http://www.eurekalert.org/pub_releases/2015-06/uoc--ede062915.php

Exit dinosaurs, enter fishes

The mass extinction event that killed the dinosaurs gave rise to the modern 'Age of Fishes,' Scripps researchers find

A pair of paleobiologists from Scripps Institution of Oceanography, UC San Diego have determined that the world's most numerous and diverse vertebrates - ray-finned fishes - began their ecological dominance of the oceans 66 million years ago, aided by the mass extinction event that killed off dinosaurs.

Scripps graduate student Elizabeth Sibert and Professor Richard Norris analyzed the microscopic teeth of fishes found in sediment cores around the world and found that the abundance of ray-finned fish teeth began to explode in the aftermath of the mass die-off of species, which was triggered by an asteroid strike in the Yucatan Peninsula. Scientists refer to this episode as the Cretaceous-Paleogene (K/Pg) extinction event.

Ninety-nine percent of all fish species in the world - from goldfish to tuna and salmon - are classified as ray-finned fishes. They are defined as species with bony skeletal structures and have teeth that are well preserved in deep ocean mud. Sharks, in contrast, have cartilaginous skeletons and are represented by both teeth and mineralized scales, also known as denticles, in marine sediments.

"We find that the extinction event marked an ecological turning point for the pelagic marine vertebrates," write the authors in the study. "The K/Pg extinction appears to have been a major driver in the rise of ray-finned fishes and the reason that they are dominant in the open oceans today."

The breakthrough for the researchers in reaching their conclusion came through their focus on fossilized teeth and shark scales. In cores from numerous ocean basins, they found that while the numbers of sharks remained steady before and after the extinction event, the ratio of ray-finned fish teeth to shark teeth and scales gradually rose, first doubling then becoming eight times more abundant 24 million years after the extinction event. Now there are 30,000 ray-finned fish species in the ocean, making this class the most numerically diverse and ecologically dominant among all vertebrates on land or in the ocean.

Scientists had known that the main diversification of ray-finned fishes had happened generally between 100 million and 50 million years ago.

"The diversification of fish had never been tied to any particular event. What we found is that the mass extinction is actually where fish really took off in abundance and variety," said Sibert, who is the recipient of an NSF Graduate Research Fellowship. "What's neat about what we found is that when the asteroid hit, it completely flipped how the oceans worked. The extinction changed who the major players were."

Sibert and Norris believe that some key changes in the oceans might have helped ray-finned fishes along. Large marine reptiles disappeared during the mass extinction, as did the ammonites, an ancient cephalopod group similar to the chambered nautilus. Those species, the researchers believe, had been either predators of ray-finned fishes or competitors with them for resources.

"What's amazing", said Norris, "is how quickly fish double, then triple in relative abundance to sharks after the extinction, suggesting that fish were released from predation or competition by the extinction of other groups of marine life."

Sibert noted that before the extinction event, ray-finned fishes existed in a state of relative ecological insignificance, just like mammals on land.

"Mammals evolved 250 million years ago but didn't become really important until after the mass extinction. Ray-finned fishes have the same kind of story," said Sibert. "The lineage has been around for hundreds of millions of years, but without the mass extinction event 66 million years ago, it is very likely that the oceans wouldn't be dominated by the fish we see today."

The paper, "New Age of Fishes initiated by the Cretaceous-Paleogene mass extinction," appears June 29 in the early edition version of the journal Proceedings of the National Academy of Sciences.

http://www.eurekalert.org/pub_releases/2015-06/uoms-fpt062915.php

First-ever possible treatments for MERS

Researchers identify 2 promising candidates

Baltimore, Md. - As the South Korean epidemic of Middle East Respiratory Syndrome (MERS) continues unabated, researchers have raced to find treatments for the deadly virus, which has killed more than 400 people since it was first discovered three years ago in Saudi Arabia.

Now, scientists at the University of Maryland School of Medicine and Regeneron Pharmaceuticals, Inc., have discovered and validated two therapeutics that show early promise in preventing and treating the disease, which can cause severe respiratory symptoms, and has a death rate of 40 percent. These therapeutics are the first to succeed in protecting and treating animal models of the MERS virus. The study appears today in the latest issue of the journal Proceedings of the National Academy of Sciences (PNAS).

"While early, this is very exciting, and has real potential to help MERS patients," says a lead researcher on the study, Matthew B. Frieman, PhD, an assistant professor of microbiology and immunology at the University of Maryland School of Medicine (UM SOM). "We hope that clinical study will progress on these two antibodies to see whether they can eventually be used to help humans infected with the virus."

The two antibodies, REGN3051 and REGN3048, showed an ability to neutralize the virus. This research, done in collaboration with Regeneron, a biopharmaceutical company based in Tarrytown, New York, used several of the company's proprietary technologies to search for and validate effective antibodies targeting the virus.

MERS was first discovered in 2012 in Saudi Arabia. It appears that the disease spread to humans from camels, who may themselves have been infected by bats. Research has shown that it is similar to Severe acute respiratory syndrome (SARS); both are caused by Coronaviruses, both cause respiratory problems, and both are often fatal.

The paper also announced the development a novel strain of mice, which will help scientists understand the disease and look for treatments. This work relied on Regeneron's VelociGene technology to create partially humanized mice that can be infected with MERS.

"Mice are typically not susceptible to MERS," said Prof. Frieman, who is an expert on both MERS and SARS, as well as other emerging viruses. "This new mouse model will significantly boost our ability to study potential treatments and help scientists to understand how the virus causes disease in people."

The South Korean outbreak began last month when a traveler returned from Saudi Arabia, and infected many people before officials realized he had the disease. So far, around 180 people have been infected in South Korea, and nearly 30 have died.

"Prof. Frieman's work provides the first glimmer of hope that we can treat and cure this threatening virus," said Dean E. Albert Reece, MD, PhD, MBA, who is also the vice president for Medical Affairs, University of Maryland, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean of the School of Medicine. "I know that they will continue to work hard to see whether these compounds can take the next steps to clinical trials."

http://www.eurekalert.org/pub_releases/2015-06/aha-cdn062415.php

Clot-removal devices now recommended for some stroke patients

American Heart Association focused update

DALLAS - For the first time, the American Heart Association/American Stroke Association recommends using a stent retrieval device to remove blood clots in select stroke patients who have clots obstructing the large arteries supplying blood to the brain, according to a new focused update published in the American Heart Association journal Stroke.

The optimal initial treatment for a clot-caused (ischemic) stroke remains intravenous delivery of the clot-busting medication tissue plasminogen activator (tPA). When given within a few hours after stroke symptoms, tPA can dissolve the clot and reestablish blood flow to the brain, limiting stroke disability.

