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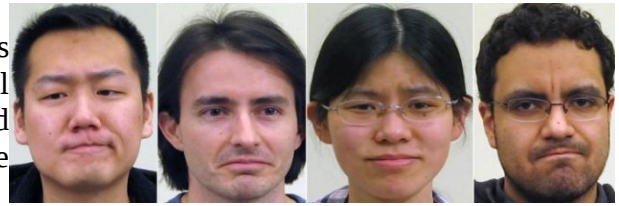
The 'Not Face' is a universal part of language, study suggests

Computer analysis shows how this facial expression acts as grammatical marker



The 'not face' in English, Spanish, Mandarin Chinese and ASL **Ohio State University**

COLUMBUS, Ohio - Researchers have identified a single, universal facial expression that is interpreted across many cultures as the embodiment of negative emotion.

The look proved identical for native speakers of English, Spanish, Mandarin Chinese and American Sign Language (ASL). It consists of a furrowed brow, pressed lips and raised chin, and because we make it when we convey negative sentiments, such as "I do not agree," researchers are calling it the "not face."

The study, published in the journal Cognition, also reveals that our facial muscles contract to form the "not face" at the same frequency at which we speak or sign words in a sentence. That is, we all instinctively make the "not face" as if it were part of our spoken or signed language. What's more, the researchers discovered that ASL speakers sometimes make the "not face" instead of signing the word "not"--a use of facial expression in ASL that was previously undocumented.

"To our knowledge, this is the first evidence that the facial expressions we use to communicate negative moral judgment have been compounded into a unique, universal part of language," said Aleix Martinez, cognitive scientist and professor of electrical and computer engineering at The Ohio State University.

"Where did language come from? This is a question that the scientific community has grappled with for a very long time," he continued. "This study strongly suggests a link between language and facial expressions of emotion."

Previously, Martinez and his team had used computer algorithms to identify 21 distinct emotional expressions--including complex ones that are combinations of more basic emotions. "Happy" and "disgusted," for instance, can be compounded into "happily disgusted," a face that we might make when watching a gross-out comedy movie or when an adorable baby poops in its diaper.

For this new study, the researchers hypothesized that if a universal "not face" existed, it was likely to be combination of three basic facial expressions that are universally accepted to indicate moral disagreement: anger, disgust and contempt.

Why focus on negative expressions? Charles Darwin believed that the ability to communicate danger or aggression was key to human survival long before we developed the ability to talk, Martinez explained. So the researchers suspected that if any truly universal facial expressions of emotion exist, then the expression for disapproval or disagreement would be the easiest to identify.

To test the hypothesis, they sat 158 Ohio State students in front of a digital camera. The students were filmed and photographed as they had a casual conversation with the person behind the camera in their native language.

The students belonged to four groups, which were chosen to represent a wide variety of grammatical structures. English is a Germanic language, while Spanish is based on Latin; Mandarin Chinese is a modern form of Middle Chinese that was formalized early in the 20th century. Like other forms of sign language, ASL combines hand gestures, head and body movements and facial expressions to communicate individual words or phrases.

The researchers were looking for a facial "grammatical marker," a facial expression that determines the grammatical function of a sentence. For example, in the sentence "I am not going to the party," there is a grammatical marker of negation: "not." Without it, the meaning of the sentence completely changes: "I am going to the party."

If the grammatical marker of negation is universal, the researchers reasoned, then all the study participants would make similar facial expressions when using that grammatical marker, regardless of which language they were speaking or signing. They should all make the same "not face" in conjunction with--or in lieu of--the spoken or signed marker of negation.

The tests went like this: The students either memorized and recited negative sentences that the researchers had written for them ahead of time, or the students were prompted with questions that were likely to illicit disagreement, such as "A study shows that tuition should increase 30 percent. What do you think?"

In all four groups--speakers of English, Spanish, Mandarin and ASL--the researchers identified clear grammatical markers of negation. The students' answers translated to statements like "That's not a good idea," and "They should not do that."

The researchers manually tagged images of the students speaking, frame by frame, to show which facial muscles were moving and in which directions. Then computer algorithms searched the thousands of resulting frames to find commonalities among them.

A "not face" emerged: the furrowed brows of "anger" combined with the raised chin of "disgust" and the pressed-together lips of "contempt." Regardless of language--and regardless of whether they were speaking or signing--the participants' faces displayed these same three muscle movements when they communicated negative sentences. Computer analysis also compared the tempo at which the students' facial muscles moved.

Here's why: Human speech typically varies between three to eight syllables per second--that is, 3-8 Hz, or hertz, a measure of frequency. Researchers believe that the human brain is wired to recognize grammatical constructs that fall within that frequency band as language.

Martinez and his team reasoned that if all the students' facial muscles moved to make the "not face" within that same frequency band, then the face itself likely functions as a universal grammatical marker of language.

In the tests, native English speakers made the "not face" at a frequency of 4.33 Hz, Spanish at 5.23 Hz, and Mandarin speakers at 7.49 Hz. Speakers of ASL made the face at a frequency of 5.48 Hz. All frequencies were within the 3-8 Hz range of spoken communication, which strongly suggests that the facial expression is an actual grammatical marker, Martinez said.

Also, something truly unique emerged from the studies of the ASL-signing students. They utilized the facial expression a different way--as if it were the unique grammatical marker in the signed sentence. People sometimes signed the word "not." Other times, they just shook their head "no" when they got to the part of the sentence where they would have signed "not." Both are accepted ways to communicate negation in ASL. But sometimes, speakers didn't make the sign for "not," nor did they shake their head. They just made the "not face," as if the face itself counted explicitly as a marker of negation in the sentence.

This is the first time researchers have documented a third way that users of sign language say "not": just by making the face.

"This facial expression not only exists, but in some instances, it is the only marker of negation in a signed sentence," Martinez said. "Sometimes the only way you can tell that the meaning of the sentence is negative is that person made the 'not face' when they signed it."

Manual analysis of the facial expressions was painstaking, Martinez admitted, but now that he and his team have shown that the experiment works, they hope to make the next phase of the project fully automatic, with new algorithms that will extract and analyze facial movements without human help. They're building those algorithms now.

Once they finish, they will take a "big data" approach to further explore the origins of language. First, they'll analyze 1,000 hours of YouTube video of people talking, which corresponds to around 100 million still frames. Ultimately, they want to amass 10,000 hours of data, or 1 billion frames. They also hope to identify the facial expressions that go along with other grammatical markers, including positive ones. "That will likely take decades," Martinez said. "Most expressions don't stand out as much as the 'not face.'"

Co-authors on the study included C. Fabian Benitez-Quiroz, a postdoctoral researcher in electrical and computer engineering, and Ronnie Wilbur, a professor of linguistics at Purdue University. This research was supported by the National Institutes of Health.

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How cancer stem cells thrive when oxygen is scarce

Hint: They borrow a trick from embryonic stem cells

Working with human breast cancer cells and mice, scientists at The Johns Hopkins University say new experiments explain how certain cancer stem cells thrive in low oxygen conditions. Proliferation of such cells, which tend to resist chemotherapy and help tumors spread, are considered a major roadblock to successful cancer treatment.

The new research, suggesting that low-oxygen conditions spur growth through the same chain of biochemical events in both embryonic stem cells and breast cancer stem cells, could offer a path through that roadblock, the investigators say.

"There are still many questions left to answer but we now know that oxygen poor environments, like those often found in advanced human breast cancers serve as nurseries for the birth of cancer stem cells," says Gregg Semenza, M.D., Ph.D., the C. Michael Armstrong Professor of Medicine and a member of the Johns Hopkins Kimmel Cancer Center. "That gives us a few more possible targets for drugs that diminish their threat in human cancer."

A summary of the findings was published online March 21 in the Proceedings of the National Academy of Sciences.

Semenza says scientists have long known that low oxygen environments affect tumor growth, but, in the case of advanced tumors, there was a paradox. "Aggressive cancers contain regions where the cancer cells are starved for oxygen and die off, yet patients with these tumors generally have the worst outcome. Our new findings tell us that low oxygen conditions actually encourage certain cancer stem cells to multiply through the same mechanism used by embryonic stem cells."

All stem cells are immature cells known for their ability to multiply indefinitely and give rise to progenitor cells that mature into specific cell types that populate the body's tissues during embryonic development. They also replenish tissues throughout the life of an organism. But stem cells found in tumors use those same attributes and twist them to maintain and enhance the survival of cancers. According to Semenza, "Chemotherapy may kill more than 99 percent of the cancer cells in a tumor but fail to kill a small population of cancer stem cells that are responsible for subsequent cancer relapse and metastasis."

"The search has been intense to find these cells' Achilles' heel. If we could get cancer stem cells to abandon their stem cell state, they would no longer have the

power to keep repopulating tumors," says Semenza, who also directs the Vascular Biology Research Program at the Institute for Cell Engineering.

Aiding their new research, Semenza says, was the knowledge that whereas the air we breathe is 21 percent oxygen, oxygen levels average around 9 percent in healthy human breast tissue but only 1.4 percent in breast tumors. Recent studies showed that low oxygen conditions increase levels of a family of proteins known as HIFs, or hypoxia-inducible factors, that turn on hundreds of genes, including one called NANOG that instructs cells to become stem cells.

Studies of embryonic stem cells revealed that NANOG protein levels can be lowered by a chemical process known as methylation, which involves putting a methyl group chemical tag on a protein's messenger RNA (mRNA) precursor. Semenza says methylation leads to the destruction of NANOG's mRNA so that no protein is made, which in turn causes the embryonic stem cells to abandon their stem cell state and mature into different cell types.

To see whether cancer stem cell renewal involves a chain of events similar to that used by embryonic stem cells, and whether the process was affected by oxygen levels, Semenza and graduate student Chuanzhao Zhang focused their studies on two human breast cancer cell lines that responded to low oxygen by ramping up production of the protein ALKBH5, which removes methyl groups from mRNAs. (Breast cancer is categorized and treated based on the presence or absence of three hormone receptors displayed on the outer membranes of cells. One human cell line they studied displays the receptors for estrogen and progesterone, and one, known as triple negative, displays none.)

Zeroing in on NANOG, the scientists found that low oxygen conditions increased NANOG's mRNA levels through the action of HIF proteins, which turned on the gene for ALKBH5, which decreased the methylation and subsequent destruction of NANOG's mRNA. When they prevented the cells from making ALKBH5, NANOG levels and the number of cancer stem cells decreased. When the researchers manipulated the cell's genetics to increase levels of ALKBH5 without exposing them to low oxygen, they found this also decreased methylation of NANOG mRNA and increased the numbers of breast cancer stem cells.

Finally, using live mice, the scientists injected 1,000 triple-negative breast cancer cells into their mammary fat pads, where the mouse version of breast cancer forms. Unaltered cells created tumors in all seven mice injected with such cells, but when cells missing ALKBH5 were used, they caused tumors in only 43 percent (six out of 14) of mice. "That confirmed for us that ALKBH5 helps preserve cancer stem cells and their tumor-forming abilities," Semenza says.

Semenza says his team will continue its mouse studies to see if metastasis -- the spread of cancer from the original tumor -- is affected by the low oxygen/ALKBH5/NANOG relationship too. The researchers also want to see what other proteins and mRNAs are involved in the relationship, and why some cancer cell lines they tested did not show the same increased ALKBH5 levels in response to low oxygen levels.

Other authors of the report include Debangshu Samanta, Haiquan Lu, John Bullen, Huimin Zhang and Ivan Chen of the Johns Hopkins University School of Medicine, and Xiaoshun He of Sun Yat-sen University in Guangzhou, China.

This work was supported by grants from the American Cancer Society (122437-RP-12-090-01-COUN), the Cindy Rosencrans Fund for Triple Negative Breast Cancer and the China Scholarship Council.

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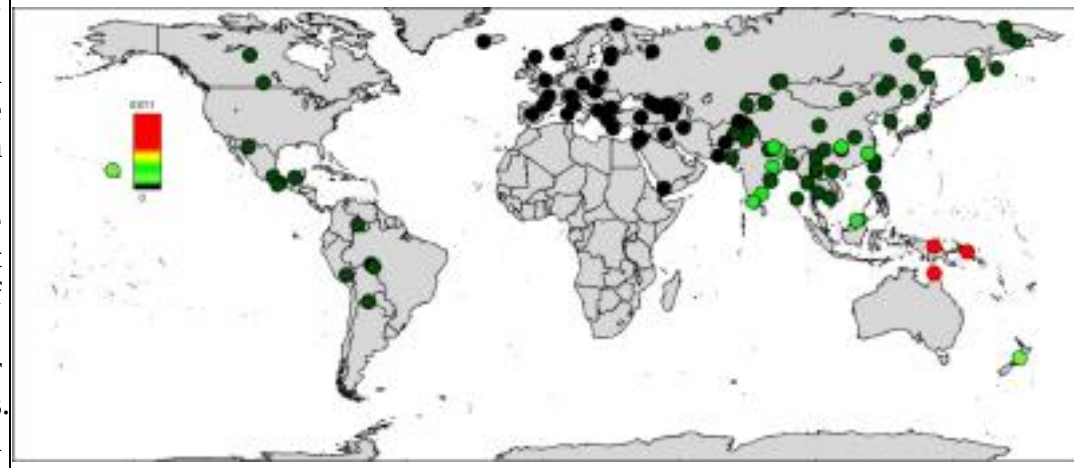
A world map of Neanderthal and Denisovan ancestry in modern humans

Many bloodlines around the world, particularly of South Asian descent, may actually be a bit more Denisovan

Most non-Africans possess at least a little bit Neanderthal DNA. But a new map of archaic ancestry--published March 28 in Current Biology--suggests that many bloodlines around the world, particularly of South Asian descent, may actually be a bit more Denisovan, a mysterious population of hominids that lived around the same time as the Neanderthals. The analysis also proposes that modern humans interbred with Denisovans about 100 generations after their trysts with Neanderthals.



This map shows the proportion of the genome inferred to be Denisovan in ancestry in diverse non-Africans. The color scale is not linear to allow saturation of the high Denisova proportions in Oceania (bright red) and better visualization of the peak of Denisova proportion in South Asia. **Sankararaman et al./Current Biology 2016**

The Harvard Medical School/UCLA research team that created the map also used comparative genomics to make predictions about where Denisovan and Neanderthal genes may be impacting modern human biology. While there is still much to uncover, Denisovan genes can potentially be linked to a more subtle sense of smell in Papua New Guineans and high-altitude adaptions in Tibetans. Meanwhile, Neanderthal genes found in people around the world most likely contribute to tougher skin and hair.

"There are certain classes of genes that modern humans inherited from the archaic humans with whom they interbred, which may have helped the modern humans to adapt to the new environments in which they arrived," says senior author David Reich, a geneticist at Harvard Medical School and the Broad Institute. "On the flip side, there was negative selection to systematically remove ancestry that may have been problematic from modern humans. We can document this removal over the 40,000 years since these admixtures occurred."

Reich and lab members, Swapan Mallick and Nick Patterson, teamed up with previous laboratory member Sriram Sankararaman, now an Assistant Professor of computer science at the University of California, Los Angeles, on the project, which found evidence that both Denisovan and Neanderthal ancestry has been lost from the X chromosome, as well as genes expressed in the male testes. They theorize that this has contributed to reduced fertility in males, which is commonly observed in other hybrids between two highly divergent groups of the same species.

The researchers collected their data by comparing known Neanderthal and Denisovan gene sequences across more than 250 genomes from 120 non-African populations publically available through the Simons Genome Diversity Project (there is little evidence for Neanderthal and Denisovan ancestry in Africans). The analysis was carried out by a machine-learning algorithm that could differentiate between components of both kinds of ancestral DNA, which are more similar to one another than to modern humans.

The results showed that individuals from Oceania possess the highest percentage of archaic ancestry and south Asians possess more Denisovan ancestry than previously believed. This reveals previously unknown interbreeding events, particularly in relation to Denisovans. In contrast, Western Eurasians are the non-Africans least likely to have Neanderthal or Denisovan genes. "The interactions between modern humans and archaic humans are complex and perhaps involved multiple events," Reich says.

The study's main limitation is that it relies on the current library of ancient genomes available. The researchers caution against drawing any conclusions about our extinct human ancestors based on the genetics and possible traits that they left behind. "We can't use this data to make claims about what the Denisovans or Neanderthals looked like, what they ate, or what kind of diseases they were susceptible to," says Sankararaman, first author on the paper. "We are still very far from understanding that."

