pointless and harmful. This is the first evidence, that we know of, indicating that IgE-associated 'allergic-type' immune responses can actually reduce the toxicity of naturally occurring venoms."
Other Stanford co-authors were instructor Laurent Lionel Reber, PhD; Janet Kalesnikoff, PhD, associate director of the Cardiovascular Institute; senior research scientist Mindy Tsai, DMSc; and Martin Metz, MD, PhD, a former postdoctoral scholar at Stanford and co-senior author of the study, now a professor of dermatology and allergy at Charité-Universitätsmedizin Berlin.
The study was funded by the German 1 Research Foundation, the National Institutes of Health (grants AI023990, CA072074 and AI070813), a Marie Curie International fellowship, the Max Kade Foundation, the Austrian Academy of Sciences and the Austrian Science Fund.

http://www.eurekalert.org/pub_releases/2013-10/aha-hud102113.php

Hands-free ultrasound device with clot-busting drug safe for stroke patients

American Heart Association Rapid Access Journal Report

A hands-free ultrasound device combined with a clot-busting drug was safe for ischemic stroke patients in a phase II pilot study, reported in the American Heart Association journal Stroke.The device is placed on the stroke patient's head and delivers ultrasound to enhance the effectiveness of the clot-busting drug tissue plasminogen activator (tPA). Unlike the traditional hand-held ultrasound probe that's aimed at a blood clot, the hands-free device used 18 separate probes and showers the deep areas of the brain where large blood clots cause severe strokes.

"Our goal is to open up more arteries in the brain and help stroke patients recover," said Andrew D. Barreto, M.D., lead author of the study and assistant professor of neurology in the Stroke Program at the University of Texas Health Science Center at Houston. "This technology would have a significant impact on patients, families and society if we could improve outcomes by another 5-10 percent by adding ultrasound to patients who've already received tPA."

In the first-in-human study, 20 moderately severe ischemic stroke patients (12 men and 8 women, average age 63 years) received intravenous tPA up to 4.5 hours after symptoms occurred and two hours exposure to 2-MHz pulsed wave transcranial ultrasound. vResearchers reported that 13 (or 65 percent) patients either returned home or to rehabilitation 90 days after the combination treatment.

After three months, five of the 20 patients had no disability from the stroke and one had slight disability.

Researchers have launched an 830-patient international, randomized efficacy study of the ultrasound approach combined with the clot buster in ischemic stroke.

The study was conducted at the University of Texas Health Science Center at Houston and the University of Alabama-Birmingham.

Co-authors are Andrei Alexandrov, M.D.; Loren Shen, B.S.N.; April Sisson, R.N.; Andrew Bursaw, M.D.; Preeti Sahoti, M.D.; Hui Peng, Ph.D.; Manouchehr Ardjomand- Hessabi, M.D.; Renganayaki Pandurengan, Ph.D.; Mohammad Rahbar, Ph.D.; Kristian Barlinn, M.D.; Hari Indupuru, M.B.B.S.; Nicole Gonzalez, M.D.; Sean Savitz, M.D.; and James C. Grotta, M.D. Author disclosures are on the manuscript.

Dr. James C. Grotta was the principal investigator of the study which was funded by the National Institutes of Health.

http://www.bbc.co.uk/news/health-24610296

Slow metabolism 'obesity excuse' true

The mocked "obesity excuse" of being born with a slow metabolism is actually true for some people, say researchers.

By James Gallagher Health and science reporter, BBC News

A team at the University of Cambridge has found the first proof that mutated DNA does indeed slow metabolism. The researchers say fewer than one in 100 people are affected and are often severely obese by early childhood. The findings, published in the journal Cell, may lead to new obesity treatments even for people without the mutation.

Scientists at the Institute of Metabolic Science, in Cambridge, knew that mice born without a section of DNA, a gene called KSR2, gained weight more easily. But they did not know what effect it may be having in people, so they analysed the DNA of 2,101 severely obese patients. Some had mutated versions of KSR2. It had a twin effect of increasing their appetite while their slowing metabolism.

"You would be hungry and wanting to eat a lot, you would not want to move because of a slower metabolism and would probably also develop type 2 diabetes at a young age," lead researcher Prof Sadaf Farooqi told the BBC. She added: "It slows the ability to burn calories and that's important as it's a new explanation for obesity."

Rare

KSR2 is mostly active in the brain and it affects the way individual cells interpret signals, such as the hormone insulin, from the blood. This in turn affects the body's ability to burn calories.

Prof Farooqi said the metabolism argument had been derided by doctors, as well as wider society, due to a lack of evidence that metabolism was slowed in obese patients. In many cases obese patients have an elevated metabolism to cope with fuelling a much larger body.

She said less than 1% of people had mutated versions of the gene and some would be a normal weight, but about 2% of children who were obese by the age of five would have the mutated gene. However, if drugs could be developed to target problems with KSR2, then it might be beneficial to anyone who is too fat.