"What we've learned in the last eight months, from six new clinical trials, is that some people will benefit from additional treatment with a stent retrieval device if a clot continues to obstruct one of the big vessels after tPA is given," said William J. Powers, M.D., lead author of the focused update and H. Houston Merritt distinguished professor and chair of the department of neurology at the University of North Carolina at Chapel Hill.

The focused update on endovascular treatment of acute ischemic stroke analyzes results from randomized clinical trials published since 2013, when the last treatment guidelines were issued.

The clot-removal procedure involves puncturing an artery in the groin and threading a thin wire tube up into the brain until it reaches the blocked vessel in one of the large arteries. At the site of the blockage, the tube with a wire mesh called a stent retriever at its end is pushed into the clot and the mesh is expanded so it grabs the clot, which is removed as the tube is pulled out.

"This additional treatment is more difficult than tPA, which can be given by most doctors in the emergency room," Powers said.

"Clot removal with a stent retriever requires a specialized center, such as Comprehensive Stroke Centers, or other healthcare facilities with specially trained people including some Primary Stroke Centers. This treatment has to be done within six hours of the onset of stroke, so in some areas it can be tricky to get you to an appropriate hospital in time." The focused update recommends that stroke patients have their clots removed with a stent retriever if they:

have no significant disability prior to the current stroke
received tPA within 4.5 hours of symptom onset
have a clot blocking a large artery supplying blood to the brain
are at least 18 years old
had an acute, severe stroke
have imaging showing more than half of the brain on the side of the stroke is not permanently damaged
can have the procedure start within six hours after symptom onset

The evidence backing this new recommendation received the highest rating based on the scientific evidence reviewed, and suggests the benefits substantially outweigh the potential risks in these patients.

"Evidence-based guidelines are based on clinical trials, which tell you that if you have a patient with the same characteristics of those in the trials, on average they will do much better with the treatment than if you treat them another way," Powers said.

The focused update states that the use of stent retrievers is indicated in preference to other mechanical thrombectomy devices, but notes that the use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances based on a physician's clinical judgment.

Both tPA and clot-retrieval procedures work better the sooner they are administered. Therefore, it's important to remember the acronym F.A.S.T. and seek immediate help if you notice anyone with the following symptoms:

Face drooping or numbness on one side.
Arm weakness with inability to hold both arms overhead.
Speech slurring or inability to repeat simple sentence.
Time to call 911.

Co-authors are Colin P. Derdeyn, M.D., vice chair; José Biller, M.D.; Christopher S. Coffey, Ph.D.; Brian L. Hoh, M.D.; Edward C. Jauch, M.D., M.S.; Karen C. Johnston, M.D., M.Sc.; S. Claiborne Johnston, M.D., Ph.D.; Alexander A. Khalessi, M.D., M.S.; Chelsea S. Kidwell, M.D.; James F. Meschia, M.D.; Bruce Ovbiagele, M.D., M.Sc., M.A.S.; and Dileep R. Yavagal, M.D., on behalf of the American Heart Association Stroke Council. Author disclosures are on the manuscript.

http://www.eurekalert.org/pub_releases/2015-06/mu-hah062515.php

His and her pain circuitry in the spinal cord

New animal research reveals fundamental sex differences in how pain is processed

New research released today in Nature Neuroscience reveals for the first time that pain is processed in male and female mice using different cells. These findings have far-reaching implications for our basic understanding of pain, how we develop the next generation of medications for chronic pain--which is by far the most prevalent human health condition--and the way we execute basic biomedical research using mice.

"Research has demonstrated that men and women have different sensitivity to pain and that more women suffer from chronic pain than men, but the assumption has always been that the wiring of how pain is processed is the same in both sexes," said co-senior author Jeffrey Mogil, Ph.D., E.P. Taylor Professor of Pain Studies at McGill University and Director of the Alan Edwards Centre for Research on Pain. "The realization that the biological basis for pain between men and women could be so fundamentally different raises important research and ethical questions if we want to reduce suffering."

The research was conducted by teams from McGill University, The Hospital for Sick Children (SickKids), and Duke University, and looked at the longstanding theory that pain is transmitted from the site of injury or inflammation through the nervous system using an immune system cell called microglia. This new research shows that this is only true in male mice. Interfering with the function of microglia in a variety of different ways effectively blocked pain in male mice, but had no effect in female mice

According to the researchers, a completely different type of immune cell, called T cells, appears to be responsible for sounding the pain alarm in female mice. However, exactly how this happens remains unknown.

"Understanding the pathways of pain and sex differences is absolutely essential as we design the next generation of more sophisticated, targeted pain medications," said Michael Salter, M.D., Ph.D., Head and Senior Scientist, Neuroscience & Mental Health at SickKids and Professor at The University of Toronto, the other co-senior author. "We believe that mice have very similar nervous systems to humans, especially for a basic evolutionary function like pain, so these findings tell us there are important questions raised for human pain drug development."

The discovery comes as there is increased attention to the inclusion of female animals and cells in preclinical research. The U.S. National Institutes of Health recently unveiled a new policy, similar to one already in force in Canada, to require the use of female animals and cell lines in preclinical research.

"For the past 15 years scientists have thought that microglia controlled the volume knob on pain, but this conclusion was based on research using almost exclusively male mice," said Mogil. "This finding is a perfect example of why this policy, and very carefully designed research, is essential if the benefits of basic science are to serve everyone."

This work was supported by grants from the Canadian Institutes of Health Research, the Louise and Alan Edwards Foundation, the U.S. National Institutes of Health and SickKids Foundation.

"Different immune cells mediate mechanical pain hypersensitivity in male and female mice", Robert E. Sorge, et al, Advance Online Publication on Nature Neuroscience's website 29 June 2015. DOI: 10.1038/nn.4053

http://www.eurekalert.org/pub_releases/2015-06/hu-tnd062915.php

The new detection method for a key drug resistant hepatitis C virus mutation

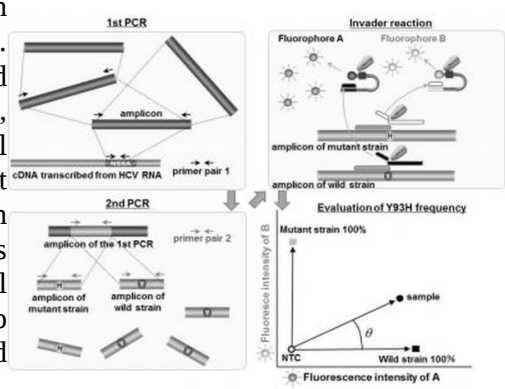
A rapid, sensitive, and accurate method to detect drug resistant hepatitis C virus (HCV) mutants has been developed.