The authors were supported by the National Institutes of Health, the National Science Foundation, and the Howard Hughes Medical Institute.

Current Biology, Sankararaman et al.: "The Combined Landscape of Denisovan and Neanderthal Ancestry in Present-Day Humans" http://dx.doi.org/10.1016/j.cub.2016.03.037

http://www.eurekalert.org/pub_releases/2016-03/osu-aak032816.php

An ancient killer: Ancestral malarial organisms traced to age of dinosaurs

First vertebrate hosts of malaria would have included the dinosaurs

CORVALLIS, Ore. - A new analysis of the prehistoric origin of malaria suggests that it evolved in insects at least 100 million years ago, and the first vertebrate hosts of this disease were probably reptiles, which at that time would have included the dinosaurs.

Malaria, a scourge on human society that still kills more than 400,000 people a year, is often thought to be of more modern origin - ranging from 15,000 to 8 million years old, caused primarily by one genus of protozoa, Plasmodium, and spread by anopheline mosquitoes.

But the ancestral forms of this disease used different insect vectors and different malarial strains, and may literally have helped shape animal survival and evolution on Earth, according to George Poinar, Jr., a researcher in the College of Science at Oregon State University.

Poinar suggested in the journal American Entomologist that the origins of this deadly disease, which today can infect animals ranging from humans and other mammals to birds and reptiles, may have begun in an insect such as the biting midge more than 100 million years ago. And in previous work, Poinar and his wife, Roberta, implicated malaria and the evolution of blood-sucking insects as disease vectors that could have played a significant role in the extinction of the dinosaurs.

"Scientists have argued and disagreed for a long time about how malaria evolved and how old it is," Poinar said. "I think the fossil evidence shows that modern malaria vectored by mosquitoes is at least 20 million years old, and earlier forms of the disease, carried by biting midges, are at least 100 million years old and probably much older."

Since the sexual reproduction stage of malaria only occurs in insects, Poinar said in the new study that they must be considered the primary hosts of the disease, not the vertebrate animals that they infect with disease-causing protozoa. And he

believes the evidence points toward the Gregarinida as a protozoan parasite group that could have been the progenitors of malaria, since they readily infect the insects that vector malaria today.

Understanding the ancient history of malaria evolution, Poinar said, might offer clues to how its modern-day life cycle works, how it evolved, and what might make possible targets to interrupt its transmission through its most common vector, the Anopheles mosquito.

Understanding the evolution of malaria also takes one on a worldwide journey, according to evidence found in insects preserved in amber. Poinar is an international expert in using plant and animal life forms preserved in this semi-precious stone to help learn more about the biology and ecology of the distant past. Poinar was the first to discover a type of malaria in a 15-20 million-year-old fossil from the New World, in what is now the Dominican Republic. It was the first fossil record of Plasmodium malaria, one type of which is now the strain that infects and kills humans.

Even further back, malaria may have been one of the diseases that arose, along with the evolution of insects, and had a huge impact on animal evolution. In a 2007 book, "What Bugged the Dinosaurs? Insects, Disease and Death in the Cretaceous," George and Roberta Poinar argued that insects carried diseases that contributed to the widespread extinction of the dinosaurs around the "K-T boundary" about 65 million years ago.

"There were catastrophic events known to have happened around that time, such as asteroid impacts and lava flows," Poinar said. "But it's still clear that dinosaurs declined and slowly became extinct over thousands of years, which suggests other issues must also have been at work. Insects, microbial pathogens and vertebrate diseases were just emerging around that same time, including malaria."

Avian malaria has been implicated in the extinction of many bird species in Hawaii just in recent decades, especially in species with no natural resistance to the disease. Different forms of malaria, which is now known to be an ancient disease, may have been at work many millions of years ago and probably had other implications affecting the outcome of vertebrate survival, Poinar said.

The first human recording of malaria was in China in 2,700 B.C., and some researchers say it may have helped lead to the fall of the Roman Empire. In 2015 there were 214 million cases worldwide, according to the World Health Organization. Immunity does not occur naturally and the search for a vaccine has not yet been achieved.

Editor's Note: The study this story is based on is available online: http://bit.ly/1ojLDqa

http://www.eurekalert.org/pub_releases/2016-03/wcmc-qtb032816.php

GI tract bacteria help decrease stroke

Certain types of bacteria in the gut can leverage the immune system to decrease the severity of stroke, according to new research from Weill Cornell Medicine.

This finding can help mitigate stroke -- which is the second leading cause of death worldwide.

In the study, published March 28 in Nature Medicine, mice received a combination of antibiotics. Two weeks later, the researcher team -- which included collaborators at Memorial Sloan Kettering Cancer Center -- induced the most common type of stroke, called ischemic stroke, in which an obstructed blood vessel prevents blood from reaching the brain. Mice treated with antibiotics experienced a stroke that was about 60 percent smaller than rodents that did not receive the medication. The microbial environment in the gut directed the immune cells there to protect the brain, the investigators said, shielding it from the stroke's full force.

"Our experiment shows a new relationship between the brain and the intestine," said Dr. Josef Anrather, the Finbar and Marianne Kenny Research Scholar in Neurology and an associate professor of neuroscience in the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine. "The intestinal microbiota shape stroke outcome, which will impact how the medical community views stroke and defines stroke risk."

The findings suggest that modifying the microbiotic makeup of the gut can become an innovative method to prevent stroke. This could be especially useful to high-risk patients, like those undergoing cardiac surgery or those who have multiple obstructed blood vessels in the brain.

Further investigation is needed to understand exactly which bacterial components elicited their protective message. However, the researchers do know that the bacteria did not interact with the brain chemically, but rather influenced neural survival by modifying the behavior of immune cells. Immune cells from the gut made their way to the outer coverings of the brain, called the meninges, where they organized and directed a response to the stroke.

"One of the most surprising findings was that the immune system made strokes smaller by orchestrating the response from outside the brain, like a conductor who doesn't play an instrument himself but instructs the others, which ultimately creates music," said Dr. Costantino Iadecola, director of the Feil Family Brain and Mind Research Institute and the Anne Parrish Titzell Professor of Neurology at Weill Cornell Medicine.

The newfound connection between the gut and the brain holds promising implications for preventing stroke in the future, which the investigators say might be achieved by changing dietary habits in patients or "at risk" individuals.

"Dietary intervention is much easier to accomplish than drug use, and it could reach a broad base," Dr. Anrather said. "This is a little far off from the current study -- it's music of the future. But diet has the biggest effect of composition of microbiota, and once beneficial and deleterious species are identified, we can address them with dietary intervention."

http://www.eurekalert.org/pub_releases/2016-03/uoo-oar032816.php

OU anthropologists reconstruct mitogenomes from prehistoric dental calculus

Human DNA enriched from dental calculus enables the reconstruction of whole mitochondrial genomes for maternal ancestry analysis

Using advanced sequencing technologies, University of Oklahoma anthropologists demonstrate that human DNA can be significantly enriched from dental calculus (calcified dental plaque) enabling the reconstruction of whole mitochondrial genomes for maternal ancestry analysis--an alternative to skeletal remains in ancient DNA investigations of human ancestry.

Christina Warinner and Cecil M. Lewis, Jr., professors in the Department of Anthropology, OU College of Arts and Sciences, collaborated with researchers from Arizona State University and Pennsylvania State University on the capture, enrichment and high-throughput sequencing of DNA extracted from six individuals at the 700-year-old Oneota cemetery, Norris Farms #36.

"We can now obtain meaningful human, pathogen and dietary DNA from a single sample, which minimizes the amount of ancient material required for analysis," said Warinner.

In recent years, dental calculus has emerged as an unexpected, but valuable, long-term reservoir of ancient DNA from dietary and microbial sources. This study demonstrates that dental calculus is also an important source of ancient human DNA. Very little dental calculus was required for analysis--fewer than 25 milligrams per individual. This makes it possible to obtain high quality genetic ancestry information from very little starting material, an important consideration for archaeological remains.

The results of this study provided high-resolution, whole mitochondrial genome information for the Oneota, a Native American archaeological culture that rose to prominence ca. AD 1000-1650, but declined sharply following European contact.

"The analysis of mitochondrial DNA allows us to better understand the population history of ancient peoples," said Anne Stone, professor in the School of Human Evolution and Social Change, Arizona State University.

Although dental calculus preserves alongside skeletal remains, it is not actually a human tissue. Dental calculus, also known as tartar, is a calcified form of dental plaque that acquires human DNA and proteins passively, primarily through the saliva and other host secretions. Once mineralized within dental calculus, however, human DNA and proteins can preserve for thousands of years. Dental calculus thus serves as an important non-skeletal reservoir of ancient human DNA.

Conventional techniques for recovering ancient human DNA typically require the destruction of bone or tooth tissue during analysis, and this has been a cause of concern for many Native and indigenous communities.

Dental calculus represents an important alternative source of ancient DNA that does not damage or disturb the integrity of skeletal remains. In addition, because dental calculus is the richest known source of DNA in the archaeological record, it presents unique opportunities for investigating archaeological sites with preservation challenges.

"Dental calculus may enable researchers to retrieve ancient DNA from samples where bone or other biological tissues are too degraded for analysis. This is particularly exciting to those of us who work in tropical or extremely old contexts, where traditional sources of DNA may be poorly preserved or even non-existent," according to Maria Nieves Colón, Ph.D. candidate, Arizona State University.

The demonstration that whole mitochondrial genomes can be reconstructed from small samples of dental calculus represents an important technological advancement for paleogenomic investigations in prehistoric North America and other regions where destructive analysis of skeletal remains is difficult or controversial.

"We hope that this research on dental calculus from the Norris Farms site acts as the first step toward future paleogenomic investigations of prehistoric North American remains in a respectful and non-destructive way that interests and benefits both descendent communities and anthropologists," said Andrew Ozga, OU doctoral graduate, and currently postdoctoral candidate at Arizona State University.

The National Science Foundation and the National Institutes of Health supported this research. The American Journal of Physical Anthropology published, "Successful enrichment and recovery of whole mitochondrial genomes from ancient human dental calculus," in a recent issue. For more information about the application of advanced genomic sequencing techniques to dental calculus, contact Christina Warinner at christina.warinner@ou.edu or Cecil M. Lewis, Jr. at cmlewis@ou.edu.

http://www.eurekalert.org/pub_releases/2016-03/isoa-cf032316.php

'I care for you,' says the autistic moral brain

A new study disproves a common stereotype about autism

"Autistic people are cold and feel no empathy." True? It is a pervasive stereotype, but when analyzed through the lens of science, reality turns out to be quite different. According to a study at SISSA, carried out in collaboration with the University of Vienna, when autistic people are placed in "moral dilemma" situations, they show an empathic response similar to the general population. The myth of coldness in autism is likely due to the presence of the subclinical trait of alexithymia, which is often associated with autism, but is distinct and can be present in the general population, and is characterized by the inability to recognize one's own, or others' emotions. The study was published in the journal Scientific Reports.

According to a Facebook post by a group called Families Against Autistic Shooters, "[Autistic people] are cold, calculating killing machines with no regard to human life." The group was created in response to the collective hysteria provoked by yet another mass shooting in an American school last October, in this case by a 26-year-old boy who was later reported to be affected by autism. The social stigma towards people with autism remains strong -- these individuals are often described as cold, antisocial, and disinterested in others, which only worsens their isolation.

But is it actually true that a person with autism does not care about the suffering of others? "According to our studies, it is quite the opposite: the autistic trait is associated with a normal empathic concern for others and is actually associated with greater tendency to avoid causing harm to others," says SISSA researcher, Indrajeet Patil, first author of a recently-published study in Scientific Reports. "The mistaken stereotype is most likely due to another personality construct, which is often found in the autistic population, but can also be found in those who are not afflicted, called alexithymia."

Autism is a neuropsychiatric disorder with a wide spectrum shared by individuals with varying degrees of cognitive skills (ranging from people with significant delays to those of above-average intelligence). Diagnostic criteria have changed over the decades (becoming more and more specific). Alexithymia, on the other hand, is a "subclinical" condition (as opposed to a disease), which can be found in the general as well as the autistic population (with an incidence rate of approximately 50% in the latter) and is characterized by an inability to understand one's own emotions and the emotions of others. "For a long time, the alexithymia trait in patients was confused with autistic symptoms, but today we know that they are distinct," says Giorgia Silani, former SISSA neuroscientist, now of the University of Vienna, who led the study. "In alexithymia, there is a lack of understanding emotions. In autism, however, we know that what is reduced is the theory of the mind, or the ability to attribute thoughts and mental states to others."

Moral Dilemmas

In the study, Patil, Silani and colleagues subjected people with high-functioning autism (high IQ) to moral dilemmas. A moral dilemma is a hypothetical situation where a decision must be made which could save lives of some individuals by sacrificing others'. In the classic moral dilemma one must decide whether or not to voluntarily take an action that will cause the death of one person, and, in so doing, save a large number of others, or do nothing, which means not killing anyone directly, but resulting in the death of other people. A "purely" rational attitude encourages the voluntary action (utilitarian), but an "empathic" attitude prevents most people from choosing to kill voluntarily.

The current investigation used advanced statistical modelling techniques to dissociated effect of autistic and alexithymic traits to see how they related to moral judgments. The results revealed that alexithymia is related to utilitarian choices on account of reduced empathic concern, while the autistic trait is linked to opposition to utilitarian choices due to increased personal distress. "Autism is associated with strong emotional stress in response to situations in which the individual tends to avoid performing harmful actions," says Patil.

The authors agree that tools for identifying and distinguishing between alexithymia and autistic disorders must be further enhanced. Their work, they add, is only an initial step in trying to define a model that can explain the complex relationship between various mutually-dependent personality traits and points to exciting new avenues for further research.

http://www.eurekalert.org/pub_releases/2016-03/asfm-nvt032916.php

Nonpathogenic viruses transferred during fecal transplants

Communities of viruses can be transferred during fecal transplants

Washington, DC - Communities of viruses can be transferred during fecal transplants, according to a study published this week in mBio, an online open-access journal of the American Society for Microbiology. Fortunately for patients who use this procedure, the viruses found to be transmitted in this study appear to be harmless to humans.

Fecal transplants are widely used for treating refractory Clostridium difficile infection, offering more than a 90% cure rate. The procedure is being tried for other gastrointestinal ailments such as irritable bowel syndrome and ulcerative colitis. During a fecal transplant, stool collected from a donor who has a healthy gastrointestinal tract is mixed with a solution (often saline), and then placed by colonoscopy, endoscopy, sigmoidsocopy, or enema into a patient with a

gastrointestinal ailment. This transfers potentially "good" bacteria into a patient. Similar to blood donations, the donating candidate is tested for high-risk viruses such as HIV.

"Fecal transplants are widely used in medicine now and they work, but you might ask what viruses are moved along with the desirable bacteria?" said principal investigator of the new study, Frederic Bushman, PhD, chair of the Department of Microbiology, Perelman School of Medicine, University of Pennsylvania. "The donors are screened very extensively for GI diseases and other infectious diseases, however you worry about the unknown unknowns, infectious agents that might be bad, but not screened for."

In the new study, the researchers analyzed the fecal transplants from a single, healthy donor to three children with chronic ulcerative colitis. The children received intensive treatment, a course of 22 to 30 transplants. The researchers purified viral particles from the poop of the donor and the recipients and conducted deep genomic sequencing to determine whether any viruses were transferred. "We could see bacterial viruses moving between humans and we were able to learn some things about transmission, but we did not see any viruses that grow on animal cells that may be of concern for infecting and harming patients," said Dr. Bushman. "We saw mostly temperate bacteriophages."

A temperate virus does not always cause immediate lysis following entry to a host, but can adopt a latent state, replicating its genome along with the host's genome after integration. These latent viruses can induce during times of stress, burst the cell, and liberate new viral particles into the environment. Some temperate bacteriophages can be of medical concern, such as ones that carry toxin genes or contribute to antibiotic resistance, but they are much less of a concern than animal cell viruses.

Temperate phages appeared to be transferred preferentially during fecal transplants. "We speculate that the temperate replication style exists, in part, to promote virus dispersal, to allow viruses to reach new environments where they can flourish," said Dr. Bushman.

The full study can be read online at: http://mbio.asm.org/content/7/2/e00322-16

http://www.eurekalert.org/pub_releases/2016-03/cu-egc032816.php

Eating green could be in your genes

Could there be a vegetarian gene?