"Other genetic disorders, such as in blood pressure, have shown that even where there's a normal gene, targeting the pathway can still help," Prof Farooqi said.

The amount and types of food eaten, as well as levels of exercise, directly affect weight, but some people at more risk of becoming obese that others.

Obesity can run in families. The other obesity genes that have been discovered tend to affect appetite.

People have two copies of the FTO gene - one from each parent - and each copy comes in a high- and a low-risk form. Those with two-high risk copies of the FTO gene are thought to be 70% more likely to become obese than those with low-risk genes. It makes fatty foods more tempting and alters levels of the hunger hormone ghrelin.

Dr Katarina Kos, from the University of Exeter Medical School, said: "It is an exciting and interesting breakthrough, this is a new pathway predisposing people to obesity. "But it does exist in obese and lean people so you still need the obesogenic environment."

http://www.sciencedaily.com/releases/2013/10/131024141436.htm

100 Percent of an Image Restored Using a Version Containing Between One and 10 Percent of the Information

Algorithms developed to reduce and optimize images; using a reduced image of 1% to 10% of the original image), allows restoration of 100% of the pixels in the initial image

In his PhD thesis, Daniel Paternain-Dallo, Computer Engineer of the NUP/UPNA-Public University of Navarre, has developed algorithms to reduce and optimize images; using a reduced image (with between 1% and 10% of the information from the original image), they allow 100% of the pixels in the initial image to be restored.

"With these algorithms we can obtain high quality images that are very similar to the original. We have shown that even if we lose 100% of the pixels of the image, we can restore a lost image with a very high level of quality just by using the information from the reduced image."

The PhD thesis is entitled Optimization of image reduction and restoration algorithms based on penalty functions and aggregation techniques.

Daniel Paternain's research comes within the framework of the digital processing of images, a discipline that has burgeoned tremendously over the last forty years. In fact, the high quality of current digital images is partly due to the fact that there is increasingly greater spatial resolution (higher number of pixels); in other words, it is possible to use a much larger quantity of information to represent the same scene.

As the researcher points out, the two main problems of high resolution images are the cost in storing or transmitting them (over the Internet, for example) and the long period of time that computers take to process them. To solve these two problems at the same time, Daniel Paternain's thesis puts forward various algorithms to reduce images in terms of both colour and greyscales.

"The aim," he explains, "is to reduce the number of pixels the image contains while trying to keep all or as much as possible of the information and properties contained in the original image."

The main idea underpinning the algorithms developed is to divide the image into small zones that are processed individually.

"For each zone we look for a value that is simultaneously the least different from all the pixels that form the zone. By following this methodology, we can design algorithms that are very efficient in terms of execution time, and capable of being adapted to the local properties of each zone of the image."

Firstly, he developed an algorithm to reduce the images on the greyscale. Aggregation functions are used to achieve this; "they are highly applicable because they study the way of combining various homogeneous or heterogeneous sources of information into a single value to represent them.

" Furthermore, for colour images in which each pixel contains a larger amount of information, he studied the so-called penalty functions. "This mathematical tool enables us by means of optimization algorithms to automatically select the aggregation function most suited to each zone of the colour image."

Image restoration

The final step in his research explored how to apply the reduction algorithms to one of the most difficult problems in image processing: restoring digital images. "Let us assume that we lose a large quantity of pixels owing to a transmission error or a problem when processing the image," explains Paternain.

The restoration algorithm seeks to estimate the original value of the pixels we have lost and to obtain an image as similar as possible to the original."

To make the restoration possible, it is necessary to have available in advance a highly reduced version of the original image that will concentrate most of its properties. The more information we have stored in the reduced image, the greater the quality of the restored image will be.

"This reduced version cannot be very big as we don't want to excessively increase the cost of storing the image. The reduced images we obtain through these algorithms account for between 1% and 10% of the original image."

After that, an optimization algorithm is generated; it is capable of estimating the value of the lost pixels using the information contained in the damaged image as well as in the reduced image.

"We have shown that by using the algorithms proposed in this thesis, we can obtain images of high quality that are very similar to the original. We have shown that even if we lose 100% of the pixels of the image, we can, with a very high level of quality, restore an image that has been completely lost, just by using the information from the reduced image."

http://www.livescience.com/40690-zombie-haiti-are-zombies-real.html

How to Make a Zombie (Seriously)

Most rational people scoff at the suggestion that zombies are real, but a number of respected medical experts and academic journals have presented evidence that zombies are, in fact, real.

By Marc Lallanilla, Assistant Editor | October 24, 2013 04:30pm ET

The slouching, flesh-eating zombie has become one of the most in-vogue creatures in current TV and movie offerings, appearing in films like "World War Z" and in the AMC series "The Walking Dead."

Most rational people scoff at the suggestion that zombies are real, but a number of respected medical experts and academic journals have presented evidence that zombies are, in fact, real.