This news release is available in Japanese.

Researchers at Hiroshima University established a system to rapidly and accurately measure the presence of HCV Y93H drug resistant mutant strains, and evaluate the proportion of patients harboring this mutation prior to treatment. Even in serum samples with low HCV titers, Y93H drug resistant mutation could be successfully detected in more than half of the samples. This new system for detecting mutant strains may provide important pre-treatment information

valuable not only for treatment decisions but also for prediction of disease progression in HCV genotype 1b patients.

HCV is a major cause of chronic liver disease, liver cirrhosis, and hepatocellular carcinoma, affecting up to 180 million people worldwide. HCV often acquires resistance against direct acting antiviral agents. Presence of the Y93H mutation prior to treatment has been reported as an important predictor of virologic failure. Direct sequencing is a commonly used method to detect this mutation. However, it is only capable of detecting viral subpopulations with frequencies of at least 10% to 20%. Next generation sequencing has recently been applied as a more sensitive method to analyze viral mutations, but it is still complex to perform and expensive for widespread clinical use.



This diagram shows the schematic flow representing a method of nested-PCR followed by Invader. **Hiroshima University**

By combining nested PCR and the Invader assay with well-designed primers and probes, the Y93H drug resistant mutation can be detected with a high success rate of 98.9% among a total of 702 Japanese HCV genotype 1b patients.

"Our assay system also showed a much lower detection limit for Y93H than using direct sequencing, and Y93H frequencies obtained by this method correlated well with those of deep-sequencing analysis." Professor Kazuaki Chayama, the principle investigator of this study at Hiroshima University, explained.

The proportion of the patients with the Y93H mutant strain estimated by this system was 23.6%, and this rate is comparable with that assayed by real-time PCR and ranked between those of deep sequencing and direct sequencing reported in the Japanese population, presumably reflecting the lower detection limit of Y93H.

This new system attained a high assay success rate and was more sensitive in detecting Y93H than direct sequencing. The evaluation of Y93H strain may provide important information for prediction of disease progression in HCV genotype 1b patients.

Rapid, Sensitive, and Accurate Evaluation of Drug Resistant Mutant (NS5A-Y93H) Strain Frequency in Genotype 1b HCV by Invader Assay

Satoshi Yoshimi , Hidenori Ochi , Eisuke Murakami, Takuro Uchida, Hiromi Kan, Sakura Akamatsu, C. Nelson Hayes, Hiromi Abe, Daiki Miki, Nobuhiko Hiraga, Michio Imamura, Hiroshi Aikata, Kazuaki Chayama

PLOS ONE DOI: 10.1371/journal.pone.0130022

http://www.eurekalert.org/pub_releases/2015-06/luhs-as062915.php

Athletes should drink only when thirsty, according to new guidelines

Drinking too much fluid can cause life-threatening hyponatremia

MAYWOOD, Ill. - At least 14 deaths of marathon runners, football players and other athletes have been attributed to a condition called exercise-associated hyponatremia, which results from drinking too much water or sports drinks.

But there's an easy way to prevent hyponatremia, according to new guidelines from an international expert panel: Simply put, drink only when you're thirsty.

"Using the innate thirst mechanism to guide fluid consumption is a strategy that should limit drinking in excess and developing hyponatremia while providing sufficient fluid to prevent excessive dehydration," according to the guidelines, published in the Clinical Journal of Sport Medicine.

Loyola University Medical Center sports medicine physician James Winger, MD, is a member of the 17-member expert panel that wrote the guidelines. Dr. Winger, who has published studies on hyponatremia in athletes, is an associate professor in the Department of Family Medicine of Loyola University Chicago Stritch School of Medicine. Corresponding author of the guidelines is Tamara Hew-Butler, DPM, PhD, of Oakland University in Rochester, Mi.

Exercise-associated hyponatremia (EAH) occurs when drinking too much overwhelms the ability of the kidneys to excrete the excess water load. Sodium in the body becomes diluted. This leads to swelling in cells, which can be life-threatening.

Symptoms of mild EAH include lightheadedness, dizziness, nausea, puffiness and gaining weight during an athletic event. Symptoms of severe EAH include vomiting, headache, altered mental status (confusion, agitation, delirium, etc.), seizure and coma.

EAH has occurred during endurance competitions such as marathons, triathlons, canoe races and swimming; military exercises; hiking; football; calisthenics during fraternity hazing; and even yoga and lawn bowling, the guidelines said.

Athletes often are mistakenly advised to "push fluids" or drink more than their thirst dictates by, for example, drinking until their urine is clear or drinking to a prescribed schedule. But excessive fluid intake does not prevent fatigue, muscle cramps or heat stroke.

"Muscle cramps and heatstroke are not related to dehydration," Dr. Winger said. "You get heat stroke because you're producing too much heat."

Modest to moderate levels of dehydration are tolerable and pose little risk to otherwise healthy athletes. An athlete can safely lose up to 3 percent of his or her

body weight during a competition due to dehydration without loss of performance, Dr. Winger said. The guidelines say EAH can be treated by administering a concentrated saline solution that is 3 percent sodium - about three times higher than the concentration in normal saline solution. The guidelines are published in an article titled "Statement of the Third International Exercise-Associated Hyponatremia Consensus Development Conference, Carlsbad, California, 2015."

The conference was supported by CrossFit, Inc. However, no members from CrossFit participated in the development of the guidelines or had access to the guidelines document before publication.

http://www.eurekalert.org/pub_releases/2015-06/mali-npp062915.php

New plan proposed to send humans to Mars

A new, cost-constrained U.S. strategy to send humans on Mars, could be achieved within projected NASA budgets by minimizing new developments and relying mainly on already available or planned NASA assets.

New Rochelle, NY - This approach is described in "A Minimal Architecture for Human Journeys to Mars," published in New Space, a peer-reviewed journal from Mary Ann Liebert, Inc., publishers. The article is available free on the New Space website until July 29, 2015.

Coauthors Hoppy Price, John Baker, and Firouz Naden, Jet Propulsion Laboratory, California Institute of Technology, Pasadena, CA, propose a long-term, stepwise series of missions to Mars that would begin with a crew landing on Mars's moon Phobos in 2033, and followed by a short-stay mission in 2039 and a year-long landing in 2043.