ITHACA, N.Y. - Cornell University researchers have found evidence of a genetic variation - called an allele - that has evolved in populations that have historically favored vegetarian diets, such as in India, Africa and parts of East Asia. They also discovered a different version of this gene adapted to a marine diet discovered among the Inuit in Greenland, who mainly consume seafood.

The vegetarian allele evolved in populations that have eaten a plant-based diet over hundreds of generations. The adaptation allows these people to efficiently process omega-3 and omega-6 fatty acids and convert them into compounds essential for early brain development and if they stray from a balanced omega-6 to omega-3 diet, it may make people more susceptible to inflammation, and by association, increased risk of heart disease and colon cancer.

In Inuit populations of Greenland, the researchers uncovered that a previously identified adaptation is opposite to the one found in long-standing vegetarian populations: While the vegetarian allele has an insertion of 22 bases (a base is a building block of DNA) within the gene, this insertion was found to be deleted in the seafood allele.

"The opposite allele is likely driving adaptation in Inuit," said Kaixiong Ye, co-lead author of the paper appearing March 29 in the journal Molecular Biology and Evolution. Ye is a postdoctoral researcher in the lab of Alon Keinan, associate professor of biological statistics and computational biology, and the paper's co-senior author.

"Our study is the first to connect an insertion allele with vegetarian diets, and the deletion allele with a marine diet," Ye said.

"It is the most interesting example of local adaptation that I have been fortunate to help study," said Keinan. "Several studies have pointed to adaptation in this region of the genome. Our analyses combine to show that the adaptation is driven by an insertion of a small piece of DNA that we know its function. Moreover, when it reached the Greenlandic Inuit, with their marine-based diet rich in omega-3, it might have become detrimental."

FADS1 and FADS2 are enzymes that are essential for converting omega-3 and omega-6 fatty acids into downstream products needed for brain development and controlling inflammation. Meat and seafood eaters have less need for increased FADS1 and FADS2 enzymes to get proper nutrition because their omega-3 and omega-6 fatty acid conversion process is simpler and requires fewer steps.

This study is based on previous work by co-senior author Tom Brenna, professor of human nutrition and of chemistry at Cornell University, who showed the insertion can regulate the expression of FADS1 and FADS2 and hypothesized it could be an adaptation in vegetarian populations.

Ye, Keinan and colleagues analyzed frequencies of the vegetarian allele in 234 primarily vegetarian Indians and 311 U.S. individuals and found the vegetarian allele in 68 percent of the Indians and in just 18 percent of Americans. Analysis using data from the 1,000 Genomes Project similarly found the vegetarian allele in 70 percent of South Asians, 53 percent of Africans, 29 percent of East Asians and 17 percent of Europeans.

"Northern Europeans have a long history of drinking milk and they absorbed enough end products from milk for long-chain fatty acid metabolism so they don't have to increase capacity to synthesize those fatty acids from precursors," said Ye. "One implication from our study is that we can use this genomic information to try to tailor our diet so it is matched to our genome, which is called personalized nutrition," he added.

The researchers are not sure yet when the adaptation first occurred, as analyses of chimpanzee or orangutan genomes did not uncover the vegetarian allele. But there is evidence for the allele in early hominid Neanderthal and Denisovan genomes.

"It is possible that in the history of human evolution, when people migrated to different environments, sometimes they ate a plant-based diet and sometimes they ate a marine-based diet, and in different time periods these different alleles were adaptive," meaning the alleles have a tendency to evolve under dietary pressures, Ye said.

Kumar Kothapalli, a senior research associate in nutritional sciences, is the paper's co-lead author. The study is funded by the National Institutes of Health and the U.S. Department of Agriculture.

http://www.eurekalert.org/pub_releases/2016-03/uoc--tko032916.php

To keep or not to keep a hookworm

UC Riverside-led research team identifies key protein that by protecting the body from damage in hookworm infections ensures benefits outweigh risks

RIVERSIDE, Calif. - Researchers in the School of Medicine at the University of California, Riverside have identified an immune protein in mice that is quickly triggered in the body following infection and serves to protect the body's tissues. Called "RELMalpha," this protein, whose homologue in humans is called "resistin," is responsible more for protecting the body than attacking the parasite.

As mammals, we have an immune system to fight pathogens that attack us. Because pathogens do us damage, the body naturally releases proteins to kill the pathogens. But these cytokines--proteins made by immune cells--can also attack the body's tissues and damage them. RELMalpha, made by mice to dampen the immune system response, focuses on protecting the body's tissues. Resistin is expected to function similarly in humans.

"This is counterintuitive," said Meera G. Nair, Ph.D., an assistant professor of biomedical sciences, whose lab led the research that focused on the hookworm as the parasite of study. "We think the immune system is all about killing the parasite. But that's not what RELMalpha sets out to do. It is important evidence that mammals have regulatory systems in place not to kill pathogens, but instead to dampen the immune response because this, overall, benefits the host."

Study results appear in the April 1 issue of the journal Infection and Immunity.

Hooked on worms

In her career, Nair has done considerable research on hookworms, soil-transmitted nematodes that infect an estimated 2 billion people worldwide--mostly in developing countries where sanitation is poor and people are often barefoot. After penetrating the skin, the hookworm--about 5 millimeters in length--travels from the bloodstream to the lung. Nair explained that the hookworm proceeds to damage the lung, the first organ it infects. When blood vessels break and hemorrhaging follows, the hookworm feeds on the blood (it cannot, however, survive in blood). When it is coughed up and swallowed, it then travels to the gut, the second organ it infects.

"The hookworm could not reach the gut if it didn't use the lung," Nair said. "In the gut, it releases thousands of eggs, which then go into the feces, completing the cycle. This is why infection is prevalent where lack of sanitation is also common, where, say, open defecation is practiced."

For their lab experiments, Nair's team used mice that were genetically deficient, meaning they lacked RELMalpha. The researchers then infected the mice with hookworms. The mice killed the worms but did not survive themselves, being unable to recover from the worm infection, which damaged their lungs.

When such genetically deficient mice were given a low dose of worms, the mice managed to kill the worms faster. But they incurred damage to their bodies. Were the mice to have RELMalpha, the researchers posit, their lung tissues would have been better protected.

Death versus worm burdens

"If you had a choice between having a parasite in your body or you dying from trying to kill it, you would choose to have the parasite live in your body," Nair explained. "Worm parasites are exceptionally good at that. They live with us for long periods without causing much damage. Essentially, a partnership is set up so that both the host and worm benefit. Worms, one of the most complex pathogens, have evolved to be the ideal parasite. They do not want you to die because that would mean they could not survive either. At doing this balancing act between inflammation and immunity, worms may be better than all other pathogens."

Nair noted that there are no vaccines available to fight worm infections. Unfortunately, distributing drugs for a disease that infects billions of people is costly and unfeasible, she said.

"RELMalpha appears to be the pivot on which the balance between inflammation and immunity is struck," she said. "This is likely true in humans as well, where resistin, the human equivalent of RELMalpha, is highly expressed in worm infections." The lab's next focus will be to investigate human resistin in this context.

Nair was joined in the research by Gang Chen (first author of the research paper), a principal scientist; Spencer H. Wang, a junior specialist at UCR; Jessica C. Jang, a UCR graduate student; and Justin I. Odegaard, a pathologist at UC San Francisco.

Nair was funded by a grant from the National Institutes of Health, specifically the National Institute of Allergy and Infectious Diseases. She has been invited to speak at the prestigious Gordon Research Conference on Tropical Infectious Diseases, which will be held next year in Galveston, Texas.

http://huff.to/1UsusAN

Dear Big Pharma: I Know I'm Going to Die. Please Stop Reminding Me

If you're not already a hypochondriac, Big Pharma will make you one.

John Blumenthal Former Playboy editor/Novelist/Screenwriter ('Blue Streak')

Back in the day, when you curled up on the couch to watch TV, it was generally a pleasurable, albeit mind-numbing experience, just as the networks intended it to be. Sure, commercials were annoying but they were about Maytag washing machines or dishwashing liquid or some other non-threatening product. You could eat a bowl of ice cream or some popcorn without suddenly being frightened out of your wits that you would get diabetes from the ice cream and high blood pressure from the salt on the popcorn. Or cancer. Or heart disease. Or uncontrollable bowel movements. Or, God help you, all three.

Curling up on the couch to watch TV used to be a way to achieve comfort; now it's a place where you curl up into a fetal position and achieve terror.

I'm sick and tired (no pun intended) of having to listen to some announcer with the hurried voice of a cattle auctioneer rushing through a list of thoroughly disgusting side effects. Here I am, happily watching a ball game or a sitcom and when the commercial break comes on I have to hear about how taking Zimethetonacxionzataphin (why do they always have a Z or an X in their names?) can cause diarrhea, unbearable headaches, projectile vomiting, anal bleeding, heart failure, total loss of muscle control, pus-filled growths, penile discharge, cancer of everything and a whole gruesome array of other revolting symptoms, all of which I am certain I will probably get because I'm a certified hypochondriac. Who needs it? Guys, I DO NOT want to have to listen to that shit, loose, watery or otherwise abnormal.

If you're not already a hypochondriac, Big Pharma will make you one. Maybe that's their goal. Stress them out enough with the commercials and hopefully they'll get sick.

If that's not bad enough, there's the lingerie-clad woman with the singsong English accent talking about erectile dysfunction which, via the power of suggestion, you will soon develop because the next time you have sex you will be reminded of the erectile dysfunction ad you just saw.

Following the Viagra commercial, a Cancer Centers of America ad pops on featuring bald people with twenty tubes up their noses. For some reason, they're all smiling as if to say, "Keep watching—-this will soon be you."

And what's with the two outdoor bathtubs? If you lug two three hundred pound bathtubs outdoors, you will definitely experience ED, not to mention permanent back problems, from which you will get temporary relief from the product in the next commercial, although you might also get lymphoma and die if you take it.

Do me a favor, Big Pharma: Enough with the pharmaceutical ads. I just want to sit back on my Barcalounger and watch actors lying on blood-soaked operating tables getting their small intestines pulled out on my favorite hospital show.

http://nyti.ms/1MN7VMw

Heroin Epidemic Is Yielding to a Deadlier Cousin: Fentanyl

When Eddie Frasca was shooting up heroin, he occasionally sought out its more potent, lethal cousin, fentanyl.

By KATHARINE Q. SEELYE MARCH 25, 2016

LAWRENCE, Mass. - "It was like playing Russian roulette, but I didn't care," said Mr. Frasca, 30, a carpenter and barber who said he had been clean for four months. When he heard that someone had overdosed or even died from fentanyl, he would hunt down that batch.

"I'd say to myself, 'I'm going to spend the least amount of money and get the best kind of high I can,' " he said.

Fentanyl, which looks like heroin, is a powerful synthetic painkiller that has been laced into heroin but is increasingly being sold by itself — often without the user's knowledge. It is up to 50 times more powerful than heroin and up to 100 times more potent than morphine. A tiny bit can be fatal.

In some areas in New England, fentanyl is now killing more people than heroin. In New Hampshire, fentanyl alone killed 158 people last year; heroin killed 32. (Fentanyl was a factor in an additional 120 deaths; heroin contributed to an additional 56.)

"It sort of snuck up on us," said Detective Capt. Robert P. Pistone of the Haverhill Police Department in Massachusetts.

He said that a jump in deaths in 2014 appeared to be caused by heroin, but that lab tests showed the culprit was fentanyl.

Fentanyl represents the latest wave of a rolling drug epidemic that has been fueled by prescription painkillers, as addicts continue to seek higher highs and cheaper fixes.

"It started out as an opioid epidemic, then heroin, but now it's a fentanyl epidemic," Maura Healey, the attorney general of Massachusetts, said in an interview.

Fentanyl has been used since the 1960s in medical settings to treat extreme pain, more recently as a patch or in a lozenge. In recent decades, illicit fentanyl has seeped into the United States from Mexico.

"For the cartels, it's their drug of choice," Ms. Healey said. "They have figured out a way to make fentanyl more cheaply and easily than heroin and are manufacturing it at a record pace."

Since New England noticed a drastic rise in drug overdose deaths in 2013, public health and law enforcement officials have begun to link more of the deaths to fentanyl.

"The severity of the situation did not become apparent until the public health community noticed the above-average number of overdoses," a report by the National Drug Intelligence Center at the Justice Department warned in 2006. Special toxicological testing is needed to detect fentanyl, but most coroners and state crime labs did not run those tests unless they had a specific reason.

The police are also finding more and more fentanyl in drug seizures, though it is not clear how much of this reflects a new invasion of the drug or just more testing and reporting.

Nationally, the total number of fentanyl drug seizures reported in 2014 by forensic laboratories jumped to 4,585, from 618 in 2012. More than 80 percent of the seizures in 2014 were concentrated in 10 states: Ohio, followed by Massachusetts, Pennsylvania, Maryland, New Jersey, Kentucky, Virginia, Florida, New Hampshire and Indiana.

Fentanyl Facts

Fentanyl is up to* 50 times *more potent than heroin and* 100 times *more potent than morphine. Because it is so strong and fast-acting, it can often lead to overdose and deaths.

Street names for fentanyl include* Apache, China girl, China white, dance fever, friend, goodfella, jackpot, murder 8, TNT, as well as Tango and Cash, *according to the National Institute on Drug Abuse.

Many state crime laboratories and coroner's offices do not track fentanyl-related deaths, so national statistics can be hard to come by.

Most of the recent fentanyl-related deaths have occurred in the Northeast, Mid-Atlantic and Appalachia, where it is sometimes mixed with another white powder, heroin. It is also starting to creep into the Midwest.

In 2015, doctors wrote 6.64 million legal fentanyl prescriptions in the U.S. Most deaths are from illegally manufactured fentanyl, but some result from diverting medical sources.

In Massachusetts in 2013, the state police crime lab found pure fentanyl, not mixed with other drugs, in just six cases; in 2015, the lab found it in 425 cases.

It was only last March that the Drug Enforcement Administration issued a nationwide alert about fentanyl, saying that overdoses were "occurring at an alarming rate throughout the United States and represent a significant threat to public health and safety."

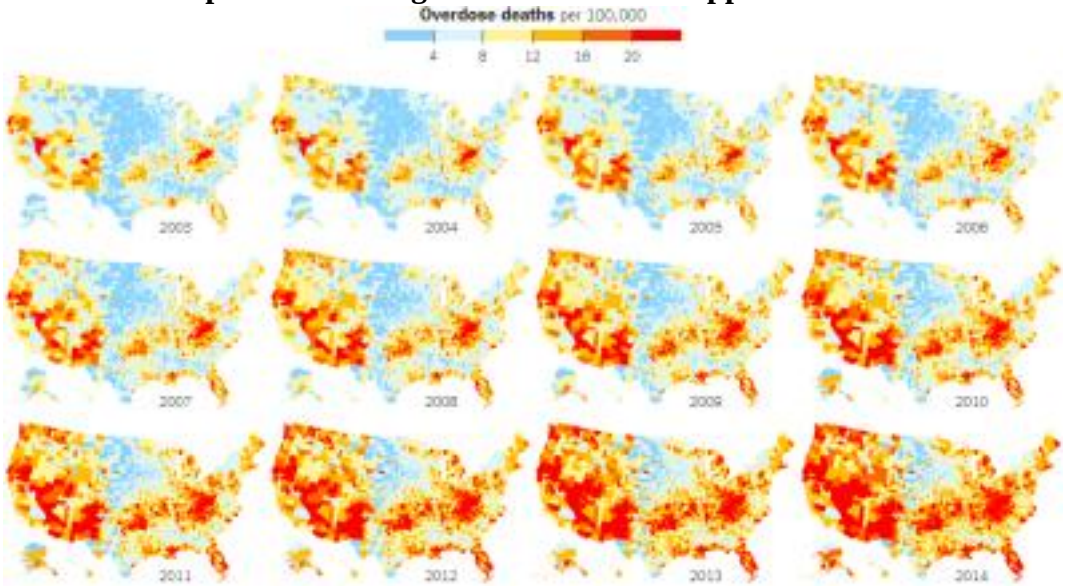
In Massachusetts, 336 people died from fentanyl-related overdoses from October 2014 to October 2015 — up from 219 deaths the previous year, an increase of 53 percent.

Vermont had 29 deaths from fentanyl in 2015, up from 18 in 2014 and 12 in 2013, a climb of 142 percent in two years.

In Maine, deaths attributed to fentanyl rose to 87 in 2015, up from 42 in 2014 and nine in 2013, an 867 percent increase in two years.