To understand the zombie phenomenon and its Haitian roots, an appreciation of the practice of vodou (sometimes spelled voodoo or vodun) is needed. A religion based in West Africa, voodou is still practiced in varying forms throughout the Caribbean, Brazil, the American South and other places with a strong African heritage.

Vodou spirituality has a rich tradition of fetish objects, including the so-called "voodoo doll." Practitioners of vodou also place a particular importance on herbal remedies and other concoctions that may include animal parts, such as bones and hair, dried plants, shells, minerals or other ingredients.

Toads, worms and human remains

Vodou priests known as bokor create a white, powdery compound called coupe poudre, according to numerous reports. The ingredients in this powder allegedly can turn a person into a zombie. In the 1980s, Harvard ethnobotanist Wade Davis traveled to Haiti to investigate zombies and "zombie powder."

Though different bokor used different ingredients in their powders, Davis found that "there are five constant animal ingredients: burned and ground-up human remains [usually bone], a small tree frog, a polychaete [segmented] worm, a large New World toad, and one or more species of pufferfish. The most potent ingredients are the pufferfish, which contain deadly nerve toxins known as tetrodotoxin,"

Davis wrote in Harper's Magazine.

Some in the scientific community have criticized Davis' research — his investigation was published in 1983 in the Journal of Ethnopharmacology — but his identification of tetrodotoxin as the active ingredient in zombie powder has considerable scientific merit.

Euphoria, then death

Several animals contain tetrodotoxin in their tissues; the liver, eyes and ovaries of the pufferfish (genus Takifugu) have especially high amounts of the lethal nerve toxin. Though regarded as a delicacy in Japan, the fish and some of its organs (especially the liver) are banned as food items in many places because of the dangers.

In small amounts, tetrodotoxin causes numbness, tingling and a not-unpleasant sensation of floating — even euphoria — according to reports from brave gourmands who have sampled carefully prepared pufferfish. High levels of the toxin, however, can cause death within minutes due to respiratory failure.

But at sublethal doses, the toxin can leave a victim in a state of suspended animation: Breathing is subdued and barely perceptible by observers, the heart rate is near zero, but the person remains conscious and aware (though unable to speak).

Zombie slavery

This toxin, then, may form the basis of the zombie phenomenon. According to Davis and other observers, a person who is exposed to a certain amount of zombie powder containing tetrodotoxin can slip into a vegetative state resembling death. Shortly after the person is buried, their body is exhumed by a bokor.

Though the exhumed zombie usually suffers from apoxia (oxygen deprivation) caused by breathing the limited amount of air inside a coffin, the bokor wields control over the person by continually administering a second drug, a psychoactive compound derived from the jimson weed (Datura stramonium). This second drug causes delirium and disorientation, rendering the person incapable of normal functioning.

The British medical journal The Lancet published three accounts of "zombification" in 1997. In one case, a woman who was presumed dead and was buried in a family tomb reappeared three years later — she was positively identified by several family members and townspeople. "After a local court authorized the opening of her tomb, which was full of stones, her parents were undecided whether to take her home, and she was admitted to the psychiatric hospital in Port-au-Prince," the authors wrote.

Because death certificates and other official niceties are rare in rural Haiti, and because burial generally occurs within a day of death, "it is not implausible for a retrieved person to be alive," the authors added. "The use of Datura stramonium to revive them, and its possible repeated administration during the period of zombie slavery, could produce a state of extreme psychological passivity."

The legal status of zombies

A well-known report of a zombie comes from the pages of ChemMatters, the publication of the American Chemical Society. In 1962, a man named Clairvius Narcisse was admitted to Albert Schweitzer Hospital in Port-au-Prince with severe respiratory problems. After slipping into a coma, Narcisse was later declared dead by two hospital doctors and was buried shortly thereafter.

Eighteen years later, in 1980, a man shuffled up to Angelina Narcisse in a village marketplace and identified himself as her brother. He related a story of being buried alive, dug up and enslaved on a distant sugar plantation. Doctors who examined Narcisse — and dozens of villagers and family members — positively identified him as the man who was buried in 1962.

But if you're tempted to make a zombie slave of your own, be aware that the zombie phenomenon is considered so real in Haiti that it's specifically outlawed.

Article 249 of the Haitian penal code states, "It shall also be qualified as attempted murder the employment which may be made against any person [using] substances which, without causing actual death, produce a lethargic coma more or less prolonged. If, after the person had been buried, the act shall be considered murder no matter what result follows."

https://theconversation.com/chemists-show-life-on-earth-was-not-a-fluke-19452

Chemists show life on Earth was not a fluke

How life came about from inanimate sets of chemicals is still a mystery. While we may never be certain which chemicals existed on prebiotic Earth, we can study the biomolecules we have today to give us clues about what happened three billion years ago.