In the Editorial "We Can Send Humans to Mars Safely and Affordably," Editor-in-Chief G. Scott Hubbard, Stanford University, describes the complex engineering, safety, and health issues related to long-term space travel that have already been overcome. "With all of these previous technical and fiscal issues addressed, we can again believe that the dream of sending people to Mars is alive," Professor Hubbard says. "The next step is to build a broad consensus around the goal and strategy for a long term, humans to Mars program." The Editorial is also available free on the New Space website until July 29, 2015.

http://www.eurekalert.org/pub_releases/2015-06/e-vma062915.php

Virus-carrying mosquitoes are more widespread than ever, and spreading

Scientists behind the first global distribution maps of two species of dengue and chikungunya-carrying mosquitoes warn they are spreading to new areas where they could cause disease.

The population of the tiger mosquito, which is known to carry dengue and chikungunya, has rapidly expanded in parts of the US, Southern Europe and China over the past 10-15 years. A new study by scientists at Oxford University reports the growth and identifies areas not yet populated by the insects that are suitable for their survival, for example in Europe. The findings are published in the journal eLife.

"Given the lack of a vaccine or any antiviral treatment for either virus and the debilitating pain they both cause, knowing where the mosquitoes are spreading to and where they might turn up next is crucial for helping to protect communities," says first author Moritz Kraemer. This is especially true in Africa, where records are sparse.

Urban areas worldwide are particularly susceptible to the spread of the yellow fever mosquito, Aedes aegypti, which also carries the viruses and lays its eggs in artificial containers such as buckets and discarded tyres. Concentrations of both mosquitoes are particularly high in Brazil, China, Taiwan and the US, though infection via Ae. Aegypti is not so widespread in the US.

Dengue fever is the world's most common insect-borne virus, causing 100 million annual infections and leaving almost half of the world's population at risk. The invasion of chikungunya into the Americas has already caused over one million cases of disease. The maps are also relevant to yellow fever, though infections from this virus are already on the decline.

Temperature is key to the survival of both species and they are mainly found in the tropics and subtropics. However, the tiger mosquito Aedes albopictus can overwinter in colder locations by becoming dormant. This allows it to extend the margins of its range. Once introduced via major shipping or travel routes, the mosquitoes spread quickly over land.

The scientists created the maps from records that include collections of the insects from national entomological surveys and published resources in many languages.

According to lead author Professor Simon Hay, "We have made our data openly available so they can be used straight away to help protect people against these viruses about which we still know so little and have so few defences."

The paper 'The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus' can be freely accessed online at http://dx.doi.org/10.7554/eLife.08347

http://www.eurekalert.org/pub_releases/2015-06/sri-srf062915.php

Small RNAs found to play important roles in memory formation

MicroRNA plays surprisingly different roles in the formation of memory in animal models

JUPITER, FL - Scientists from the Florida campus of The Scripps Research Institute (TSRI) have found that a type of genetic material called "microRNA" plays surprisingly different roles in the formation of memory in animal models. In some cases, these RNAs increase memory, while others decrease it.

"Our systematic screen offers an important first step toward the comprehensive identification of all miRNAs and their potential targets that serve in gene networks important for normal learning and memory," said Ron Davis, chair of TSRI's Department of Neuroscience who led the study. "This is a valuable resource for future studies."

The study was published in the June 2015 edition of the journal Genetics.

Unlike some types of RNA, microRNAs (miRNAs) do not code for proteins but instead regulate various biological processes by modulating the level of gene expression.

A number of studies have shown that miRNAs are critical for normal development and cellular growth and may contribute to the complexity of neurodegenerative diseases.

In the new study, 134 different miRNAs were tested for roles in learning and memory in the central nervous system of Drosophila melanogaster, the common fruit fly, which is a recognized animal model for memory studies.

The researchers tested the potential involvement of miRNAs in intermediate-term memory by silencing them individually and identified at least five different miRNAs involved in memory formation or retention.

"Among the five miRNAs identified in this study, we found one that is necessary for memory formation," said Research Associate Germain U. Busto, a first author of the study with Research Associate Tugba Guven-Ozkan.

"Interestingly, its human counterpart is altered in several neurodegenerative diseases, including Alzheimer's and Huntington's. It's possible that this might be a potential model to study and solve some specific aspects of those disorders."

Surprisingly, the researchers found some miRNAs decreased memory formation, while others increased it. The identified miRNAs affected either neuronal physiology underlying memory formation or the development of the nervous system.

"These microRNAs are highly regulated during brain development and for adult brain function," said Guven-Ozkan. "When misregulated, they may exacerbate brain diseases like autism, and Alzheimer's and Huntington's diseases. We'd like to pinpoint learning and memory pathways to understand how they may lead to human disease."

In addition to Davis, Busto and Guven-Ozkan, other authors of the study, "microRNAs That Promote or Inhibit Memory Formation in Drosophila melanogaster," include Tudor A. Fulga and David Van Vactor of Harvard Medical School. For more information, see http://www.genetics.org/content/200/2/569.abstract.

The work was supported by National Institutes of Health (grants R37 NS19904 and R01 NS069695).

http://bit.ly/1NHldGq

Pre-Crastination: The Opposite of Procrastination

Why we do some tasks before their time—and why pigeons do, too

By David A. Rosenbaum and Edward A. Wasserman

Procrastination is a well-known and serious behavioral problem involving both practical and psychological implications. Taxpayers commonly put off submitting their annual returns until the last minute, risking mathematical errors in their frenzy to file. Lawmakers notoriously dawdle and filibuster before enacting sometimes rash and ill-advised legislation at the eleventh hour. And, students burn the midnight oil to get their term papers submitted before the impending deadline, precluding proper polishing and proofreading. For these reasons, we are cautioned not to procrastinate: *Don't put off until tomorrow what you can do today. He who hesitates is lost. Procrastination is the thief of time.*

However, the opposite of procrastination can also be a serious problem — a tendency we call "pre-crastination." Pre-crastination is the inclination to complete tasks quickly just for the sake of getting things done sooner rather than later. People answer emails immediately rather than carefully contemplating their replies. People pay bills as soon as they arrive, thus failing to collect interest income. And, people grab items when they first enter the grocery store, carry them to the back of the store, pick up more groceries at the back, and then return to the front of the store to pay and exit, thus toting the items farther than necessary. Familiar adages also warn of the hazards of pre-crastinating: *Measure twice, cut once. Marry in haste, repent at leisure. Look before you leap.*

We first found striking evidence of pre-crastination in a laboratory study exploring the economics of effort. College students were asked to carry one of a pair of buckets: one on the left side of a walkway and one on the right side of the same walkway. The students were instructed to carry whichever bucket seemed easier to take to the end of the walkway. We expected students to choose the bucket closer to the end because it would have to be carried a shorter distance. Surprisingly, they preferred the bucket closer to the starting point, actually carrying it farther. When asked why they did so, most students said something like, "I wanted to get the task done as soon as possible," even though this choice did not in fact complete the task sooner.