Some of the biggest fentanyl busts have occurred in and around Lawrence, an old mill town 30 miles north of Boston, near New Hampshire; it has long served as a major drug hub.

How the Epidemic of Drug Overdose Deaths Ripples Across America



Drug deaths have surged in nearly every U.S. county, reaching a new peak in 2014.

"Massachusetts is the epicenter for the heroin/fentanyl trade," Ms. Healey said. "From Lawrence, it's being trafficked and sold all over the New England states."

In one seizure last year, law enforcement officers from Massachusetts and New Hampshire confiscated 33 pounds of fentanyl and heroin with a street value of

$2.2 million, most from a house in Lawrence. In January, the police seized 66 pounds of fentanyl-laced heroin, worth millions, in nearby Tewksbury.

Two Lawrence men were indicted in June in connection with an extensive fentanyl and heroin distribution operation involving more than $1 million in drugs. Lawrence sits at the nexus of major highways, and the police say many drug deals occur at fast-food restaurants off the exits for nearby towns. And those deals are highly lucrative.

One middleman would meet his dealer from Lawrence weekly off an exit in Haverhill, and would buy 100 “fingers” (10 grams each) of fentanyl for $400 apiece, Captain Pistone said. He would sell each finger for $750 in New Hampshire and Maine, making $35,000 a week.

“It’s just everywhere,” Heather Sartori, 38, a former nurse who is on methadone after years of shooting up heroin, said as she sat at a busy McDonald’s here. “It would be really hard to navigate through this city without being touched by it.”

She said she had lost several friends to fentanyl and called Lawrence’s drug-infested landscape “the treacherous terrain where the ghosts of the fallen linger.”

“It’s cheaper, and the high is better, so more addicts will go to a dealer to get that quality and grade,” she said, even if it means they could die.

“That is the phenomenon of the addicted mind,” she said. “It’s beyond the scope of a rational thinker to understand.”

Fentanyl is abundant, too, in the tent cities of homeless people here under the bridges over the Merrimack River.

“It’s all there is out there right now,” said a 24-year-old who lives under one of the bridges and goes by G. “I couldn’t find real heroin if I tried.”

Its chief characteristic is that it is fast acting.

“You can’t move,” said a 46-year-old woman, who kept nodding off during an interview at the Haverhill police station. She agreed to talk about fentanyl on the condition that she not be identified.

“When you inject it, it hits before you’re even done giving the shot,” she said. “That’s why so many people get caught with the needle still hanging out of their arm. It’s bam! To your brain.”

Joanne Peterson, executive director of Learn to Cope, a statewide support network for families involved with addiction, said fentanyl works so quickly that there is often little time to administer naloxone, which reverses the effects of an overdose.

“At least with heroin, there is a chance that if someone relapses, they can get back into recovery,” she said.

But with fentanyl, she said, it is only a matter of moments before an addict can be dead.

http://www.eurekalert.org/pub_releases/2016-03/uot-tss032816.php

Tsukuba scientists solved the Spallanzani's dilemma

Newts are the masters of regeneration.

Imagine losing an eye, an arm or even your spinal cord. When we are wounded, our bodies, and those of other mammals, generally respond by sealing the wound with scar tissue. The newt, however, has evolved unique strategies that allow it to repeatedly regenerate lost tissues, even as an adult.

Newts are the masters of regeneration. No other animal can match their regenerative abilities in body parts including the limbs, the tail and spinal cord, parts of the eye (such as the retina and the lens), the brain, the heart and the jaws. What happens when a newt loses, for example, a leg? A mass of cells, called a blastema, is generated at the stump, from which a new, fully functional leg is eventually regenerated.

The newt is unique in having this ability even as an adult. Other amphibians with regenerative potential, such as axolotls, lose this ability once they metamorphose from a larva to a juvenile. Research led by Chikafumi Chiba at the University of Tsukuba, Japan and Panagiotis Tsonis at the University of Dayton, Ohio, and published in the current volume of the prestigious journal Nature Communications, has shed some light on the newt's exceptional regenerative ability and may provide further insight into regeneration in other species, including mammals.

The researchers made the exciting discovery that the mechanism for regeneration in the larval newt is different to the one used after metamorphosis. This discovery was made using transgenic newts, the use of which has only recently been made possible. One of the researchers on the team, Martin Casco-Robles, from the Faculty of Life and Environmental Sciences, University of Tsukuba, is a pioneer in developing techniques for the creation of transgenic newts.

Using transgenic Japanese fire bellied newts, the team were able to track different types of muscle cells during limb regeneration in both larval and metamorphosed animals. It had been suggested previously that either skeletal muscle fiber cells (SMFCs) or muscle stem/progenitor cells (MPCs) contribute to new muscle in regenerated limbs of newts. SMFCs make up skeletal muscles, which are one of the three major types of muscles. MPCs are the dormant predecessors of muscle fiber cells and are located within muscle fibers. They can be triggered to proliferate for both self-renewal and specialization into muscle fiber cells.

The researchers inserted a gene known to be active in SMFCs into single-celled newt embryos. The transgenic newt embryos were then reared until the swimming larval stage, at 3 months of age, or the metamorphosed juvenile stage, at 16 months. The gene was linked to a red fluorescent protein which could be switched on and off at precise times with the addition of a particular chemical to the rearing

solution.Selected transgenic newts had a limb removed under anesthesia. The fluorescence of the tissues in the living newts was monitored under a microscope during development and limb regeneration. In addition, tissue samples were collected for further MPC cell-specific staining. Lead author, Hibiki Tanaka, of the Graduate School of Life and Environmental Sciences, University of Tsukuba, explains that "we found that larval newts did not require muscle fiber cells to regenerate their amputated limbs."

These experiments showed that the new muscle in larval newt regeneration tissue is primarily derived from muscle stem/progenitor cells, not skeletal muscle fiber cells. In contrast, after metamorphosis, the team found that the skeletal muscle fiber cells in the stump temporarily regress to a more primitive state, that is, they become dedifferentiated. The cells then re-enter the cell cycle and proliferate to produce more muscle cells. Hibiki Tanaka says "larval newts use stem/progenitor cells for new muscle in a regenerated limb while metamorphosed newts recruit muscle fiber cells in the stump for the same purpose."

Next the researchers looked at whether or not the tissues in the limb strictly regenerated the same tissue types using reporter-gene expressing tissue transplantation experiments. The principal tissues of the adult limb, skin, bone, muscle and nerve tissues, were obtained from transgenic newts and grafted onto or into the corresponding regions of normal newts. These newts were then used in regeneration experiments. The team discovered that skin, bone, muscle and nerve tissues faithfully regenerated themselves.

Chikafumi Chiba explains these remarkable discoveries, saying "the newt switches the cellular mechanism for limb regeneration from a stem/progenitor-based mechanism (larval mode) to a dedifferentiation-based one (adult mode) as it transits beyond metamorphosis". He says "delineating the mechanisms of these strategies will undoubtedly provide clues for regeneration in other species including mammals".

Thus, while we may never have the incredible regenerative powers of the newt, it is likely that this little amphibian will continue to provide us with insights into mammalian tissue regeneration, wound healing and repair.

http://www.eurekalert.org/pub_releases/2016-03/ru-hal033016.php

Heart and liver disease linked to shutdown of body's antioxidant

Rutgers scientists identify a protein causing damage and serious illness

A protein that should help fight infection and keep us healthy may be targeted for treating devastating illnesses like heart and liver disease, according to a new Rutgers study.

In research published in Molecular Cell, Rutgers scientists discovered that a protein (p62), which is supposed to act as an antioxidant to prevent cell damage, was not working efficiently in laboratory mice with liver and heart disease that mimicked these conditions in humans.

This caused oxidative stress - too much oxygen that damages healthy cells - and allowed the release of harmful molecules, called free radicals, which resulted in serious illness. One of the body's first lines of defense, the cells antioxidant response system is supposed to prevent these harmful invaders from causing a domino effect and damaging other cells.

Wei-Xing-Zong, a professor in the Department of Chemical Biology in the Ernest Mario School of Pharmacy and leader of the study, said the damage occurred because another protein, (TRIM21) - which should activate the body's response system to fight off bacteria and virus - did the opposite in these seriously ill mice and shut the antioxidant protein down, preventing it from doing its job.

"The (TRIM21) protein exists naturally in our body; without it, we could easily succumb to other manageable infections," said Zong. "But this study has shown us that when we run into severe pathological conditions like heart and liver disease it would be more beneficial to inhibit the TRIM21 protein because it is preventing the cell from protecting itself against damage."

In the Rutgers study, Zong and lead author Ji-An Pan, a scientist in his laboratory, looked at liver and heart damage in laboratory mice and found that the mice in which the TRIM21 gene was inactivated suffered little heart or liver damage when put through the same laboratory procedures used to produce tissue damage in mice with the gene.

"The hearts and livers of the mice without the TRIM21 gene seemed to be well protected which was opposite of the mice with the gene," said Zong. "We believe this evidence is a truly important step to determining how to effectively treat these conditions in humans."

Heart disease is the leading cause of death in the United States while one in 10 Americans has some form of liver disease. Rutgers scientists said this study indicates how critical it is to carefully control oxidative stress - which can also lead to neurodegenerative diseases like Parkinson's and Alzheimer's, chronic fatigue syndrome, cancers and gene mutations as well as liver and heart disease - so that cell or tissue damage doesn't occur.

They believe that drugs could be developed that would reduce or stop the activity of the protein that is causing damage and preventing the antioxidant response from occurring.

"These exciting new results suggest that drugs that reduce the activity of TRIM21 could be highly effective new tools for the treatment of conditions that are driven by high oxidative stress, including liver and heart disease," Zong said.

http://www.eurekalert.org/pub_releases/2016-03/uoc--sdr032416.php

Successful dying: Researchers define the elements of a 'good death'

For most people, the culmination of a good life is a "good death," though what that means exactly is a matter of considerable consternation.

Researchers at the University of California, San Diego School of Medicine surveyed published, English-language, peer-reviewed reports of qualitative and quantitative studies defining a "good death," ultimately identifying 11 core themes associated with dying well. The findings are published in the April 2016 issue of the American Journal of Geriatric Psychiatry.

The research team, headed by senior author Dilip Jeste, MD, Distinguished Professor of Psychiatry and Neurosciences and director of the Sam and Rose Stein Institute for Research on Aging at UC San Diego School of Medicine, focused on three groups of stakeholders: patients, family members (before or during bereavement) and health care providers.

"This is the first time that data from all of the involved parties have been put together," said Jeste, who is also associate dean for healthy aging and senior care at UC San Diego School of Medicine. "Death is obviously a controversial topic. People don't like to talk about it in detail, but we should. It's important to speak honestly and transparently about what kind of death each of us would prefer."

The literature search culled through 32 qualifying studies. It identified 11 core themes of good death: preferences for a specific dying process, pain-free status, religiosity/spirituality, emotional well-being, life completion, treatment preferences, dignity, family, quality of life, relationship with the health care provider and "other."

The top three themes across all stakeholder groups were preferences for specific dying process, pain-free status and emotional well-being. For other themes, however, different stakeholders put somewhat different levels of emphasis. For example, patients more often cited religiosity/spirituality as important than did family members, who believed dignity and life completion were more critical to a good death. Health care providers tended to represent a middle ground between patients and family members.

"Clinically, we often see a difference between what patients, family members and health care providers value as most important near the end of life", said first author Emily Meier, PhD, a psychologist at Moores Cancer Center at UC San Diego Health. "Ultimately, existential and other psychosocial concerns may be prevalent among patients, and this serves as a reminder that we must ask about all facets of care that are essential at the end of life."

The bottom line, said Jeste, is "ask the patient."

"Usually, patients know what they want or need and there is relief in talking about it. It gives them a sense of control. I hope these findings spur greater conversation across the spectrum. It may be possible to develop formal rating scales and protocols that will prompt greater discussion and better outcomes. You can make it possible to have a good death by talking about it sometime before."

Co-authors include Jarred V. Gallegos, Lori P. Montross Thomas, Colin A. Depp and Scott A. Irwin, all at UC San Diego.

Funding for this research came, in part, from the Sam and Rose Stein Institute for Research on Aging and the Moores Cancer Center at UC San Diego, and the American Cancer Society (grant MRSG-13-233-01 PCSM).

http://www.eurekalert.org/pub_releases/2016-03/uoc-mor033016.php

Map of rocky exoplanet reveals a lava world

Most detailed 'fingerprint' of a rocky planet outside our solar system to date

An international team of astronomers, led by the University of Cambridge, has obtained the most detailed 'fingerprint' of a rocky planet outside our solar system to date, and found a planet of two halves: one that is almost completely molten, and the other which is almost completely solid.

VIDEO: *This is an illustration of 55 Cancri e* **NASA/JPL-Caltech**

According to the researchers, conditions on the hot side of the planet are so extreme that it may have caused the atmosphere to evaporate, with the result that conditions on the two sides of the planet vary widely: temperatures on the hot side can reach 2500 degrees Celsius, while temperatures on the cool side are around 1100 degrees. The results are reported in the journal Nature.

Using data from NASA's Spitzer Space Telescope, the researchers examined a planet known as 55 Cancri e, which orbits a sun-like star located 40 light years away in the Cancer constellation, and have mapped how conditions on the planet change throughout a complete orbit, the first time this has been accomplished for such a small planet.

55 Cancri e is a 'super Earth': a rocky exoplanet about twice the size and eight times the mass of Earth, and orbits its parent star so closely that a year lasts just 18 hours. The planet is also tidally locked, meaning that it always shows the same face to its parent star, similar to the Moon, so there is a permanent 'day' side and a 'night' side. Since it is among the nearest super Earths whose composition can be

studied, 55 Cancri e is among the best candidates for detailed observations of surface and atmospheric conditions on rocky exoplanets.

Uncovering the characteristics of super Earths is difficult, since they are so small compared to the parent star and their contrast relative to the star is extremely small compared to larger, hotter gas giant planets, the so-called 'hot Jupiters'.

"We haven't yet found any other planet that is this small and orbits so close to its parent star, and is relatively close to us, so 55 Cancri e offers lots of possibilities," said Dr Brice-Olivier Demory of the University's Cavendish Laboratory, the paper's lead author. "We still don't know exactly what this planet is made of - it's still a riddle. These results are like adding another brick to the wall, but the exact nature of this planet is still not completely understood."

55 Cancri e has been extensively studied since it was discovered in 2011. Based on readings taken at different points in time, it was thought to be a water world, or even made of diamond, but researchers now believe that it is almost completely covered by lava.

"We have entered a new era of atmospheric remote sensing of rocky exoplanets," said study co-author Dr Nikku Madhusudhan, from the Institute of Astronomy at Cambridge. "It is incredible that we are now able to measure the large scale temperature distribution on the surface of a rocky exoplanet."

Based on these new infrared measurements, the 'day' side of the planet appears to be almost completely molten, while the 'night' side is almost completely solid. The heat from the day side is not efficiently circulated to the night side, however. On Earth, the atmosphere aids in the recirculation of heat, keeping the temperature across the whole planet within a relatively narrow range. But on 55 Cancri e, the hot side stays hot, and the cold side stays cold.

According to Demory, one possibility for this variation could be either a complete lack of atmosphere, or one which has been partially destroyed due to the strong irradiation from the nearby host star. "On the day side, the temperature is around 2500 degrees Celsius, while on the night side it's about 1100 degrees - that's a huge difference," he said. "We think that there could still be an atmosphere on the night side, but temperatures on the day side are so extreme that the atmosphere may have evaporated completely, meaning that heat is not being efficiently transferred, or transferred at all from the day side to the night side."

Another possibility for the huge discrepancy between the day side and the night side may be that the molten lava on the day side moves heat along the surface, but since lava is mostly solid on the night side, heat is not moved around as efficiently.

What is unclear however, is where exactly the 'extra' heat on 55 Cancri e comes from in the first place, since the observations reveal an unknown source of heat that makes the planet hotter than expected solely from the irradiation from the star - but the researchers may have to wait until the next generation of space telescopes are launched to find out.

For Demory, these new readings also show just how difficult it will be to detect a planet that is similar to Earth. The smaller a planet is, the more difficult it is to detect. And once a rocky planet has been found, there is the question of whether it lies in the so-called habitable zone, where life can be supported. "The problem is, people don't agree on what the habitable zone is," said Demory. "For example, some studies consider Mars and Venus to be in the habitable zone, but life as we know it is not possible on either of those planets. Understanding the surface and climate properties of these other worlds will eventually allow us to put the Earth's climate and habitability into context."