How life came about from inanimate sets of chemicals is still a mystery. While we may never be certain which chemicals existed on prebiotic Earth, we can study the biomolecules we have today to give us clues about what happened three billion years ago.

Now scientists have used a set of these biomolecules to show one way in which life might have started. They found that these molecular machines, which exist in living cells today, don't do much on their own. But as soon as they add fatty chemicals, which form a primitive version of a cell membrane, it got the chemicals close enough to react in a highly specific manner.

This form of self-organisation is remarkable, and figuring out how it happens may hold the key to understanding life on earth formed and perhaps how it might form on other planets.

The 1987 Nobel Prize in Chemistry was given to chemists for showing how complex molecules can perform very precise functions. One of the behaviours of these molecules is called self-organisation, where different chemicals come together because of the many forces acting on them and become a molecular machine capable of even more complex tasks. Each living cell is full of these molecular machines.

Pasquale Stano at the University of Roma Tre and his colleagues were interested in using this knowledge to probe the origins of life. To make things simple, they chose an assembly that produces proteins. This assembly consists of 83 different molecules including DNA, which was programmed to produce a special green fluorescent protein (GFP) that could be observed under a confocal microscope.

The assembly can only produce proteins when its molecules are close enough together to react with each other. When the assembly is diluted with water, they can no longer react. This is one reason that the insides of living cells are very crowded, concentrated places: to allow the chemistry of life to work.

In order to recreate this molecular crowding, Stano added a chemical called POPC to the dilute solution. Fatty molecules such as POPC do not mix with water, and when placed into water they automatically form liposomes. These have a very similar structure to the membranes of living cells and are widely used to study the evolution of cells.

Stano reports in the journal Angewandte Chemie that many of these liposomes trapped some molecules of the assembly. But remarkably, five in every 1,000 such liposomes had all 83 of the molecules needed to produce a protein. These liposomes produced large amount of GFP and glowed green under a microscope.

Computer calculations reveal that even by chance, five liposomes in 1,000 could not have trapped all 83 molecules of the assembly. Their calculated probability for even one such liposome to form is essentially zero. The fact that any such liposomes formed and that GFP was produced means something quite unique is happening.

Stano and his colleagues do not yet understand why this happened. It may yet be a random process that a better statistical model will explain. It may be that these particular molecules are suited to this kind of self-organisation because they are already highly evolved. An important next step is to see if similar, but less complex, molecules are also capable of this feat.

Regardless of the limitations, Stano's experiment has shown for the first time that self-assembly of molecular machines into simple cells may be an inevitable physical process. Finding out how exactly this self-assembly happens will mean taking a big step towards understanding how life was formed.

Andrew Bissette does not work for, consult to, own shares in or receive funding from any company or organisation that would benefit from this article, and has no relevant affiliations.

http://www.eurekalert.org/pub_releases/2013-10/cmc-lgd102513.php

Lou Gehrig's disease: From patient stem cells to potential treatment strategy in one study

Translational research goes seamless: After creating neurons from patients' skin cells, cedars-sinai-led researchers 'treat' gene defect in a dish, indicating the therapy may work

LOS ANGELES - Although the technology has existed for just a few years, scientists increasingly use "disease in a dish" models to study genetic, molecular and cellular defects. But a team of doctors and scientists led by researchers at the Cedars-Sinai Regenerative Medicine Institute went further in a study of Lou Gehrig's disease, a fatal disorder that attacks muscle-controlling nerve cells in the brain and spinal cord.

After using an innovative stem cell technique to create neurons in a lab dish from skin scrapings of patients who have the disorder, the researchers inserted molecules made of small stretches of genetic material, blocking the damaging effects of a defective gene and, in the process, providing "proof of concept" for a new therapeutic strategy – an important step in moving research findings into clinical trials.

The study, published Oct. 23 in Science Translational Medicine, is believed to be one of the first in which a specific form of Lou Gehrig's disease, or amyotrophic lateral sclerosis, was replicated in a dish, analyzed and "treated," suggesting a potential future therapy all in a single study.

"In a sense, this represents the full spectrum of what we are trying to accomplish with patient-based stem cell modeling. It gives researchers the opportunity to conduct extensive studies of a disease's genetic and molecular makeup and develop potential treatments in the laboratory before translating them into patient trials," said Robert H. Baloh, MD, PhD, director of Cedars-Sinai's Neuromuscular Division in the Department of Neurology and director of the multidisciplinary ALS Program. He is the lead researcher and the article's senior author.

Laboratory models of diseases have been made possible by a recently invented process using induced pluripotent stem cells – cells derived from a patient's own skin samples and "sent back in time" through genetic manipulation to an embryonic state. From there, they can be made into any cell of the human body.

The cells used in the study were produced by the Induced Pluripotent Stem Cell Core Facility of Cedars-Sinai's Regenerative Medicine Institute. Dhruv Sareen, PhD, director of the iPSC facility and a faculty research scientist with the Department of Biomedical Sciences, is the article's first author and one of several institute researchers who participated in the study.