Nine experiments involving more than 250 students failed to reveal what might have been so compelling about picking up the nearer bucket. Although some hidden benefit may await discovery, a simple hypothesis is that getting something done, or coming closer to getting it done, is inherently rewarding. No matter how trivial the achievement, even something as inconsequential as picking up a bucket may serve as its own reward.

Is pre-crastination — exhibited by college students, bill payers, e-mailers, and shoppers — a symptom of our harried lives? The other study from our laboratories suggests it is not: that experiment was done with pigeons. The birds could earn food by pecking a touchscreen three times: first, into a square in the center of the screen; second, into the same square or into a square that randomly appeared to the left or right of it; and third, into a side square after a star appeared within it. Critically, food was given after the final peck regardless of whether the second peck struck the center square or the side square where the star would be presented. The pigeons directed their second peck to the side square, hence moving to the goal position as soon as they could even though there was no obvious or extra reward for doing so. Thus, the pigeons pre-crastinated.

Finding pre-crastination in the pigeon is particularly important because the evolutionary ancestors of pigeons and people went their separate ways 300 million years ago. Following a popular line of thinking in comparative psychology, the fact that both pigeons and people pre-crastinate suggests that this behavioral tendency may have emerged even earlier in phylogeny.

Why would our evolutionary kin have pre-crastinated, and why do we humans and our pigeon contemporaries do so now? It is possible, as suggested above, that pre-crastination amounts to grabbing low-hanging fruit. If grain is nearby or if a bucket is close at hand, then it may be best to get it while it's available. Another explanation is that completing tasks immediately may relieve working memory. By doing a task right away, you don't have to remember to do it later; it can be taxing to keep future tasks in mind. Requiring people to delay performance of a task often worsens their performance of it. Yet, we doubt this is the whole story. Lifting a bucket doesn't tax working memory very much, and it's not obvious why directing the second peck to the future goal location would reduce the load on the pigeons' working memory. A simpler account is that task completion is rewarding in and of itself. Tasks that can be completed quickly woo us more than tasks that must delayed. All potential tasks, or their underlying neural circuits, compete for completion. Neural circuits for tasks that get completed may endure longer than neural circuits for tasks that don't.

Another benefit of completing tasks as soon as possible is to provide us with as much information as possible about the costs and benefits of task-related behaviors. Trial-and-error learning is the most reliable way we discover what does and doesn't succeed in everyday life. Such learning can even prompt practical behavioral innovations. Given these benefits, it may be better to gain experience from several trials than only a few.

Pre-crastination clearly adds to the challenge of coping with procrastination. Not only must procrastinators start sooner to begin tasks they'd rather defer, but they must also inhibit the urge to complete small, trivial tasks that bring immediate rewards just for being completed. The discovery of pre-crastination may suggest a way to counter the ills of procrastination. Break larger tasks into smaller ones. Such smaller tasks, when completed, will promote a sense of accomplishment, will bring one closer to the final goal, and, via trial-and-error learning, may support the discovery of even more adaptive or innovative ways of behaving.

ABOUT THE AUTHOR(S)

David A. Rosenbaum, a professor of psychology at Pennsylvania State University, is the author of "It's a jungle in there: How competition and cooperation in the brain shape the mind" (Oxford University Press, 2014) and co-author of "MATLAB For Behavioral Scientists" (Routledge, 2015). Edward A. Wasserman, a professor of psychology at the University of Iowa, is the co-author of "How Animals See the World" and "Oxford Handbook of Comparative Cognition" (both published by Oxford University Press, 2012).

http://www.eurekalert.org/pub_releases/2015-06/p-iis062915.php

Innovative imaging study shows that the spinal cord learns on its own

May offer new opportunities for rehabilitation after spinal cord injury

The spinal cord engages in its own learning of motor tasks independent of the brain, according to an innovative imaging study publishing on June 30th in Open Access journal PLOS Biology. The results of the study, conducted by Shahabeddin Vahdat, Ovidui Lungu, and principal investigator Julien Doyon, of the University of Montreal, Quebec, Canada, may offer new opportunities for rehabilitation after spinal cord injury.

Learning a complex motor task, such as touch typing or playing the piano, induces changes in the brain, which can be monitored using functional magnetic resonance imaging (fMRI). During learning, sensory information and motor commands pass through the spinal cord, but to date it has been challenging to perform fMRI on the brain and spinal cord simultaneously, and thus it has been difficult to determine whether observed changes in the spinal cord during motor skill acquisition depend entirely on signals from the brain, or occur independently. That barrier was overcome for the first time in this study by taking advantage of the fact that the 3.0T MRI scanner had a field of view long enough to image the brain and the cervical spinal cord, which relays signals to and from the hand muscles. Using this technique on subjects performing a complex finger tapping task, the authors showed that learning-related changes in blood flow in the spinal cord were independent of changes in blood flow in the brain regions involved in the task.

The results of the study indicate that the spinal cord plays an active role in the very earliest stages of motor learning. Future work will be needed to confirm that

the changes seen in the spinal cord persist over time and generalize to other stages of learning and other forms of motor skills. The discovery of an independent role in learning for the spinal cord may provide new avenues for relearning motor tasks after spinal cord injury, when the connections between brain and cord are impaired.

Vahdat S, Lungu O, Cohen-Adad J, Marchand-Pauvert V, Benali H, Doyon J (2015) Simultaneous Brain-Cervical Cord fMRI Reveals Intrinsic Spinal Cord Plasticity during Motor Sequence Learning. PLoS Biol 13(6): e1002186. doi:10.1371/journal.pbio.1002186

Funding:

This work was funded by Natural Sciences and Engineering Research Council of Canada, RGPIN-2014-06318, JD http://www.nserc-crsng.gc.ca/index_eng.asp SensoriMotor Rehabilitation Research Team (SMRRT), Canadian Institutes of Health Research, RMF111622, JD http://www.cihr-irsc.gc.ca/e/193.html; and SensoriMotor Rehabilitation Research Team (SMRRT), Canadian Institutes of Health Research, postdoctoral fellowships, SV and OL; http://www.cihr-irsc.gc.ca/e/193.html. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

http://www.eurekalert.org/pub_releases/2015-06/foas-vas063015.php

Vitamin A supplementation may cause the immune system to 'forget' past infections

New research published in the Journal of Leukocyte Biology suggests that vitamin A inhibits trained immunity, leading to tolerance of the innate immune cells upon stimulation with mitogens and antigens

Although vitamin A supplementation can have profound health benefits when someone is deficient, new evidence is emerging to show that vitamin A supplementation above and beyond normal levels may have negative health consequences. A new research report published in the July 2015 issue of the Journal of Leukocyte Biology may help to explain why too much vitamin A can be harmful. Too much vitamin A shuts down the body's trained immunity, opening the door to infections to which we would otherwise be immune. This study adds to the arguments that vitamin A supplementation should only be done with clear biological and clinical arguments. Furthermore, it also suggests that low vitamin A concentrations in certain situations may even be "normal."