One possibility might be to look at stars which are much cooler and smaller than our sun, such as the M-dwarfs, which would mean that planets could be much closer to their star and still be in the habitable zone. The sizes of such planets relative to their star would be larger, which make them more detectable from Earth.

But for the time being, Demory and his colleagues plan to keep studying 55 Cancri e, in order to see what other secrets it might hold, including the possibility that it might be surrounded by a torus of gas and dust, which could account for some of the variations in the data. And in 2018, the successor to Hubble and Spitzer, the James Webb Space Telescope, will launch, allowing astronomers to look at planets outside our solar system with entirely new levels of precision.

http://www.eurekalert.org/pub_releases/2016-03/gu-im032916.php

Indonesian 'Hobbits' may have died out sooner than thought

An ancient species of pint-sized humans discovered in the tropics of Indonesia may have met their demise earlier than once believed, according to an international team of scientists who reinvestigated the original finding.

Published in the journal Nature this week, the group challenges reports that these inhabitants of remote Flores island co-existed with modern humans for tens of thousands of years.

They found that the youngest age for Homo floresiensis, dubbed the 'Hobbit', is around 50,000 years ago not between 13,000 and 11,000 years as initially claimed.

Led by Indonesian scientists and involving researchers from Griffith University's Research Centre of Human Evolution (RCHE) the team found problems with prior dating efforts at the cave site, Liang Bua.

"In fact, Homo floresiensis seems to have disappeared soon after our species reached Flores, suggesting it was us who drove them to extinction," says Associate Professor Maxime Aubert, a geochronologist and archaeologist at

RCHE, who with RCHE's Director Professor Rainer measured the amount of uranium and thorium inside Homo floresiensis fossils to test their age.

"The science is unequivocal," Aubert said.

youngest Hobbit skeletal remains occur at 60,000 years ago but evidence for their simple stone tools continues until 50,000 years ago. After this there are no more traces of these humans."

While excavating at the limestone cave of Liang Bua in 2003, archaeologists found bones from diminutive humans unlike any people alive today. The researchers concluded the tiny cave dwellers evolved from an older branch of the human family that had been marooned on Flores for at least a million years. It was thought that this previously unknown population lived on Flores until about 12,000 years ago.

Liang Bua, a limestone cave on the Indonesian island of Flores. **Liang Bua Team**

"The But the site is large and complex and the original excavators dug only a tiny portion of it. Years of further excavation has led to a much clearer understanding of the order of archaeological layers. It is now evident that when the original team collected samples for dating the main layer containing Hobbit bones they mistakenly took them from an overlying layer that is similar in composition, but far younger.

"This problem has now been resolved and the newly published dates provide a more reliable estimate of the antiquity of this species," Aubert said.

But the mystery of what happened to these creatures remains.

RCHE archaeologist Dr Adam Brumm, who also participated in the study, said Hobbits are likely to have inhabited other Flores caves which may yield more recent signs of their existence.

He believes Homo floresiensis probably suffered the same fate that befell Europe's Neanderthals - our species simply out-competed and replaced them within a few thousand years.

"They might have retreated to more remote parts of Flores, but it's a small place and they couldn't have avoided our species for long. I think their days were numbered the moment we set foot on the island."

http://www.eurekalert.org/pub_releases/2016-03/uok-amm033016.php

Asthma-free? Maybe Mom experienced a sunny second trimester

Health economists tested hypothesized link between vitamin D and asthma

LAWRENCE -- The best way to reduce a child's chances of developing asthma might be making sure Mom had enough vitamin D during the second trimester, a new study from the University of Kansas shows.

The most cost-effective way to get Mom more vitamin D could be as simple as health recommendations that consider the benefits of soaking up a little more sun, a practical and cost-effective way to get a dose of D.

According to the Centers for Disease Control and Prevention, 1 in 12 of us in the U.S. suffers from asthma.

"Our health system spends billions and billions treating asthma, and there's lots and lots of opportunity costs," said David Slusky, assistant professor of economics. "Pain and suffering, loss of productivity and premature death -- asthma has all of those."

When resources are being used inefficiently, that's when Slusky and his fellow economists like to step in.

They knew about a recent medical hypothesis by Scott Weiss and Augusto Litonjua, both of whom are physicians with Brigham and Women's Hospital in Boston and professors at Harvard Medical School. Weiss and Litonjua hypothesize that vitamin D levels in the second trimester of pregnancy influence the probability that a fetus will develop asthma later in life.

Slusky and colleagues Nils Wernerfelt of the Massachusetts Institute of Technology and Richard Zeckhauser of Harvard's Kennedy School put the medical hypothesis to the test using an economist's tools, such as survey and health data.

"This is the golden age in the way that data about hospital discharges, insurance claims, birth certificates and death certificates are more and more available and more and more set up for researchers," Slusky said. "And that allows economists to get really large sample sizes with not a lot of cost."

Using data from hospital discharges in two states and from a national survey, Slusky and his colleagues looked at where and when asthmatics were born.

Then the economists looked at the measurements of sunlight in the birth locations when the asthmatics' mothers would have been in their second trimesters. Sunlight is where Americans get more than 90 percent of our vitamin D.

What the economists found was that a mother's increased sunlight exposure -- and therefore, vitamin D -- during this period lowers her child's chance of developing asthma. Because of concerns about individuals in different parts of the country

being systematically different, Slusky and his co-authors looked at relative differences.

"We're not looking at sunny places versus non-sunny places," Slusky said "We looked at the relative differences of the level of sunlight at a particular place at a particular time of year."

In other words, people born in Georgia in July of 1978 received a different exposure to sunlight in utero than did their fellow Georgians born a year later.

"If that place is relatively more sunny during the second trimester, we found relatively lower rates of asthma," Slusky said.

The findings indicate that the way pregnant women can get more vitamin D -- and lessen the likelihood of asthma in their children -- may be as simple as 10 minutes in the sun, which medical literature indicates is all most of us need for a daily dose of the "sunshine vitamin."

"Skin cancer is a very serious disease, and I don't want to minimize it, but at some point that extra minute you spend inside is costing you more vitamin D than it's helping you not get skin cancer," Slusky said.

Vitamin D can be acquired from dietary supplements, too, but Slusky and his colleagues point out that the prenatal vitamins many pregnant women take already include vitamin D and that they may not be getting the full benefit from them.

Moreover, sunshine is free.

"Calibrating this into the proper policy recommendation is something I'll leave to others, but I think that's where this research is going," Slusky said.

Case in point, health officials in Australia are becoming more aware of vitamin D deficiencies. They have begun urging schools to relax requirements that students wear hats while outside during that continent's winter months of June and July.

"Clearly if I'm going to the beach or going to spend all day outside, I need to put on sunscreen," Slusky said. "But spending 10 minutes outside without it may not be such a bad idea."

The research will appear in a coming issue of the American Journal of Health Economics.

http://www.eurekalert.org/pub_releases/2016-03/idso-siv032916.php

Seasonal influenza vaccination during pregnancy may reduce risk of stillbirth

Seasonal influenza vaccination may guard against stillbirth, a new study published in Clinical Infectious Diseases and available online suggests.

Researchers in Western Australia analyzed data from nearly 60,000 births that occurred during the southern hemisphere's 2012 and 2013 seasonal influenza epidemics, and found that women who received the trivalent influenza vaccine during pregnancy were 51 percent less likely to experience a stillbirth than unvaccinated mothers.

The retrospective study used midwives' records to examine a cohort of 58,008 births: 52,932 to mothers who had not received the vaccine and 5,076 to mothers who had been vaccinated during pregnancy. All births took place in Western Australia between April of 2012 and December of 2013. The adjusted risk of stillbirth among vaccinated mothers was 51 percent lower than the risk among women who had not been vaccinated.

Researchers also observed that stillbirth rates increased after periods of influenza virus circulation and decreased during the months prior to the influenza season, although the seasonal differences were not statistically significant. The study's results are consistent with those of a 2000 study in Switzerland that recorded increased incidence of stillbirth in relation to the northern hemisphere's influenza season, as well as with similar research conducted during the influenza A/H1N1 pandemic.

"During the 2009 H1N1 pandemic, we saw a similar reduction in stillbirths following vaccination," said study author Annette Regan, MPH, of the Western Australia Department of Health. "Our results are particularly exciting since they show we can get the same protection during seasonal epidemics, which occur every winter. Unfortunately, we know that about 40 percent of pregnant women go unvaccinated, missing out on these benefits."

The U.S. Centers for Disease Control and Prevention recommends annual flu vaccination for everyone 6 months of age and older, including pregnant women during any trimester of their pregnancy. Pregnancy puts women at an increased risk of developing serious complications related to influenza, including acute respiratory distress syndrome and pneumonia. Infection during pregnancy has also been linked to fetal mortality and premature births. But concern for the safety of the fetus dissuades many expectant mothers from vaccination.

The new study's findings not only support the safety of influenza vaccination during pregnancy, but also suggest that vaccination protects against stillbirth. The authors noted that the protective benefits they observed "may be an underestimate of the true effect measure" due to the methods of data analysis employed in their study.

Over 3 million stillbirths occur worldwide each year, and in developed countries, stillbirth accounts for 70 percent of infant deaths around the time of birth. Establishing a connection between influenza season and stillbirth could have global implications for infant mortality.

Further research is needed to confirm the possible links between stillbirth, influenza season, and vaccination, the study's findings indicate. But the researchers are hopeful that their data will be useful for communicating vaccination's potential health benefits to expectant mothers and health care

providers. "I'm hoping results like these can convince more pregnant women to get vaccinated each year," Regan said.

Fast Facts

In this retrospective cohort study, women in Western Australia who received the seasonal trivalent influenza vaccine during pregnancy showed a 51 percent lower risk of experiencing a stillbirth than unvaccinated expectant mothers.

Observed rates of stillbirth increased just after periods of influenza virus circulation, suggesting a link between incidence of stillbirth and the influenza season.

Over 3 million stillbirths occur worldwide each year, and in developed countries, stillbirth accounts for 70 percent of infant deaths around the time of birth.

Editor's note: The study was funded by the Western Australia Department of Health. The study authors' affiliations, acknowledgments, and disclosures of financial support and potential conflicts of interests, if any, are available in the article. For an embargoed copy of the study, please contact Emily Zaideman (312-558-1770, ezaideman@pcipr.com).

http://bit.ly/1RHZ63A

Stop Making Fun of Tyrannosaurs' Tiny Arms

The stubby limbs may seem out of place, but they may have been key to the T. rex's terrifying bite

By Brian Switek smithsonian.com

We often ridicule what we love, and, in the realm of dinosaurs, that may explain our complicated relationship with the late, great *Tyrannosaurus rex*. The gigantic carnivore is the A-list celebrity of the Mesozoic, making repeated appearances on the silver screen as well as holding an obligatory presence in most museum exhibits. Yet, we just can't stop ourselves from poking fun at the tyrant's dinky arms. Maybe, though, it's time we stifle our laughter.

T. rex *had tiny arms. But that's no reason to mock the dinosaur.* (Momatiuk - Eastcott/Corbis)

You'd expect that any saurian that lived up to the title of apex predator would have had burly arms tipped in wicked, curved claws. But instead, the king of the lizards bears nothing more than a pair of two fingered stubs. The ferocity of the dinosaur is always undercut by the silliness of its twiddly little forelimbs.

T. rex isn't even the most extreme of the stubby-armed carnivorous dinosaurs. The Jurassic *Ceratosaurus* also had comparatively tiny arms with little, stubby-clawed fingers that would have been little help at all in catching or killing anything, as paleontologists Matthew Carrano of the Smithsonian National Museum of Natural History and Jonah Choiniere of the University of Witwatersrand pointed out in a recent paper in the *Journal of Vertebrate Paleontology*. This sharp-toothed dinosaur must have been all mouth when hunting.

Its later relative *Carnotaurus* took the trend even further. While the entire dinosaur measured about 30 feet long, its arms were no longer then yours, the fingers and bones of the lower arm mashed together into a useless mitt that confirm *Carnotaurus* was not much for upper-body workouts.

But we may have been looking at these dinosaurs all wrong.

To the eyes of University of Southern California paleontologist Michael Habib, it's the predatory dinosaurs with longer arms and giant claws, such as the Jurassic-era *Allosaurus*, that don't make sense.

Everyone jabs at *T. rex*, but "*Allosaurus* arms were awfully out of the way, too," Habib says. The Jurassic carnivore's relatively longer arms and larger claws look more impressive, yet their superiority has always been assumed rather than demonstrated. In Habib's view, this has given us a skewed view of how these dinosaurs hunted.

"There is actually no way to get the hands of *Allosaurus* anywhere near its mouth," Habib says, meaning that these dinosaurs would have to attack impossibly large prey in order to use both teeth and claws in tandem. More than that, *Allosaurus* and similarly equipped dinosaurs probably couldn't even see their arms while on the hunt. For these carnivores to use their arms at all, Habib says, they "would have to miss with the mouth, keep charging forward, hit the prey animal hard with its chest and then try to grab it blindly" with arms that were not especially flexible or dexterous. Bigger might not be better after all.

While the smaller arms of dinosaurs like *Tyrannosaurus* and *Ceratosaurus* might be good for a laugh, Habib notes that there are biomechanical reasons why smaller limbs may have the advantage. "The bones of the chest and shoulder, such as the coracoids and scapula, are anchor points for muscles going into the arm," Habib says, "but they are also anchor points for neck muscles." Only so much muscle can attach to any given bone. But by reducing the size of the arms and the muscles needed to move them, evolution may have allowed dinosaurs like *Tyrannosaurus* to allot more space to the neck muscles that gave them devastating bites.

"Keeping the bones around the chest and shoulder large, while reducing the forelimbs, provided more room for big neck muscles, which actually makes a lot of sense for predators that relied on large heads as their primary weapons," Habib says. Think less lion, and more hyena or wild dog.

If shorter arms were better for big, knife-toothed dinosaurs, though, this raises the question of why *Allosaurus* and similar dinosaurs weren't shaped

like *Tyrannosaurus*. One possibility, Habib says, is that dinosaurs like *Allosaurus* hunted and fed in such a way that they did not require super-powerful bites. "They could have been jaw slashers or grabbers that focused on small to medium prey," Habib says, and so there just wasn't pressure to evolve more powerful neck muscles. It's also possible that dinosaurs with longer torsos could use their arms for a bit of a push while getting up from a nap, but there's no definitive answer just yet.

Much remains unknown about the way our favorite snaggletoothed dinosaurs went about hunting and killing prey. The discrepancy Habib sees is a brain-teaser that awaits detailed study, even as comparative anatomy hints that carnivorous dinosaurs behaved differently than we immediately expect. That's the difficulty of being over 66 million years too late to watch them in action.

But for now, Habib says, we should give *Tyrannosaurus* a break. "The key bit isn't that it had small arms, but that it had an enormous head! …That giant set of bone-crushing, muscle-rending jaws was made possible, in part, by having small arms." And this, Habib says, "made *T. rex* a tougher animal, not a weaker one."

http://bit.ly/1M9kQZm

The Lazarus Phenomenon, Explained: Why Sometimes, the Deceased Are Not Dead, Yet

What does CPR have to do with the curious case of clinically dead patients coming "back to life"?

By Adam Hoffman smithsonian.com March 31, 2016

By 1:56 p.m., the intensive care unit had tried everything: aggressive CPR, four shocks to the chest, seven doses of adrenaline and two bags of fluids. But the 11-month-old girl lay still, her body in cardiac arrest. At 1:58 p.m., after two minutes flatlining without a pulse, she was pronounced dead.

"The family wanted a little time to just be with the patient," says Louis Daugherty, an associate professor of pediatrics at the University of Rochester Medical Center and a member of the team handling the case. After about 15 minutes, the mother asked for the breathing tube to be removed so that she could hold her daughter. And then, the team witnessed the unimaginable.

"Soon after the breathing tube was removed, she started to have spontaneous breathing. Her heart rate came back, her color improved and she had a gag reflex," says Daugherty. "I had never seen anything like this." Although the young girl's condition stabilized, she succumbed to progressive heart failure in a chronic care facility four months later.

The girl had experienced a rare resurrection called the "Lazarus Phenomenon," in which patients who appear to be clinically dead sometimes spontaneously return to life. While the majority of these patients eventually succumb to death's grip, as many as a third make a full recovery. But according to several surveys, this marvel may be more common than most people suspect due to under-reporting tied to legal concerns.