"In these studies, we turned skin cells of patients who have ALS into motor neurons that retained the genetic defects of the disease," Baloh said. "We focused on a gene, C9ORF72, that two years ago was found to be the most common cause of familial ALS and frontotemporal lobar degeneration, and even causes some cases of Alzheimer's and Parkinson's disease. What we needed to know, however, was how the defect triggered the disease so we could find a way to treat it." Frontotemporal lobar degeneration is a brain disorder that typically leads to dementia and sometimes occurs in tandem with ALS.

The researchers found that the genetic defect of C9ORF72 may cause disease because it changes the structure of RNA coming from the gene, creating an abnormal buildup of a repeated set of nucleotides, the basic components of RNA.

"We think this buildup of thousands of copies of the repeated sequence GGGGCC in the nucleus of patients' cells may become "toxic" by altering the normal behavior of other genes in motor neurons," Baloh said.

"Because our studies supported the toxic RNA mechanism theory, we used two small segments of genetic material called antisense oligonucleotides – ASOs – to block the buildup and degrade the toxic RNA. One ASO knocked down overall C9ORF72 levels. The other knocked down the toxic RNA coming from the gene without suppressing overall gene expression levels. The absence of such potentially toxic RNA, and no evidence of detrimental effect on the motor neurons, provides a strong basis for using this strategy to treat patients suffering from these diseases." Researchers from another institution recently led a phase one trial of a similar ASO strategy to treat ALS caused by a different genetic mutation and reportedly uncovered no safety issues.

Clive Svendsen, PhD, director of the Regenerative Medicine Institute and one of the article's authors, has studied ALS for more than a decade. "ALS may be the cruelest, most severe neurological disease, but I believe the stem cell approach used in this collaborative effort holds the key to unlocking the mysteries of this and other devastating disorders. Within the Regenerative Medicine Institute, we are exploring several other stem cell-based strategies in search of treatments and cures," he said, adding that ALS affects 30,000 to 50,000 people in the U.S., but unlike other neurodegenerative diseases, it is almost always fatal, usually within three to

five years. Svendsen recently received a $17.8 million grant from the California Institute for Regenerative Medicine. In collaboration with Baloh and the ALS clinical team at Cedars-Sinai, this study will support a novel stem cell and growth factor therapy for ALS.

Researchers from UCLA; the Mayo Clinic in Jacksonville, Fla.; the University of California, San Diego; Washington University School of Medicine in St. Louis, Mo.; and Isis Pharmaceuticals contributed to the C9ORF72 study.

The research was supported by National Institutes of Health grants NS055980, NS069669, NIH-U24NS07837; and California Institute of Regenerative Medicine grant RT2-02040. Baloh holds a Career Award for Medical Scientists from the Burroughs Wellcome Fund. Analytical work was partially supported by the UCLA Muscular Dystrophy Core Center funded by the National Institute of Arthritis, Musculoskeletal and Skin Disorders (P30 AR057230) within the Center for Duchenne Muscular Dystrophy at UCLA.

Citation: Science Translational Medicine, "Targeting RNA foci reduces pathology in iPSC-derived motor neurons from C9ORF72 repeat patients."

http://www.sciencedaily.com/releases/2013/10/131024182424.htm

Study Finds That Paying People to Become Kidney Donors Could Be Cost-Effective

Paying kidney donors $10,000, with the assumption that this strategy would increase the number of transplants performed by 5% or more

A strategy where living kidney donors are paid $10,000, with the assumption that this strategy would increase the number of transplants performed by 5% or more, would be less costly and more effective than the current organ donation system, according to a study appearing in an upcoming issue of the Clinical Journal of the American Society of Nephrology (CJASN). The findings demonstrate that a paid living donor strategy is attractive from a cost-effectiveness perspective, even under conservative estimates of its effectiveness.

Kidney transplantation is the best treatment for patients with kidney failure. Unfortunately, there's a shortage of kidneys available to those in need of a transplant, and donation rates from both living and deceased donors have remained relatively unchanged over the last decade. There is considerable debate around the use of financial incentives in living kidney donation regarding legal, ethical, and moral issues. By estimating the likely costs and consequences of paying donors, experts can determine whether a strategy of paying donors is worth pursuing with the goal of clarifying these remaining issues.

Lianne Barnieh, PhD, Braden Manns, MD (University of Calgary, in Canada), and their colleagues studied whether a government or third party administered program of paying living donors $10,000 would be cost-effective. In other words, would it save money and, by increasing the number of transplants, improve patient outcomes?

According to their model, a strategy to increase the number of kidneys for transplantation by 5% (a very conservative estimate) by paying living donors $10,000 could result in an incremental cost savings of $340 and a gain of 0.11 quality-adjusted life years over a patient's lifetime compared with the current organ donation system. Increasing the number of kidneys for transplantation by 10% and 20% would translate into an incremental cost savings of $1,640 and $4,030 and a quality-adjusted life year gains of 0.21 and 0.39, respectively.