"This study helps to explain the mechanisms of anti-inflammatory effects of vitamin A and by doing so opens the door to identifying novel ways to modulate the immune response and restore its function in situations in which it is dysregulated," said Mihai G. Netea, M.D., Ph.D., a researcher involved in the work from the Department of Internal Medicine at Radboud University Medical Center in Nijmegen, The Netherlands.

To make this discovery, Netea and colleagues stimulated immune cells, isolated from volunteers, with Vitamin A and saw that the cells produced fewer cytokines, key proteins that help ward off microbes, upon stimulation with various mitogens and antigens. Furthermore, the cells were also stimulated with various microbial structures, which resulted in long-term activation or training of the cells. When the same experiments were performed in the presence of vitamin A, the microbial structures were no longer able to activate the immune cells.

"The interface of nutrition and immunity is an area of considerable importance, especially in an age when dietary supplements and vitamins are quite common," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "These new findings shed light on an importance balance in vitamin A levels for optimal immunity. These studies have implications for how we think about daily vitamins, but also for the developing world, where improving diet could have dramatic benefits on how the immune system is trained to respond to different infections."

Details: Rob J. W. Arts, Bastiaan A. Blok, Reinout van Crevel, Leo A. B. Joosten, Peter Aaby, Christine Stabell Benn, and Mihai G. Netea. Vitamin A induces inhibitory histone methylation modifications and down-regulates trained immunity in human monocytes. J. Leukoc. Bio.l July 2015 98:129-136; doi:10.1189/jlb.6AB0914-416R ;

http://www.jleukbio.org/content/98/1/129.abstract

http://www.eurekalert.org/pub_releases/2015-06/foas-osa063015.php

Omega-3 supplements and antioxidants may help with preclinical Alzheimer's disease

New research in The FASEB Journal suggests that clinical trials of omega-3 and antioxidant supplementation should be undertaken for people with Alzheimer's disease with mild clinical impairment

Here's more evidence that fish oil supplementation and antioxidants might be beneficial for at least some people facing Alzheimer's disease: A new report published in the July 2015 issue of The FASEB Journal describes the findings of a very small study in which people with mild clinical impairment, such as those in the very early stages of the disease, saw clearance of the hallmark amyloid-beta protein and reduced inflammation in neurological tissues. Although the findings involved just 12 patients over the course of 4 to 17 months, the findings suggest further clinical study of this relatively inexpensive and plentiful supplement should be conducted.

"Prevention of mild cognitive impairment progression is one of the best hopes," said Milan Fiala, M.D., Research Professor at the University of California's Department of Surgery in Los Angeles. "In addition to physical and mental exercises recommended by experts, this study suggests that nutrition is equally important."

To make their discovery, Fiala and colleagues investigated the effects of 4 to 17 months of supplementation with omega-3 fatty acids and antioxidants in 12 patients with minor cognitive impairment, 2 patients with pre-mild cognitive impairment, and 7 patients with Alzheimer disease. They measured the phagocytosis of amyloid-beta 1-42 by flow cytometry and microscopy, the transcription of inflammatory genes by RT-PCR, the production of resolvin D1 by enzyme immunoassay, and the cognitive status by MMSE. In patients with mild clinical impairment and pre-mild clinical impairment, phagocytosis of amyloid-beta by monocytes increased from 530 to 1306 mean fluorescence intensity units. The increase in patients with Alzheimer's disease was not significant. The lipidic mediator resolvin D1, which stimulates amyloid-beta phagocytosis in vitro, increased in macrophages in 80 percent of patients with mild clinical impairment and pre-mild clinical impairment. The transcription of inflammatory genes' mRNAs was increased in a subgroup of patients with low transcription at baseline, whereas it was not significantly changed in patients with high transcription at baseline.

"We've known for a long time that omega-3 fatty acids and some antioxidants can be beneficial to people with a wide range of health problems, as well as protective for healthy people," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Now, we know that the effects of these supplements may extend to Alzheimer's disease as well. Although these supplements are considered to be generally safe and are very easy to obtain, full-scale clinical trials are necessary to verify the findings of this research and to identify who might benefit the most."

Details: Milan Fiala, Ramesh C. Halder, Bien Sagong, Olivia Ross, James Sayre, Verna Porter, and Dale E. Bredesen. ω-3 Supplementation increases amyloid-β phagocytosis and resolvin D1 in patients with minor cognitive impairment. FASEB J. July 2015 29:2681-2689; doi:10.1096/fj.14-264218 ; http://www.fasebj.org/content/29/7/2681.abstract

http://bit.ly/1dF2hLG

Fruity Alternative to Toxic Insect Repellents

A natural compound already used in flavoring keeps flies away from blueberries

By Ida Emilie Steinmark and ChemistryWorld | June 26, 2015

A compound found in fruit could be the safe insect repellent of the future, according to a group of scientists from the University of California, Riverside in the US.

Insects annually destroy huge amounts of agricultural produce. Finding safe and effective repellents is, therefore, a top priority for agrichemical producers. In recent years interest has grown in examining plants' defences against pests, with one group, for instance, recently investigating how a plant's chemical distress signal can be converted into a weapon to combat insects.

To find alternatives to existing insecticides, the California team investigated a series of DEET substitutes that are already approved as food additives. DEET is a widely used insect repellent but has been the subject of some safety concerns and is only meant to be applied to skin and clothing.

One DEET substitute, butyl anthranilate, is found in fruit and is often used in flavours and fragrances thanks to its pleasant scent. The team found that spraying blueberries with a 10% solution of butyl anthranilate provided nearly total protection for blueberry samples from the spotted wing Drosophila. This fruit fly is a major pest and causes hundreds of millions of dollars of agricultural damage worldwide each year, meaning new ways to fight the flies are urgently needed.