For centuries, people have had anxieties about incorrect death pronouncement and premature burials. In the 1800s, the fear of being buried alive, known as taphophobia, was so widespread that many people included provisions in their wills calling for tests to confirm death, such as pouring hot liquids on their skin or making surgical incisions. Others were buried with crowbars and shovels. This paranoia eventually led to a new class of "safety coffins" with breathing tubes and a variety of flags, bells or pyrotechnics that would allow anyone buried prematurely to signal passersby.

Auto-resuscitation in hospitals wasn't reported in medical literature until 1982. Anesthesiologist Jack Bray, Jr. gave the phenomenon its moniker in 1993, based on the Biblical story of Lazarus of Bethany, who died and was resurrected by Jesus Christ four days later. Since then, though, the phenomenon has remained scarce in the scientific literature.

Vedamurthy Adhiyaman, a consultant geriatrician at Glan Clwyd Hospital in North Wales, became interested in the Lazarus Phenomenon after encountering it firsthand in the early 2000s. His team had conducted CPR on an elderly man in is his late 70s for about 15 minutes with no response.

"There isn't any definite time frame for how long you should attempt CPR before you stop," says Adhiyaman. "It really varies on a case by case basis." Although Adhiyaman did not officially declare death immediately after stopping CPR, a member from his team told the family that the man had died. As it turns out, the situation was not that straightforward.

"After about 15 to 20 minutes, he started breathing," recalls Adhiyaman. "But he remained unconscious in a coma for the next two days until he died on day three." The family believed that the CPR should not have been stopped and that the team had provided substandard care, so they took Adhiyaman to court. "It was around that time that I began researching this phenomenon, because I had to show evidence that these things do happen," he says.

After scouring the medical literature, Adhiyaman unearthed 38 cases of Lazarus Phenomenon, which proved sufficient to demonstrate its legitimacy and exonerate him of negligence. In his 2007 review of the subject, published in the *Journal of the Royal Society of Medicine*, Adhiyaman found that on average, these patients returned from death's door seven minutes after stopping CPR, though close monitoring in many cases was inconsistent. Three patients were left unattended for several minutes, with one making it all the way to the hospital mortuary before being discovered alive.

While the vast majority of patients died soon after auto-resuscitation, 35 percent of them were eventually sent home with no significant neurological consequences. Adhiyaman's analysis also showed that these positive outcomes were not really affected by the duration of CPR or the amount of time it took for patients to auto-resuscitate.

Coming back from the brink this way is undoubtedly rare. In 2010, a team at McGill University conducted an extensive review of medical literature and found just 32 cases of the Lazarus Phenomenon since 1982. That same year, a German team was able to round up 45 articles on the subject. Many of the same cases appear in both reports.

A spattering of new cases has emerged since then. In 2012, a 65-year-old patient in Malaysia was found with a pulse 40 minutes after he was pronounced dead. In 2013, an 89-year-old woman in New Haven regained a pulse five minutes after resuscitation efforts were abandoned. And in 2015, two cases popped up—one in a 67-year-old man in Denmark and another in the 11-month-old girl in Rochester.

In addition, recent investigations suggest that the phenomenon may be underreported. A 2013 study indicated that nearly half of all French emergency room physicians claim to have seen a case of auto-resuscitation during their career, while according to a 2012 survey, more than one-third of Canadian critical care doctors reported encountering at least one case.

It may be that doctors are not reporting it officially due to the embarrassing professional and legal consequences associated with a premature declaration of death. Adhiyaman also believes that many cases go unreported due to privacy laws.

"In order to publish a case report in the scientific literature, you need the consent of the family. And it's going to be really hard to get them to agree when all trust between the medical profession and the family has been broken," he says.

This all makes auto-resuscitation extremely difficult to study, and the exact mechanisms that produce the phenomenon remain speculative. Notably, though, all official reports of auto-resuscitation have one thing in common—the use of CPR.

One popular theory is dynamic hyperinflation, which can occur during CPR if the lungs are rapidly filled with air without adequate time to exhale. The increased pressure in the lungs could limit blood flow back to the heart and even inhibit the heart's ability to pump altogether, producing cardiac arrest.

"When we breathe we suck in air, which creates negative pressure, whereas a ventilator [or CPR] blows in air, which creates positive pressure," says Daugherty. "If someone has an abnormal heart that is not functioning normally, and then you add this pressure to the chest, it decreases the amount of blood that is being returned to the heart, which further impairs its function."

In theory, when emergency doctors stop CPR, the lung pressure caused by dynamic hyperinflation returns to normal and the blood begins to circulate with greater ease, producing an auto-resuscitation effect.

Other researchers have proposed that dynamic hyperinflation instead plays a role in delaying drugs administered during CPR from reaching the heart. Once CPR is curtailed and blood flow returns to normal, the drugs reach their destination and may produce further improvements in circulation.

Hyperkalemia, or an elevated level of potassium in the blood, has also been proposed as a contributing cause in some cases of auto-resuscitation. These heightened levels interfere with heart function. After physicians prescribe calcium, glucose and insulin, sodium bicarbonate or other drugs that reduce potassium levels, the heart is able to resume beating.

While the nuts and bolts of the "Lazarus Phenomenon" remain an enigma, doctors can still take precautions to ensure that they don't quit on a patient too early. Adhiyaman recommends that physicians notify family members that CPR has been stopped and then monitor the patient for at least 10 to 15 minutes before declaring death.

"Death is not an event, it is a process. It happens gradually as your organs start shutting down. And so unless you are absolutely certain, you should not certify death," he says.

But in some situations, physicians are under time pressure and must draw a discrete line between life and death as quickly as possible—especially when it comes to organ donation and transplantation.

The dead donor rule, which serves as the ethical standard for organ transplantation, states that "vital organs should only be taken from dead patients and, correlatively, living patients must not be killed by organ retrieval." For organs to be transplanted successfully, they must be quickly removed to minimize any damage from lack of blood supply.

For brain-dead patients, the answer is simple: Keep them hooked up to a ventilator, which ensures circulation. But for patients who are donating after a cardiac death, doctors are put in the difficult situation of waiting long enough to ensure that a patient can be declared dead, but short enough to be left with viable organs that could save another life.

"There is an inherent tension, because the longer you wait, the more time the organs are not getting enough blood, which increases the likelihood that they go bad. So it cannot be too long," says James Kirkpatrick, an associate professor of medicine and a member of the ethics consultation committee at the University of

Washington School of Medicine. “But you also want to make sure the patient is not going to auto-resuscitate, because theoretically their heart and lungs are not irreversibly damaged and could come back.”

Right now, recommendations for wait times in cases of organ donation after a cardiac death vary significantly. The Institute of Medicine suggests at least five minutes, while the American Society of Transplant Surgeons and the Society for Critical Care Medicine each propose two minutes. A 2012 study, for instance, closely tracked 73 potential organ donors after cardiac death. That research found no occurrence of auto-resuscitation after two minutes—but none of those patients had received CPR.

Also, adopting national guidelines may be challenging, because some people remain skeptical about auto-resuscitation. “Frankly, some people don’t really believe in it,” says Daugherty. “And so a couple of examples like this are not going to change everything in how physicians declare someone dead.”

In the meantime, advancements in life-sustaining medical technologies and resuscitation techniques have only added nuance and complexity—prompting further questions, such as at what point death, clinically speaking, becomes irreversible?

“Although this is such a rare phenomenon and it is poorly understood, a lot of caution still needs to be taken on when we should declare someone dead,” says Daugherty. “It’s definitely a cause for concern.”

http://www.bbc.com/news/health-35933692

GlaxoSmithKline to 'drop patents in poor countries for better drug access'

Pharmaceutical firm GlaxoSmithKline has said it wants to make it easier for manufacturers in the world's poorest countries to copy its medicines.

The British company said it would not file patents in these countries.

Chief executive Sir Andrew Witty said he wanted to take a "graduated" approach to the company's "intellectual property" based on the wealth of nations around the globe. Experts have described the plans as "brave and positive".

GSK hopes that by removing any fear of it filing for patent protection in poorer countries it will allow independent companies to make and sell versions of its drugs in those areas, thereby widening the public access to them.

'Clear and simple'

Sir Andrew said he hoped Africa would benefit most from the move.

In accordance with international guidelines set out by the United Nations and World Bank, the company has drawn up a list of 50 countries with a combined population of about 1 billion people, where it has said it will not file for patents.

In what GSK describes as lower middle income countries it will continue to file patents, but will grant licences to generic manufacturers in exchange for a "small royalty".

Sir Andrew added: "The changes we are setting out aim to make it as clear and simple as possible for generic manufacturers to make and supply versions of GSK medicines."

The company has said it also wants to put all its future cancer drugs into a Medicines Patent Pool in an effort to address what it described as "the increasing burden of cancer in developing countries".

The patents pool was established in 2010 and has proved successful in accelerating access to treatments such as HIV, tuberculosis and hepatitis C through voluntary licensing arrangements, which allow generic versions of GSK's drugs to be made and distributed in poorer countries.

Expanding the pool to include cancer drugs will "add to the wider contribution GSK makes to improve access to effective healthcare around the world", the company said.

Sir Andrew added: "The experience GSK has with the Medicines Patent Pool for Tivicay - our newest HIV medicine and one of our most commercially successful products - gives us confidence that increasing access, incentivising innovation appropriately and achieving business success can go hand in hand."

GSK said it would continue to seek full patent protection in richer parts of the world.

'Broadening access'

Prof Raymond Hill, former President of the British Pharmacological Society, said GSK's plans set a precedent for other major pharmaceutical companies to follow.

He said: "This is a brave and positive step towards broadening the access to important new medicines in the developing world.

"The impact of this move on the treatment of cancer and other diseases in each individual country will depend on whether there is a local adequate healthcare infrastructure that will allow the safe use of powerful new drugs in an appropriate group of patients.

"Many new cancer drugs are most valuable when used in sub-groups of patients identified by advanced diagnostic techniques that may not be available."

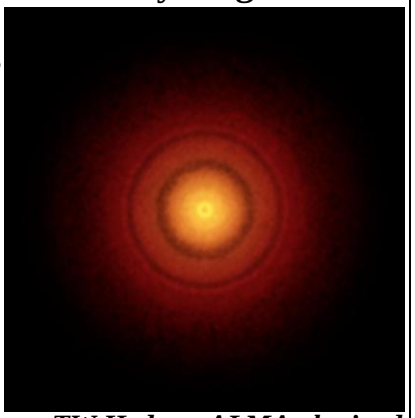
Prof Alan Boyd, from the Royal Colleges of Physicians, described the plans as "good news" and "significant"

He added: "Access to medicines for patients on a global basis is vital and it is good to see an innovative approach like this to ensure this happens."

http://www.eurekalert.org/pub_releases/2016-03/nrao-pfi033116.php

Planet formation in Earth-like orbit around a young star

ALMA's best image yet of a protoplanetary disk



The disks of dust and gas that surround young stars are the formation sites of planets. New images from the Atacama Large Millimeter/submillimeter Array (ALMA) reveal never-before-seen details in the planet-forming disk around a nearby Sun-like star, including a tantalizing gap at the same distance from the star as the Earth is from the Sun. This structure may mean that an infant version of our home planet, or possibly a more massive "super-Earth," is beginning to form there.

This is an ALMA image of the disk around the young star TW Hydrae. ALMA obtained its best image of a protoplanetary disk to date, revealing the classic rings and gaps that signify planets are in formation in this system. **S. Andrews (CfA); B. Saxton (NRAO/AUI/NSF); ALMA (ESO/NAOJ/NRAO**

The star, TW Hydrae, is a popular target of study for astronomers because of its proximity to Earth (approximately 175 light-years away) and its status as a veritable newborn (about 10 million years old). It also has a face-on orientation as seen from Earth. This affords astronomers a rare, undistorted view of the complete disk.

"Previous studies with optical and radio telescopes confirm that this star hosts a prominent disk with features that strongly suggest planets are beginning to coalesce," said Sean Andrews with the Harvard-Smithsonian Center for Astrophysics in Cambridge, Mass., and lead author on a paper published today in Astrophysical Journal Letters. "The new ALMA images show the disk in unprecedented detail, revealing a series of concentric dusty bright rings and dark gaps, including intriguing features that suggest a planet with an Earth-like orbit is forming there."

Other pronounced gap features are located 3 billion and 6 billion kilometers from the central star, similar to the distances from the Sun to Uranus and Pluto in our own Solar System. They too are likely the result of particles that came together to form planets, which then swept their orbits clear of dust and gas and shepherded the remaining material into well-defined bands.

For the new TW Hydrae observations, astronomers imaged the faint radio emission from millimeter-size dust grains in the disk, revealing details on the order of one astronomical unit (about 150 million kilometers, or the distance between the Earth and the Sun). These detailed observations were made possible with ALMA's high-resolution, long-baseline configuration. When ALMA's dishes are at their maximum separation, up to nearly 15 kilometers apart, the telescope is able to resolve finer details.

"This is the highest spatial resolution image ever of a protoplanetary disk from ALMA, and that won't be easily beaten going forward," said Andrews.

"TW Hydrae is quite special. It is the nearest known protoplanetary disk to Earth and it may closely resemble our Solar System when it was only 10 million years old," said co-author David Wilner, also with the Harvard-Smithsonian Center for Astrophysics.

Earlier ALMA observations of another system, HL Tau, show that even younger protoplanetary disks - a mere one million years old - can display similar signatures of planet formation. By studying the older TW Hydrae disk, astronomers hope to better understand the evolution of our own planet and the prospects for similar systems throughout the Galaxy.

The astronomers' next phase of research is to investigate how common these kinds of features are in disks around other young stars and how they might change with time or environment. The National Radio Astronomy Observatory is a facility of the National Science Foundation, operated under cooperative agreement by Associated Universities, Inc.

http://www.eurekalert.org/pub_releases/2016-03/uoc--sof032916.php

Short overnight fasting linked to increased risk of breast cancer recurrence

Researchers suggest increasing duration of nightly fasting may improve prognosis

In patients with breast cancer, a short overnight fast of less than 13 hours was associated with a statistically significant, 36 percent higher risk of breast cancer recurrence and a non-significant, 21 percent higher probability of death from the disease compared to patients who fasted 13 or more hours per night, report University of California, San Diego School of Medicine researchers.

The study, publishing online in the Journal of the American Medical Association Oncology on March 31, also found a non-significant, 22 percent higher risk of mortality from any cause among patients with breast cancer who fasted for shorter periods compared to those who fasted for 13 hours or more overnight.

Researchers also reported that fasting fewer hours per night was associated with significantly less sleep and higher levels of glycated hemoglobin (HbA1c), which is a measure of average blood sugar levels over a period of months. These findings are relevant to cancer prevention and control efforts because elevated HbA1c and poor sleeping habits have been linked to an increased risk of breast

cancer. These findings corroborate a paper published in April 2015, in which researchers demonstrated that shorter overnight fasts were associated with worse blood sugar control.

"Prolonging the overnight fasting interval may be a simple, non-pharmacological strategy for reducing a person's risk of breast cancer recurrence and even other cancers," said Catherine Marinac, lead author and doctoral candidate at UC San Diego Moores Cancer Center. "Previous research has focused on what to eat for cancer prevention, but when we eat may also matter because it appears to affect metabolic health."

The study included 2,413 non-diabetic breast cancer survivors between the age of 27 and 70 who participated in a multi-institutional research study conducted between 1995 and 2007, with follow up for breast cancer recurrence and mortality. Participants were 86 percent non-Hispanic white and 55 percent were college educated.

"If future trials confirm that habitual prolonged nightly fasting improves metabolic health, this would be an important discovery in prevention that could reduce the risk of cancers, type 2 diabetes, and cardiovascular disease," said Ruth Patterson, PhD, senior author and leader of the cancer prevention program at Moores Cancer Center.

Randomized trials to test whether prolonging overnight fasting reduces the risk of chronic diseases are needed, said the authors.

Additional study co-authors include Caitlin I. Breen, Sheri J. Hartman, Loki Natarajan, John P. Pierce, Shirley W. Flatt, and Dorothy D. Sears, UCSD; Sandahl H. Nelson, UCSD and San Diego State University.