"Such a program could be cost saving because of the extra number of kidney transplants and, consequently, lower dialysis costs. Further, by increasing the number of people receiving a kidney transplant, this program could improve net health by increasing the quality and quantity of life for patients with end-stage renal disease," said Dr. Barnieh.

In an accompanying editorial, Matthew Allen, BA, and Peter Reese, MD, MSCE (University of Pennsylvania) have proposed a research agenda and necessary elements for a limited trial of incentives. "Current trends regarding the use of financial incentives in medicine suggest that the time is ripe for new consideration of payments for living kidney donation," they wrote. "Reassurance about the ethical concerns, however, can come only through empirical evidence from actual experience," they added.

Lianne Barnieh, John S. Gill, Scott Klarenbach, and Braden J. Manns. The Cost-Effectiveness of Using Payment to Increase Living Donor Kidneys for Transplantation. Clinical Journal of the American Society of Nephrology, October 2013

http://www.eurekalert.org/pub_releases/2013-10/uadb-aaf102513.php

An antibody fragment designed at the UAB ameliorates first hallmarks of Alzheimer's disease in mice

Beneficial effects were seen at the behavioural, cellular and molecular levels five days after administration

Researchers at the Biosciences Unit of the Department of Biochemistry and Molecular Biology at the Universitat Autònoma de Barcelona (UAB), in collaboration with the UAB Institute of Neurosciences (INc), have conducted trials with mice by injecting a specific antibody fragment against soluble aggregates of the A peptide, responsible for the toxicity and cell death characteristic of Alzheimer's disease. The beneficial effects

were seen at the behavioural, cellular and molecular levels five days after an intraperitoneal dose was administered.
Since the first case of Alzheimer's disease was described, the disease has been associated with the presence of insoluble deposits known as amyloid plaques. However, in the past decade researchers have been able to conclude that the neuronal death characteristic of the disease is not due to the presence of these plaques but rather to the toxicity of the soluble aggregates preceding them (and called oligomers), formed by the Aβ peptide.
Immunotherapy, consisting of the use of antibodies as a treatment for disease, is turning out to be an encouraging tool for the treatment of certain types of cancer and has also been used in clinical trials to treat Alzheimer's disease. Nevertheless, the clinical trial which had advanced the most in treating Alzheimer's through passive vaccination - using the bapineuzumab antibody - was halted in 2012 during its last trial phase due to controversial adverse effects and benefits of the treatment. Many scientists think the effects were the result of administering complete antibodies, which produce inflammation in the brain. For this reason, they propose that administering antibody fragments instead would be much safer.
The research group directed by Dr Sandra Villegas, from the Biosciences Unit of the Department of Biochemistry and Molecular Biology at the UAB, designed a recombinant antibody fragment (the single-chain variable fragment scFv-h3D6), a derivative of bapineuzumab, which only consists of the active part trapping the etiological agent of the disease: the domains of the antibody responsible for the binding of Aβ oligomers. Scientists observed how this antibody fragment protected from cell death in human cell-cultures and described the molecular mechanism by which this antibody fragment removed the Aβ oligomers that cause the disease.
In the latest edition of mAbs (monoclonal antibodies), a journal specialized in immunotherapy, the research group has published three articles which demonstrate the benefits of the treatment using the antibody fragment scFv-h3D6 in mice, and have redesigned the molecule to make it even more efficient.
The mice come from the 3xTg-AD colony, an animal model of Alzheimer's disease, provided by Dr Lydia Giménez-Llort of the UAB Institute of Neurosciences (INCs).
Researchers observed how a single injection into the abdomen of the animals and five days later, the mice reversed their levels of anxiety to normal levels and the learning and memory deficits were ameliorated. At the molecular level, researchers demonstrated two important facts: first, the treatment cleared from the cerebral cortex the Aβ peptide oligomers, the elements causing the disease; and second, this clearence is linked to the recovery of the levels of certain apolipoproteins suspected to be the natural removers of Aβ peptide aggregates. The study on these apolipoproteins was conducted in collaboration with Dr Jose L. Sánchez-Quesada, from the Research Institute of the Sant Pau Hospital.
The results of the studies at the cellular level were also very encouraging. In addition to demonstrating that in young mice with the disease neuronal death occurs even in the cerebellum, UAB scientists observed how the antibody fragment protected the neurons, either fully in the less involved areas or partially in the most involved ones.
With the goal of improving the molecule, especially in regard to how long it can remain in the blood stream, the UAB group redesigned the molecule based on a molecular model developed in collaboration with Dr Baldo Oliva from the UPF-IMIM. The mutations introduced increase the thermodynamic stability by 25% and decrease the tendency to aggregate to some 4ºC, traits which clearly increase the therapeutic potential of the scFv-h3D6 fragment to treat Alzheimer's disease. Additionally, the published redesign can also be useful for other antibody fragments being produced in other laboratories with the aim of finding effective treatments for several diseases.

http://www.livescience.com/40704-spaying-changing-cat-personalities.html

Are Humans Reversing Cat Domestication?