Senior author Anandasankar Ray has patented the technology and wants to give farmers the option of using naturally-occurring repellents. He is also considering similar approaches to protect humans and animals from insects.

http://www.eurekalert.org/pub_releases/2015-06/uotm-sbe063015.php

Similarities between embryos and breast tumors identified

MD Anderson researchers find that metastatic tumors behave like embryonic stem cells

It may seem incredulous, but breast tumors may have something in common with embryos ... at least in mice, say researchers at The University of Texas MD Anderson Cancer Center.

A study led by Sendurai Mani, Ph.D., associate professor of Translational Molecular Pathology and Jeffrey Chang, Ph.D., assistant professor of Integrative Biology at The University of Texas Health Science Center at Houston, found that tumors that resemble six-day-old mouse embryos are more prone to metastasize than those that look like tissues from adult mice.

Specifically, they noticed that the same genes that are turned on in developing mice are also present in metastatic tumors.

Although every cell contains the same set of genes, which ones are activated are unique across tissues and medical conditions.

This pattern of activation, also called a gene expression signature, may indicate different subtypes of a disease, including those that predict disease survival or prognosis. Gene expression signatures are thought to be useful for identifying effective treatments for select groups of patients.

"Looking at the embryo to learn more about cancer is a novel and important finding for researchers," said Mani. "It is difficult to predict metastasis by merely analyzing the primary tumor and often, no mutations can be found. Clinicians still need to know whether a tumor is going to metastasize."

The researchers aimed to isolate a marker from the gene expression signature and identified one marker based on the biology of a developing embryo.

One process that is activated in early embryonic development is called the epithelial-mesenchymal transition (EMT). Tumors that form in the linings of organs known as the epithelium, which account for over 85 percent of solid tumors, can activate this complex biochemical program which leads to metastasis in the lab. They found that the EMT gene expression signature did not predict metastasis in human tumors.

A key insight to this problem is that for cancer cells to metastasize, they must change their characteristics. In the primary tumor, cancer cells must grow quickly before they stop growing and enter a "migratory state" where they disseminate to the metastatic site.

To establish tumor spread, they need to switch back to a fast-growing cell. Scientists call this ability to change characteristics "plasticity."

"Recent findings have shown that carcinomas have to shed off their EMT features and activate the reverse process, MET, in order to promote metastasis and create heterogeneous tumors at distant sites," said Mani.

Mani's team wondered if tumors likely to spread would behave like embryos, in particular, early stage embryos.

"During early stages of embryo development, this phenomenon of plasticity is more prevalent compared to that in embryos at later stages or even in adult tissues, and our findings clearly demonstrate that metastatic tumors bear remarkable similarities in gene expression profiles to that of mouse embryos at day 6.5 of early gestation," said Mani.

"Our findings clearly demonstrated that metastatic tumors are more like the embryo," he said. "We found that tumors having gene expression signatures similar to mouse embryonic development day 6.5 were more prone to develop metastasis compared to tumors with more adult-differentiated signatures."

This first-of-its-kind signature stands out in its ability to predict metastatic propensity in cancer patients by analyzing the bulk of the primary tumor rather than residual issues or scarce circulating tumor cells. More importantly, the signature is applicable to a wide class of breast tumor subtypes.

Study results were published in the June 30 issue of Nature Scientific Reports.

Other MD Anderson team members included Rama Soundararajan, Ph.D., Anurag Paranjape, Ph.D., and Valentin Barsan, M.D., all from Translational Molecular Pathology at MD Anderson.

The study was funded by the National Institutes of Health/National Cancer Institute (CA155243-01 and R00LM009837).

http://www.eurekalert.org/pub_releases/2015-06/iop-frb062915.php

Friction reduction breakthrough is no snake oil

Snake skin inspired surfaces smash records, providing an astonishing 40 percent friction reduction in tests of high performance materials

Snake skin inspired surfaces smash records, providing an astonishing 40% friction reduction in tests of high performance materials.

These new surfaces could improve the reliability of mechanical components in machines such as high performance cars and add grist to the mill of engineers designing a new generation of space exploration robots.

A paper discussing this finding is published today (1 June 2015) in IOP Publishing's Bioinspiration & Biomimetics journal.

The skin of many snakes and lizards has been studied by biologists and has long been known to provide friction reduction to the animal as it moves. It is also resistant to wear, particularly in environments that are dry and dusty or sandy.

Dr Greiner and his team used a laser to etch the surface of a steel pin so that it closely resembled the texture of snake skin. They then tested the friction created when the pin moved against another surface.

In dry conditions, i.e. with no oil or other lubricant, the scale-like surface created far less friction--40% less--than its smooth counterpart.

Lead researcher, Dr Christian Greiner said "If we'd managed just a 1% reduction in friction, our engineering colleagues would have been delighted; 40% really is a leap forward and everyone is very excited!"

Applications are likely to be in mechanical devices that are made to a micro or nano scale. Familiar examples include the sensors in car anti-lock braking systems, computer hard disk drives, and the component called an accelerometer, which means your mobile phone can tell if it is in portrait or landscape mode, and your activity band can count your steps as you move.

"Our new surface texture will mainly come into its own when engineers are really looking to push the envelope," Dr Greiner said.

The snake skin surface could be used in very high end automotive engineering, such as Formula 1 racing cars; in highly sensitive scientific equipment, including sensors installed in synchrotrons such as the Diamond Light Source in the UK or the Large Hadron Collider in Switzerland; and anywhere the engineering challenge is to further miniaturise moving parts.

There is interest in snake skin inspired materials from the robotics sector, too, which is designing robots, inspired by snakes, which could aid exploration of very dusty environments on earth or even in space. This raises a new challenge for Dr Greiner's team--to make a material that decreases friction in only one direction.

Anyone who has felt a snake's skin will know that the scales all lie in the same direction and are articulated to aid the snake in its forward motion, whilst resisting backwards motion. The steel pins tested in this research mimic only the overall surface texture of snake skin and reduce friction in at least two directions.

Dr Greiner has made some progress with polymers that even more closely mimic snake skin to reduce friction in only one direction. It is, he says, early days and this later work is not yet scheduled for publication.

The only caution is that this new surface doesn't work well in an environment where oil or another lubricant is present. In fact, the snake skin effect created three times more friction, with lubricant, than an equivalent smooth surface.

"This wasn't a huge surprise," Dr Greiner explained, "since we were looking to nature for inspiration and the species we mimicked - the royal python and a lizard called a sandfish skink--live in very dry environments and don't secrete oils or other liquids onto their skin."

The published version of the paper 'Bio-inspired scale-like surface textures and their tribological properties' (Bioinspiration Biomimetics 10 044001) will be freely available online from Tuesday 30 June. It will be available at http://iopscience.iop.org/1748-3190/10/3/044001.

http://www.eurekalert.org/pub_releases/2015-06/vu-nmo063015.php

New model of cosmic stickiness favors 'Big Rip' demise of universe

The universe can be a very sticky place, but just how sticky is a matter of debate.