This research was funded, in part, by the National Cancer Institute of the National Institutes of Health (F31CA183125, K07CA181323, U54CA155435, R01CA166293).

http://www.eurekalert.org/pub_releases/2016-03/nioa-soz033016.php

Structure of Zika virus determined

NIH-funded research could aid quest for vaccines, drugs

Credit: Courtesy of Kuhn and Rossmann research groups, Purdue University

A near-atomic level map of Zika virus shows its structure to be largely similar to that of dengue virus and other flaviviruses, but with a notable difference in one key surface protein, report scientists funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The variation in the Zika envelope (E) glycoproteins-- 180 of which are packed on the virus's outer shell-- may provide clues to better understand how Zika virus enters human cells and suggests ways to combat the virus with drugs or vaccines aimed at the newly detailed region.

NIAID grantees Richard Kuhn, Ph.D., Michael Rossmann, Ph.D., and their colleagues at Purdue University created the picture of a mature Zika virus particle with a technique called cryo-electron microscropy. The process involves freezing virus particles and firing a stream of high-energy electrons through the sample to create tens of thousands of two-dimensional electron micrograph images that are then combined to yield a composite high-resolution, three-dimensional view of the virus. The team included NIAID investigator Theodore Pierson, Ph.D.

The difference visualized by the researchers is in a region of the E glycoprotein that flaviviruses may use to attach to some human cells. The variation in the E glycoprotein of Zika virus could explain the ability of the virus to attack nerve cells, as well as the associations of Zika virus infection with birth defects and the autoimmune-neurological Guillian-Barré syndrome. The structure could inform vaccine development, as the Zika E glycoprotein is a key target of immune responses against the virus. The information may also be useful for designing treatments such as antiviral drugs or antibodies that interfere with E glycoprotein function. Further, details on the structural differences between E glycoprotein of Zika virus and the same protein in dengue virus may make it possible to create diagnostic tests that can distinguish Zika virus infection from dengue infection, a critical need in countries where both Zika and dengue viruses are circulating.

D Sirohi et al. The 3.8Å resolution cryo-EM structure of Zika virus. Science DOI: 10.1126/science.aaf5316 (2016).

This research was supported by NIAID grants R01AI073755 and R01AI076331.

http://www.eurekalert.org/pub_releases/2016-03/aaft-cds032816.php

Compact drug synthesizer could revolutionize drug delivery

System the size of a household fridge can synthesize a variety of pharmaceuticals

Researchers have developed a system the size of a household fridge that can synthesize a variety of pharmaceuticals in short periods of time, including an antihistamine, an antidepressant, a common local anesthetic, and a central nervous system depressant. Pharmaceutical manufacturing often requires multiple compounds and steps of synthesis at different sites, making the production process slow, inefficient and cumbersome. This disjointed process means that pharmaceuticals are often produced in batches, a main contributing factor to drug shortages. The condensed system developed by Andrea Adamo and colleagues offers continuous production of a drug - from start to finish - over the course of several hours or days, at a quality that meets U.S. Pharmacopeial standards. This advancement holds numerous important implications, such as for drug delivery in the face of disease epidemics or after natural disasters. The system consists of reconfigurable units that can be added or removed depending on the drug being

synthesized. As proof of principle, the researchers demonstrate the production of diphenhydramine hydrochloride (common trade name Benadryl®, often used to treat allergies), lidocaine hydrochloride (a common local anesthetic and antiarrhythmic drug), diazepam (commonly known as Valium®), and fluoxetine hydrochloride (a widely used antidepressant, e.g. Prozac®). The synthesizer was able to produce 4500, 810, 3000 and 1100 doses per day, respectively. Switching production from the simplest to the most complex drug took two hours. The system currently only produces liquid forms of drugs, but the authors note that new approaches, such as three-dimensional printing, could facilitate on-the-spot production of pharmaceuticals in pill form. A Perspective by Rainer Martin discusses this development in more detail, highlighting the scientific advantages that the system has by harnessing flow processes.

http://bit.ly/1SwiqJq

Something new under a (dead) sun

A white dwarf that appears to be made almost entirely of oxygen

Alan Duffy

For all their enormous size and furious energies, stars are remarkably simple. Knowing just their mass and the smattering of elements heavier than hydrogen we can predict their lives from cradles to grave. But every now and then, nature throws us something truly bizarre as as reminder that we ain't seen everything yet. As reported in Science, just such an oddity has been found in a search of over 30,000 white dwarfs, the end state of stars similar to our sun. This white dwarf appears to be made almost entirely of oxygen. And how it formed is truly a puzzle.

Life cycle

A star is a fusion bomb, burning light elements like hydrogen and helium through nuclear fusion to form heavier elements like carbon and oxygen. The bigger the star, the brighter it burns and the faster it uses up this fuel.

Stars no more than ten times the mass of our Sun will tend to throw out their nuclear "ash" of heavy elements into space, forming planetary nebulaes, which will eventually condense to form new stars, rocky planets and ultimately maybe even give rise to life like us that breathes the oxygen and eats this carbon. As Carl Sagan noted, we're made of star-stuff.

What's left behind in a dying star is a glowing cinder with the mass of our sun crushed to the size of the Earth. This incredible density means that a teaspoon worth of this object would be about the mass of a truck. We call this a white dwarf and it is the fate of our own sun in 5 billion years time.

End of the road, not the story

This newly discovered white dwarf has half of our sun's mass in a size no bigger than Earth, meaning the surface gravity is 100,000 times that of Earth. For you to walk on this would be like trying to walk with 40 blue whales on your back. That's assuming you haven't burnt to a crisp on it's glowing white hot surface, with temperatures over 20,000K (red hot would be just 1,000K).

Like the ash of campfire, you can tell what's been burnt by examining what's left over. In your camp you might wood ash or melted plastic perhaps but with the tremendous nuclear fires in stars we are left with individual elements. The bigger the initial star, the hotter it burns, and the heavier the elements left over.

In the case of this white dwarf we only see oxygen, meaning all the carbon has been fused into this heavier element. The puzzle is, our models tell us that it can't have produced the conditions to fuse carbon, meaning there's something we're missing in our models of how stars can die.

One idea is that towards the end of the progenitor star's life it began to "pulse" as it's outer layers were raised up by the intense pressure of the radiation only for this material to crash back to the surface and temporarily create intense conditions to fuse all the carbon into oxygen.

Then any remaining lighter elements like hydrogen and helium might also have been gravitationally stolen by a nearby companion (that has yet to be found) finally leaving a white dwarf containing only oxygen.

In having oxygen 25 times more common than any other element, this object is unique amongst the tens of thousands white dwarfs that have been surveyed. Yet the fact it exists at all has implications for the way that amazingly destructive events in our universe, called supernovae.

In some supernovae, white dwarfs detonate like ticking time bombs, all with the same brightness. This means we can use them as "standard candles" to measure distances based on how faint they appear. Measuring the expansion of the universe with these standard candles earned ANU Vice Chancellor Professor Brian Schmidt a share of the Nobel Prize in Physics 2011.

While a white dwarf is the end of the road for a star, this latest discovery shows there's still much to be learnt about these extreme objects.

http://www.eurekalert.org/pub_releases/2016-03/asfm-iin033116.php

Investigators identify new pneumonia epidemic in Beijing

Mycoplasma found in more than half of hospitalized children suffering from pneumonia in Beijing

Washington, DC - Mycoplasma pneumoniae infections began rising in Beijing last spring, and by December, this pathogen was found in more than half of hospitalized children suffering from pneumonia in that city, according to investigators from the Capital Institute of Pediatrics, Beijing, China. Now these investigators predict that this epidemic will likely continue well into 2016, and possibly longer. Their data may help clinicians slow the epidemic. The research is

published February 24th in the Journal of Clinical Microbiology, a publication of the American Society for Microbiology.

From May to December, 2015, the rate of diagnoses positive for M. pneumoniae in children nearly doubled, from 30 percent to 57 percent, said Hongmei Sun, MD, a pediatrician who is Director in the Department of Bacteriology, Capital Institute of Pediatrics. As the epidemic continues in Beijing, the investigators predict related outbreaks will occur elsewhere in China, and possibly in other Asian countries, said Sun.

As a result of these findings, Beijing doctors are being advised to be alert for M. pneumoniae, said Sun. The news media is publicizing the epidemic, and advising parents to cooperate with diagnosis and treatment, in an effort to stanch the epidemic's spread, she added.

"We have started investigating the rate of M. pneumoniae infection in several other regions of China, along with other Chinese Mycoplasma experts," said Sun. The researchers are hoping to be able to publish the resulting data before this coming autumn, in order to use it to help control the epidemic in these other regions, she said.

The foundation of the research is monitoring of the pathogen in children that Sun and collaborators have conducted since 1977. Since then, seven epidemics have taken place in Beijing. In the wake of the 1990 epidemic, a national training course for laboratory diagnosis of M. pneumoniae was held in 1992, said Sun.

The investigators have genotyped samples from patients from this and earlier epidemics. Genotyping can help clinicians identify and treat disease, as different genotypes of the same pathogen may produce slightly different symptoms, and different susceptibilities to drugs. One particular genotype, "MLVA4572", appears to harbor drug resistance, said Sun.

Children infected with M. pneumoniae typically come down with chest colds. Sore throat, fever, fatigue, headache, and a slowly worsening cough that can last for months are common symptoms, according to the Centers for Disease Control and Prevention. Children under five typically do not have fevers, but may suffer from vomiting and diarrhea. People at highest risk live or work in crowded conditions, such as schools, hospitals, and dormitories.

http://www.eurekalert.org/pub_releases/2016-03/cp-3g032416.php

3-D 'mini-retinas' grown from mouse and human stem cells

Stem cell science has progressed so that researchers can now share recipes for making human retinas--the part of the eye that is sensitive to light.

The first protocols enabled the generation of retinal cells in laboratory plates and more recently as complex tissue in the form of tiny eye-like cups. Researchers in Germany now have another efficient way to make 3-D retina organoids, which mimic the organ's tissue organization, from mouse or human stem cells. Their version of "mini-retinas," published online on March 31 by Stem Cell Reports, offers new perspectives on retina growth, injury, and repair.

"The goal isn't just to make the closest thing next to a real retina, but also to possibly harness the flexibility of the system to create more diverse ways of studying retina tissue," says senior author Mike Karl of the German Center for Neurodegenerative Diseases (DZNE). "We need to respect that each protocol is a new beast with different tastes, wrappings, and purposes."

Stem cell technologies have the potential to develop therapies for the treatment of diseases such as age-related blindness, and as clinical researchers work to apply the cells into new therapies, stem cell biologists such as Karl have been working to understand the regeneration of neurons from lower vertebrates to humans, which can aid regenerative medicine in more indirect ways.

For example, the 3-D retinal organoids developed in Karl's lab (an effort led by first author Manuela Völkner) efficiently replicate the formation of the retina. This specifically includes the light-detecting cone cells, which now can be produced in high quantities in their mini-retinas. Cone photoreceptors, which are responsible for high acuity and color vision, are the most precious retinal cell type with regard to potential future cell replacement therapies in patients affected by retinal degeneration.

Karl and colleagues' comparative studies on pluripotent stem cell-derived human and mouse retina organoids and mouse retina in vivo support the power of the new organoid protocol. "Tissue heterogeneity is a major challenge in organoid systems, and here our work provides new insight, which will help to develop specific organoid-based models, specifically to reliably study retinal disease mechanism," says Karl, who is also a part of the Center for Regenerative Therapies (CRTD) at Technische Universit?t Dresden.

"Even with our new additions to existing organoid systems, we have not yet reached that tipping point of robustness that we need for people without the expertise to grow these models," says Karl, "By working out the details, we also hope to help those who are not developmentally or stem cell-minded to just go and study what they want."

The Karl Lab's change to the mini-retina protocol involves cutting a retina organoid grown from stem cells into three pieces at an early stage of eye development. Each of these pieces, which look like little half moons, eventually grows into the full suite of cells found in the retina, thereby increasing the yield of retinal organoids up to 4-fold compared to previous protocols. A trisection also spurs the surviving organoids to grow to reach sizes similar to uncut organoids.

These mini-retinas swim around in the dish and because they're not attached to a surface, better reflect the structure of retinal tissue during development.

Karl's next objective is to make his 3-D "mini-retinas" even more complex, perhaps by bringing in blood vessels, as well as to use the organoids to study regeneration and the function of different neural cell types--specifically, from the human retina.

This work was supported by the Funding Programs for DZNE Helmholtz, TU Dresden CRTD, DFG, MedDrive TU Dresden UKD-Medical Faculty, research award Novartis Pharma GmbH, Volkswagen Foundation Freigeist fellowship, and the European Union's 6th Framework Program ESTOOLS.

Stem Cell Reports, Völkner et al.: "Retinal organoids from pluripotent stem cells efficiently recapitulate retinogenesis." http://dx.doi.org/10.1016/j.stemcr.2016.03.001

http://www.eurekalert.org/pub_releases/2016-03/wuis-lot033016.php

Living off the fat of the land

Do cancer cells synthesize the parts for new cells or scavenge them from the environment?

Cancer cells are defined by their ability for uncontrolled growth, one cell quickly becoming two becoming many. "It's a fascinating process," said Gary Patti, PhD, associate professor of chemistry at Washington University in St. Louis. "Imagine creating two copies of yourself every few days instead of just maintaining the one you have. In the past 15 or 20 years people have become really interested in how a cell does that."

For more than 80 years the reigning idea has been that cancer cells fuel their explosive growth by soaking up glucose from the blood, using its energy and atoms to crank out duplicate sets of cellular components. One of the reasons so much glucose is taken up is to make the lipids, or fats, that are assembled into cell membranes, the thin veils that separate the contents of a cell from its environment.

In 1970s and '80s, scientists working with radioactively tagged glucose showed that practically all the lipids inside tumor cells were made from glucose the cells took up from the extracellular environment, a finding that seemingly corroborated the "glucose hypothesis." The hypothesis makes sense, but like many other things that make sense, it may not be right.

While pursuing other work, the Patti lab discovered that proliferating fibroblasts make most of their lipids from glucose only if they are grown in standard cell-culture medium, which is nutrient-rich but lipid-poor.

When the scientists spiked the culture medium with lipids, raising concentrations to those typical of blood, the cells preferred to scavenge lipids from the medium rather than synthesizing them. And under these conditions, rapidly dividing cells took up no more glucose than cells that weren't dividing.

This effect was discovered in cultures of fibroblasts, which divide until they touch one another and then stop, giving scientists a chance to compare the metabolism of proliferating and quiescent cells. But intrigued by the "lipid effect," the scientists checked for it in two cancer-cell lines, the famous HeLa cells and a lung cancer cell line called H460. These cell lines responded less strongly but similarly to lipid concentrations.

The startling result, published online in the March 31, 2016, issue of *Cell Chemical Biology*, calls into question aspects of cancer research and treatment founded on the glucose hypothesis.

"It has only been possible to think about glucose metabolism at the systems level for the past few years," Patti said, referring to the new discipline of metabolomics. "Before that the technology to follow glucose through all the possible metabolic pathways just didn't exist."

Are glucose-uptake images accurate?

"The idea that increased glucose uptake is a metabolic hallmark of cancer cells is deeply embedded in our thinking. It's the basis for how we diagnose cancer and manage its treatment in the clinic," Patti said.

In diagnostic FDG-PET scans, patients are injected with a small amount of a glucose analog that includes a radioactive atom and are then scanned to create images of glucose uptake by various organs. Bright spots on these images indicate potential cancer.

Our study raises questions about the sensitivity of these scans, Patti said. "Perhaps cancer cells can live off fats floating in the blood rather than making them all out of glucose, particularly in the case of obese or diabetic patients whose blood lipid concentrations can be higher than normal."

Could this allow cancer cells to fly under the radar, leading to false negatives?

Should cancer drugs target glucose metabolism?

Because of the glucose hypothesis, scientists have devoted a lot of attention to developing cancer therapies that inhibit either glucose metabolism or lipid synthesis.

But if the assumption is wrong, would blocking glucose metabolism slow cell growth? Wouldn't the cells just scavenge lipids from their surroundings?

To test this possibility, the scientists tried dosing their cell lines with 2DG, a glucose molecule with a hydrogen atom substituted for a hydroxyl (OH-) group that gets stuck in the pathway that breaks down glucose. They found that if they spiked the cultures with lipids as well, 2DG was much less effective in slowing the growth of cancer cells.

This finding challenges the reasoning behind one strategy for killing cancer cells, Patti said. 2DG is now in clinical trials.

What about targeting lipid uptake?