When your cat sees a stranger, does he come and snuggle close or hiss and run away?

By Tia Ghose, Staff Writer | October 25, 2013 01:09pm ET

Whether a feline friend is a lap cat or a claws-out kitty is largely affected by their socialization as young kittens. But at least part of cats' friendliness may be in their genes. And the widespread practice of spaying or neutering cats before they are adopted may be inadvertently selecting for aloof cats, by ensuring the friendliest animals don't reproduce, one researcher says.
"The very cats that are the friendliest and the ones that don't do much hunting are the very ones we are told we should be neutering," said John Bradshaw, an anthrozoologist at the University of Bristol in England, and the author of "Cat Sense: How the New Feline Science Can Make You a Better Friend to Your Pet" (Basic Books, 2013). But not everyone is convinced.
Domestic and feral cats are genetically indistinguishable, so spay/neuter programs are unlikely to nudge the gene pool one way or the other, said Carlos Driscoll, a University of Oxford biologist who is studying the

genome of the wildcat from which the domestic cat emerged at the National Institutes of Health in Bethesda, Md.

Subtle differences

Domestic cats arose from a subspecies of cat called Felis silvestris lybica between 10,000 and 20,000 years ago in the Near East or North Africa. But the genetic differences between this wildcat ancestor and its tamer offshoot are very subtle: Wild cats and domestic cats look alike and are able to mate with one another, Driscoll said. Just 10 to 20 gene changes may be responsible for domestication in the tame cats, though scientists don't know which ones.

Because so few genes are associated with domestication, spay and neuter policies that ensure the friendliest cats don't reproduce could be "pushing domestication backward" to a noticeable degree in the next 50 to 100 years, Bradshaw told LiveScience.

Selecting for less-friendly cats?

To support that notion, Bradshaw conducted a simple test of cat personality in Southampton, England: He had strangers enter the houses of kittens in the area, try to pick up and stroke the cats, and then watched the kitties purr or hide.

In an area where spaying and neutering rates were highest — more than 98 percent —kitties tended to be a bit more skittish around strangers, possibly because they have to "import" their fluffy friends since their own pals aren't able to reproduce. Less-affluent areas had bolder, friendlier cats.

"What we suggest is people [in affluent areas] are getting kittens in from the countryside from feral cats that are a little bit wilder," or from a few feral females and just a few tomcats that are "living in the shadows," Bradshaw said.

Therefore, intensive spay and neuter programs may be artificially selecting for the less-tame cats, he said.

"Neutering is — in terms of biology, in terms of population dynamics — a mortality factor," Bradshaw said. "If you neuter, you've removed its genes from the pools, so when you look at the next population, you have to rule it out." The study has a few caveats: It hasn't been published in a peer-reviewed journal, and the team only looked at about 70 cats in all.

Other solutions

And even if the findings are borne out, Bradshaw isn't suggesting a return to the old days, when cats mated freely and the unwanted kittens were tossed in a sack and drowned.

Cats kill billions of animals a year, so cities rightly want to keep feral-cat colonies in check. But if that's cities' aim, Bradshaw said, they should find the ultimate source of the problem: food.

"Are there people feeding them, are they stealing the food, is it bad hygiene in restaurants?" Bradshaw said. Reduce the available food, and the feral-cat population will naturally decrease, he said.

Identifying the genes involved in cat personality could also help, by allowing breeders, for the first time, to select for traits such as friendliness and gentleness, rather than just looks, he said.

Skeptics remain

Driscoll doesn't think spay and neuter programs will make cats any less friendly. For one, no studies have ever shown any genetic differences between house kitties and feral cats — which are, after all, just domestic cats that fend for themselves and haven't been socialized to live with humans.

Moreover, simply too many cats with too much freedom are on the prowl for spay and neuter programs to change the entire gene pool. "The population of domestic cats has been stable for a very long time," Driscoll said. "There's a lot of genetic inertia there. You can go out and spay and neuter all the damn cats you want, and the next year, they're all going to be back."

http://www.sciencedaily.com/releases/2013/10/131025091951.htm

Experimental Drug Reduces Brain Damage, Eliminates Brain Hemorrhaging in Rodents Afflicted by Stroke

An experimental drug called 3K3A-APC appears to reduce brain damage, eliminate brain hemorrhaging and improve motor skills in older stroke-afflicted mice and stroke-afflicted rats with comorbid conditions such as hypertension, according to a new study from Keck Medicine of USC.