If the work in the Patti lab suggests that cancer cells might not respond as hoped to drugs that block the glucose uptake, it also suggests blocking lipid uptake might be effective .

he scientists tested this idea by dosing their cultures with a drug called SSO that irreversibly binds to a lipid transporter in the cell membrane, inhibiting lipid uptake. When they did this, all three cells lines were slower to grow and divide.

Perhaps we should be thinking more about inhibiting lipid uptake, Patti said.

Cells in culture are artifacts

'The last point," Patti said, "and I think most people accept this, is that cell cultures are highly artificial systems that often give misleading results. Whether cell culture findings translate to animal models or patients is really questionable; it's hard to place a lot of trust in them," he said.

"In this case, the standard cell culture media that everyone uses has such low lipid concentrations that it really skews what the cells in culture are doing.

"Even though we all do the same cell culture in the same way it is dangerous to assume the results apply to the clinic," he said.

http://www.eurekalert.org/pub_releases/2016-04/tes-imo040116.php

In mildly obese patients, sleeve-it surgery may increase weight loss and glycemic control

Sleeve-IT surgery results in better glycemic control than either gastric bypass or clinical treatment

Boston, MA-- In mildly obese ("class I") patients, sleeve with ileal transposition (sleeve-IT) surgery results in better glycemic control than either gastric bypass or clinical treatment, a new study from Brazil suggests. The results will be presented Friday, April 1, at ENDO 2016, the annual meeting of the Endocrine Society, in Boston.

"This recent technique that combines sleeve gastrectomy with ileal transposition was an effective and safe choice for treating patients with mild obesity," said lead study author Ana Priscila Soggia, MD, endocrinologist in the Division of Clinical Research at the Hospital Sirio-Libanês in São Paulo.

Bariatric surgery for weight loss has been performed for many years, and in 80 percent to 90 percent of patients with moderate or severe obesity, bariatric surgery leads to remission of Type 2 diabetes. But not much is known about the corresponding impact of bariatric surgery on mildly obese patients who have diabetes.

"Although in 2010, the International Diabetes Federation recommended surgery for diabetic patients with mild obesity if clinical treatment is not successful, few related studies on this topic have been published," Soggia said. "The first surgical choice is gastric bypass. However, sleeve-IT, a recent technique not yet approved, increases the beneficial effects of traditional surgery, due to intestinal physiological mechanisms, without increasing the risk of side effects."

Soggia and her colleagues explored the possibility of bariatric surgery as a treatment for diabetes in patients with mild obesity (body mass index 30 to 35) by comparing two different types of surgery for weight loss with clinical treatment for diabetes in their hospital patients.

The 42 mildly obese study participants with poorly controlled Type 2 diabetes were, on average, 51 years of age and 62 percent were women. The researchers randomly assigned them to receive one of three treatments: sleeve-IT surgery, gastric bypass surgery, or clinical diabetes treatment.

After one year of treatment, 100 percent of patients having sleeve-IT and 46 percent of those having gastric bypass weight-loss procedures reached glycemic control (glycated hemoglobin 6.5 percent or less), compared with 8 percent of those treated clinically for diabetes. And overall, 75 percent of patients having sleeve-IT and 30 percent of those having gastric bypass reached remission (glycemic control without medication).

Weight loss was greater in the sleeve-IT and gastric bypass than in the clinical group. On average, participants in the sleeve-IT group lost 18.6 kg (40.9 lb), and those in the gastric bypass group lost 22.5 kg (49.5 lb), while those treated clinically lost only 4.7 kg (10.3 lb). Four patients experienced serious adverse events, but no deaths or life-threatening complications occurred.

The research team plans to continue to assess the results during 24 to 36 months of follow up. The Hospital Sirio-Libanês, through its philanthropic program PROADI, sponsored the study.

http://www.eurekalert.org/pub_releases/2016-04/uosc-nsl033016.php

New study links coffee consumption to decreased risk of colorectal cancer

Coffee consumption decreases the risk of colorectal cancer

LOS ANGELES -- Whether you like your coffee black, decaf, half-caff or even instant, feel free to drink up. Researchers at the University of Southern California (USC) Norris Comprehensive Cancer Center of Keck Medicine of USC have found that coffee consumption decreases the risk of colorectal cancer.

The study examined over 5,100 men and women who had been diagnosed with colorectal cancer within the past six months, along with an additional 4,000 men and women with no history of colorectal cancer to serve as a control group. Participants reported their daily consumption of boiled (espresso), instant,

decaffeinated and filtered coffee, as well as their total consumption of other liquids. A questionnaire also gathered information about many other factors that influence the risk of colorectal cancer, including family history of cancer, diet, physical activity and smoking.

"We found that drinking coffee is associated with lower risk of colorectal cancer, and the more coffee consumed, the lower the risk," said Stephen Gruber, MD, PhD, MPH, director of the USC Norris Comprehensive Cancer Center and senior author of the study.

The data showed that even moderate coffee consumption, between one to two servings a day, was associated with a 26 percent reduction in the odds of developing colorectal cancer after adjusting for known risk factors. Moreover, the risk of developing colorectal cancer continued to decrease to up to 50 percent when participants drank more than 2.5 servings of coffee each day. The indication of decreased risk was seen across all types of coffee, both caffeinated and decaffeinated.

"We were somewhat surprised to see that caffeine did not seem to matter," Gruber said. "This indicates that caffeine alone is not responsible for coffee's protective properties."

Coffee contains many elements that contribute to overall colorectal health and may explain the preventive properties. Caffeine and polyphenol can act as antioxidants, limiting the growth of potential colon cancer cells. Melanoidins generated during the roasting process have been hypothesized to encourage colon mobility. Diterpenes may prevent cancer by enhancing the body's defense against oxidative damage.

"The levels of beneficial compounds per serving of coffee vary depending on the bean, roast and brewing method," said first author Stephanie Schmit, PhD, MPH. "The good news is that our data presents a decreased risk of colorectal cancer regardless of what flavor or form of coffee you prefer."

This extensive study was conducted by a research team led by Gad Rennert, MD, PhD, director of the Clalit National Israeli Cancer Control Center in Haifa, Israel, together with investigators at USC Norris. One advantage of this large, population-based study is that the results are representative of many coffee-drinking populations.

"Although coffee consumption in Israel is less common and with more type-variability than in the United States, our results indicate similarities in risk reduction with use consumption of various types of coffee," Rennert said.

The study is available in the April 1, 2016 issue of Cancer Epidemiology, Biomarkers & Prevention, which is published by the American Association of Cancer Research.

"While the evidence certainly suggests this to be the case, we need additional research before advocating for coffee consumption as a preventive measure," Gruber added. That being said, there are few health risks to coffee consumption, I would encourage coffee lovers to revel in the strong possibility that their daily mug may lower their risk of colorectal cancer."

Colorectal cancer is the third most common cancer that is diagnosed in both men and women in the United States, with nearly five percent of men and just over four percent of women developing the disease over their lifetime. The American Cancer Society (ACS) estimates that in the United States, over 95,000 new cases of colon cancer and 39,000 new cases of rectal cancer will be diagnosed in this year alone.

http://www.eurekalert.org/pub_releases/2016-04/imc-ns032516.php

New study: Waist circumference is stronger predictor of heart disease than BMI

Researchers found that abdominal obesity, or having an apple-shaped body, is a strong predictor of serious heart disease in patients who have type 1 or type 2 diabetes, and haven't displayed any symptoms of heart disease

A new study from the Intermountain Medical Center Heart Institute in Salt Lake City and John Hopkins Hospital in Baltimore lends more evidence to the idea that it's better to be shaped like a pear -- with weight around the hips -- as opposed to an apple -- with weight around the abdomen.

Researchers from the two centers found that abdominal obesity -- or having an apple-shaped body -- is a strong predictor of serious heart disease in patients who have type 1 or type 2 diabetes, and haven't displayed any symptoms of heart disease.

Apple-shaped bodies are already associated with metabolic syndrome (which includes high blood pressure, high sugar levels and high cholesterol), as well as coronary artery disease and heart failure, but this new study found that waist circumference is also a strong predictor of left ventricular dysfunction in patients. Metabolic syndrome is often accompanied by excess body fat around the abdomen.

The collaborative team of researchers studied 200 diabetic men and women who had not yet exhibited any coronary disease. The researchers found that even independently of total body weight and body mass index or BMI, abdominal obesity was strongly associated with regional left ventricular dysfunction, which is a common cause of heart disease, including congestive heart failure.

Results of the study will be reported at the 2016 American College of Cardiology Scientific Session in Chicago on Saturday, April 2.

"Our research examined patients with diabetes, who are considered high risk for developing heart disease already, and found that the shape of your body determined if you were at a greater risk to develop left ventricular dysfunction," said Brent Muhlestein, co-director of research at the Intermountain Medical Center Heart Institute in Salt Lake City.

"This study confirms that having an apple-shaped body -- or a high waist circumference -- can lead to heart disease, and that reducing your waist size can reduce your risks," adds Dr. Muhlestein.

Studies show a strong correlation between weight gain and regional left ventricular function -- and obesity is a major worldwide health risk. One in three people will have cardiovascular disease in their lifetime, and about a third of them will die from a heart attack or similar malfunction before their heart disease is diagnosed.

The results of the new research expands on the results of a previously published study called faCTor-64, also conducted by researchers at Intermountain Medical Center Heart Institute and Johns Hopkins, which showed that the greater a person's body mass index, the greater their risk of heart disease.

FaCTor-64 enrolled patients with diabetes who were considered to be at high risk for heart attacks, strokes, or death but had no evidence of heart disease as of yet. Study participants completed randomized screening for coronary artery disease by CT coronary angiography, then received recommendations to change their care or their lifestyles, or continue routine standard diabetes care, based on their results. They were then followed to track future adverse heart events.

During the new study, 200 participants who received CT screenings also had echocardiography to assess their left ventricular function. The left ventricle is the chamber of the heart that pumps oxygen-rich blood to the brain and the body. When there's a dysfunction in the left ventricle, blood backs up into the lungs and lower extremities, which often leads to heart failure and increases the risk of sudden cardiac arrest.

Although any form of obesity can produce stress on the heart, the new Intermountain Medical Center Heart Institute/Johns Hopkins study shows that abdominal obesity, more so than total body weight or BMI (weight to height ratio), is a strong predictor of left ventricle dysfunction.

"We specifically found that waist circumference appears to be a stronger predictor for left ventricle dysfunction than total body weight or body mass index," says Boaz D. Rosen, MD, of Johns Hopkins, who is the study's principal investigator

Dr. Rosen says further studies are needed to verify these findings. "It will be important to see if these patients are indeed at risk of developing heart failure or coronary artery disease in the future," he added.

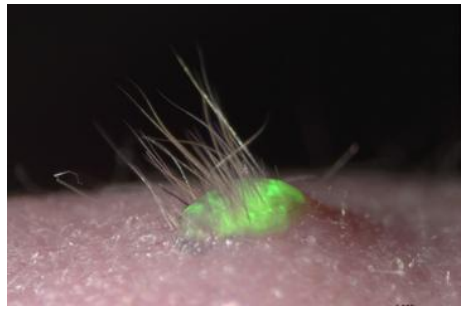
Other members of the research team include Ravi K. Sharma, MD, Kenneth D. Horton, Heidi T. May, MD, Yitzhak Rosen, Jeffery L. Anderson, MD, Donald L. Lappé, MD, and Joao A. C. Lima, MD.

http://bit.ly/1M9nMVI

Lab-Grown Skin Sweats and Sprouts Hair

In a lab in Japan, researchers have grown complex skin tissue, complete with hair follicles and sweat glands, according to a new study.

by Agata Blaszczak-Boxe



The new lab-grown skin tissue, once transplanted onto a mouse, sprouted hair.

Takashi Tsuji, RIKEN

The researchers implanted the tissue into living mice, and found that the tissue formed connections with the animals' nerves and muscle fibers. The findings may one day help researchers create better skin transplants for human patients with severe burns or skin diseases.

Prior to the new study, researchers had already developed a more basic type of skin substitute that had been used successfully in human patients, said Takashi Tsuji, a team leader at RIKEN Center for Developmental Biology in Japan. But that skin had only one or two layers of tissue, and lacked features such as hair follicles and the glands that secrete sweat and oil called sebum, he said.

In the new research, the scientists generated skin that had not only those features but also all three layers of tissue that normal skin has.

The work began with cells collected from mouse gums. The researchers used chemicals to transform these cells into cells that were similar to stem cells. Then, the researchers used these cells to generate three-layered, fully functioning skin tissue in lab dishes. Then, they transplanted this tissue, complete with hair follicles and glands that produce sebum, into mice.

The researchers found that the tissue made normal connections with surrounding nerves and muscle tissues in the mice, and those connections allowed the tissue to function normally. The mice's immune systems did not reject the transplanted tissues.

Moreover, 14 days after the tissue had been transplanted, the researchers noticed that hair had sprouted from the bioengineered hair follicles and started to grow.

"Our present outcomes indicate a proof of concept of regenerative therapy of [a] fully functional and integrated skin organ system that will have a potential for the application of the future clinical treatment," Tsuji told Live Science.

However, the researchers noted that, to generate human tissue for use in people, they would have to start with human cells, and would still have to figure out how to grow skin tissue from those cells, the researchers said.

Besides its potential application in human patients, the newly developed skin tissue also could be used as an alternative to testing cosmetics on animals, the researchers said.

The researchers are currently trying to generate other organs that are associated with skin tissue, such as teeth and salivary glands, Tsuji said.

The new study was published today (April 1) in the journal Science Advances.

http://www.eurekalert.org/pub_releases/2016-04/mu-rf033116.php

Researchers find 'simple' methods to prevent heart attacks and stroke worldwide

Statins and antihypertensives studied

Hamilton, ON - Three simple solutions to prevent heart attacks and stroke worldwide have been proven effective by an international team led by Hamilton medical researchers.

The research team from the Population Health Research Institute (PHRI) of McMaster University and Hamilton Health Sciences studied more than 12,000 patients from 21 countries to evaluate drugs that can prevent cardiovascular diseases (CVD). These diseases lead to 18 million deaths and about 50 million heart attacks and strokes globally every year.

"These are incredibly important findings with potential for significant global impact," said Dr. Salim Yusuf, principal investigator and executive director of PHRI. "If just 10 percent of the world's population at intermediate risk of CVD is impacted, we're talking about 20 to 30 million people who could be helped by these drugs."

The three methods examined included two forms of therapy: Statins, a group of cholesterol-lowering drugs, and antihypertensives, a class of drugs used to treat high blood pressure. In addition, a combination of statins and antihypertensives was reviewed.

Three studies on the methods were published today in the New England Journal of Medicine. Under the name of HOPE-3, or Heart Outcomes Prevention Evaluation-3, the studies involved 228 centres looking at the effects of the three treatments in people at intermediate risk of, but without, clinical heart disease.

Statins proved to significantly and safely reduce CVD events by 25 per cent in patients at intermediate risk without CVD. Antihypertensives did not reduce major CVD events overall in the population studied, but did reduce such events in the group of people with hypertension, but not in those without hypertension. When combined, statins and antihypertensives reduced CVD events by 30 per cent--with a 40% benefit in those with hypertension, suggesting that patients with hypertension should not only lower their BP but also consider taking a statin.

The HOPE-3 research reports were led by Yusuf and Dr. Eva Lonn, both professors of medicine of McMaster's Michael G. DeGroote School of Medicine, and Jackie Bosch, an associate professor of the university's School of Rehabilitation Science.

"The HOPE-3 trial brings clarity in the management of blood pressure and cholesterol, two of the most common cardiovascular risk factors," said Lonn. "Primary prevention can be greatly simplified and made available to most intermediate-risk people worldwide."

Bosch added: "Treatment with a statin was remarkably safe and beneficial in our study, regardless of cholesterol or blood pressure levels, age, gender or ethnicity. We are incredibly encouraged by the study's results."

HOPE-3's findings will have a major influence on primary care in developed nations, where statins and antihypertensives are inexpensive, Yusuf added. While still relatively inexpensive in developing nations, the drugs are less affordable in relation to income. Still, Yusuf said the study's results hold promise everywhere as the price of these drugs start to come down.

"These simple methods can be used practically everywhere in the world, and the drugs will become even cheaper as more and more systems and people adopt these therapies," he said.

Yusuf, Lonn and Bosch are presenting the HOPE-3 trials at the 2016 American College of Cardiology (ACC) Scientific Session and Expo in Chicago this weekend.

The HOPE-3 study is funded by the Canadian Institutes of Health Research and AstraZeneca.