The study, which appears online today in the journal Stroke, provides additional evidence that 3K3A-APC may be used as a therapy for stroke in humans, either alone or in combination with the FDA-approved clot-busting drug therapy tPA (tissue plasminogen activator). Clinical trials to test the drug's efficacy in people experiencing acute ischemic stroke are expected to begin recruiting patients in the U.S. in 2014.

"Currently, tPA is the best treatment for stroke caused by a blocked artery, but it must be administered within three hours after stroke onset to be effective," said Berislav V. Zlokovic, MD, PhD, director of the Zilkha

Neurogenetic Institute (ZNI) at the Keck School of Medicine of USC and the study's lead investigator.
"Because of this limited window, only a small fraction of those who suffer a stroke reach the hospital in time to be considered for tPA. Our studies show that 3K3A-APC extends tPA's therapeutic window and counteracts tPA's tendency to induce bleeding in the brains of animals having a stroke."
Zlokovic is the scientific founder of ZZ Biotech, a Houston-based biotechnology company he co-founded with USC benefactor Selim Zilkha to develop biological treatments for stroke and other neurological ailments. ZZ Biotech's 3K3A-APC is a genetically engineered variant of the naturally occurring activated protein C (APC), which plays a role in the regulation of blood clotting and inflammation. 3K3A-APC has been shown to have a protective effect on the lining of blood vessels in rodent brains, which appears to help prevent bleeding caused by tPA.
In collaboration with Cedars-Sinai Medical Center and The Scripps Research Institute, Zlokovic and his team gave tPA -- alone and in combination with 3K3A-APC -- to mature female mice and male hypertensive rats four hours after stroke. They also gave 3K3A-APC in regular intervals up to seven days after stroke. They measured the amount of brain damage, bleeding and motor ability of the rodents up to four weeks after stroke. The researchers found that, under those conditions, tPA therapy alone caused bleeding in the brain and did not reduce brain damage or improve motor ability when compared to the control. The combination of tPA and 3K3A-APC, however, reduced brain damage by more than half, eliminated tPA-induced bleeding and significantly improved motor ability.
"Scientists all around the globe are studying potential stroke therapies, but very few have the robust preclinical data package that 3K3A-APC has," said Kent Pryor, PhD, MBA, ZZ Biotech's chief operating officer. "The results from Dr. Zlokovic's studies have been very promising."
Zlokovic's team previously reported similar results in young, healthy male rodents. A Phase 1 trial testing the safety of 3K3A-APC in healthy human volunteers, led by study co-author Patrick D. Lyden, M.D., of Cedars-Sinai, concluded in February.
"We now have opened an investigational new drug application at the FDA to conduct a Phase 2 clinical trial of 3K3A-APC in patients experiencing acute ischemic stroke," said Joe Romano, CEO and president of ZZ Biotech. "We are excited to see 3K3A-APC move from healthy volunteers to real patients suffering from this terrible disease."
Wang, Y., Zhao, Z., Chow, N., Rajput, P.S., Griffin, J.H., Lyden, P.D. & Zlokovic, B.V. An activated protein C analog protects from ischemic stroke and extends the therapeutic window of tPA in aged female mice and hypertensive rats. Stroke, October 2013

http://www.eurekalert.org/pub_releases/2013-10/aaop-poh101713.php

Prevalence of household gun ownership linked to child gun shot wounds

Reducing the number of household firearms, especially handguns, may reduce childhood gunshot injuries

ORLANDO, Fla. –There are approximately 7,500 child hospitalizations and 500 in-hospital deaths each year due to injuries sustained from guns. In an abstract presented Oct. 27 at the American Academy of Pediatrics (AAP) National Conference and Exhibition in Orlando, researchers also identified a link between the percentage of homes with guns and the prevalence of child gunshot injuries.
In "United States Gunshot Violence—Disturbing Trends," researchers reviewed statistics from the Kids' Inpatient Database (KID) from 1997, 2000, 2003, 2006 and 2009 (for a total of 36 million pediatric hospital admissions), and estimated state household gun ownership using the most recent Behavioral Risk Factor Surveillance System data (2004).
The study found that approximately 7,500 children are admitted to the hospital for the treatment of injuries sustained from guns each year, and more than 500 children die during hospital admission from these injuries. Between 1997 and 2009, hospitalizations from gunshot wounds increased from 4,270 to 7,730, and in-hospital deaths from 317 to 503.
The study also found a significant association between the percentage of gunshot wounds occurring in the home and the percentage of households containing any firearms, loaded firearms and unlocked loaded firearms.
"Handguns account for the majority of childhood gunshot wounds and this number appears to be increasing over the last decade," said lead study author Arin L. Madenci, MD, MPH. "Furthermore, states with higher percentages of household firearm ownership also tended to have higher proportions of childhood gunshot wounds, especially those occurring in the home."
Many current gun control efforts focus on limiting the availability of military-style semi-automatic assault rifles. "Policies designed to reduce the number of household firearms, especially handguns, may more effectively reduce the number of gunshot injuries in children," said Dr. Madenci.