That is because for decades cosmologists have had trouble reconciling the classic notion of viscosity based on the laws of thermodynamics with Einstein's general theory of relativity. However, a team from Vanderbilt University has come up with a fundamentally new mathematical formulation of the problem that appears to bridge this long-standing gap.

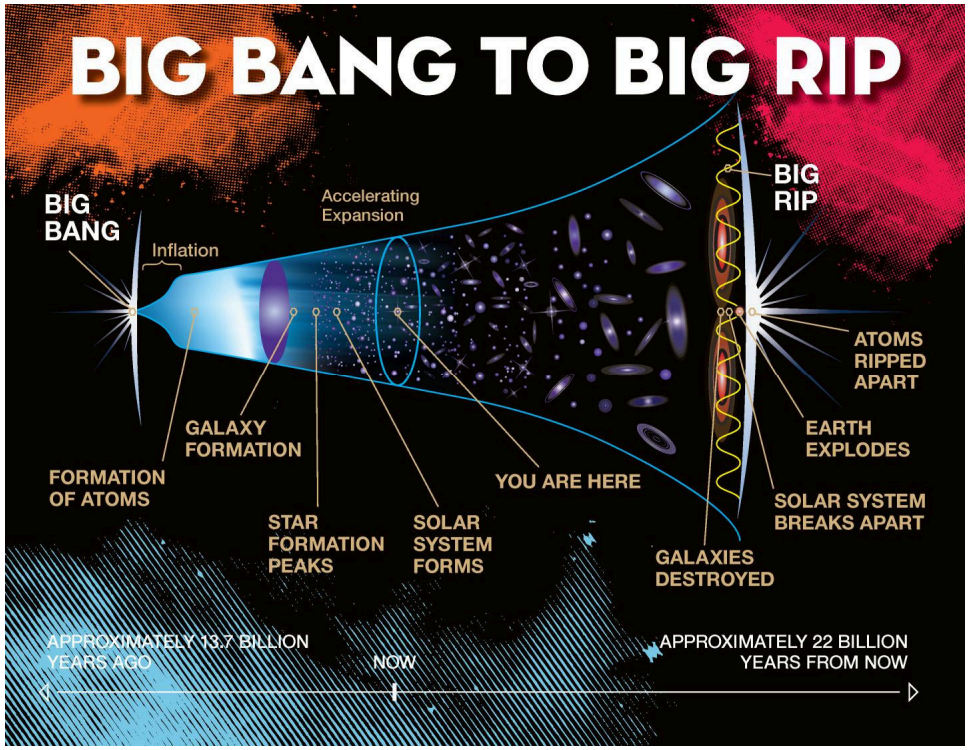
The new math has some significant implications for the ultimate fate of the universe. It tends to favor one of the more radical scenarios that cosmologists have come up with known as the "Big Rip." It may also shed new light on the basic nature of dark energy.

The new approach was developed by Assistant Professor of Mathematics Marcelo Disconzi in collaboration with physics professors Thomas Kephart and Robert Scherrer and is described in a paper published earlier this year in the journal Physical Review D.

"Marcelo has come up with a simpler and more elegant formulation that is mathematically sound and obeys all the applicable physical laws," said Scherrer.

The type of viscosity that has cosmological relevance is different from the familiar "ketchup" form of viscosity, which is called shear viscosity and is a measure of a fluid's resistance to flowing through small openings like the neck of a ketchup bottle. Instead, cosmological viscosity is a form of bulk viscosity, which is the measure of a fluid's resistance to expansion or contraction. The reason we don't often deal with bulk viscosity in everyday life is because most liquids we encounter cannot be compressed or expanded very much.

Disconzi began by tackling the problem of relativistic fluids. Astronomical objects that produce this phenomenon include supernovae (exploding stars) and neutron stars (stars that have been crushed down to the size of planets).



This is a time line of life of the universe that ends in a Big Rip. **Jeremy Teaford, Vanderbilt University**

Scientists have had considerable success modeling what happens when ideal fluids - those with no viscosity - are boosted to near-light speeds. But almost all fluids are viscous in nature and, despite decades of effort, no one has managed to come up with a generally accepted way to handle viscous fluids traveling at relativistic velocities. In the past, the models formulated to predict what happens when these more realistic fluids are accelerated to a fraction of the speed of light have been plagued with inconsistencies: the most glaring of which has been

predicting certain conditions where these fluids could travel faster than the speed of light.

"This is disastrously wrong," said Disconzi, "since it is well-proven experimentally that nothing can travel faster than the speed of light."

These problems inspired the mathematician to re-formulate the equations of relativistic fluid dynamics in a way that does not exhibit the flaw of allowing faster-than-light speeds. He based his approach on one that was advanced in the 1950s by French mathematician André Lichnerowicz.

Next, Disconzi teamed up with Kephart and Scherrer to apply his equations to broader cosmological theory. This produced a number of interesting results, including some potential new insights into the mysterious nature of dark energy.

In the 1990s, the physics community was shocked when astronomical measurements showed that the universe is expanding at an ever-accelerating rate. To explain this unpredicted acceleration, they were forced to hypothesize the existence of an unknown form of repulsive energy that is spread throughout the universe. Because they knew so little about it, they labeled it "dark energy."

Most dark energy theories to date have not taken cosmic viscosity into account, despite the fact that it has a repulsive effect strikingly similar to that of dark energy. "It is possible, but not very likely, that viscosity could account for all the acceleration that has been attributed to dark energy," said Disconzi. "It is more likely that a significant fraction of the acceleration could be due to this more prosaic cause. As a result, viscosity may act as an important constraint on the properties of dark energy."

Another interesting result involves the ultimate fate of the universe. Since the discovery of the universe's run-away expansion, cosmologists have come up with a number of dramatic scenarios of what it could mean for the future.

One scenario, dubbed the "Big Freeze," predicts that after 100 trillion years or so the universe will have grown so vast that the supplies of gas will become too thin for stars to form. As a result, existing stars will gradually burn out, leaving only black holes which, in turn, slowly evaporate away as space itself gets colder and colder.

An even more radical scenario is the "Big Rip." It is predicated on a type of "phantom" dark energy that gets stronger over time. In this case, the expansion rate of the universe becomes so great that in 22 billion years or so material objects begin to fall apart and individual atoms disassemble themselves into unbound elementary particles and radiation.

The key value involved in this scenario is the ratio between dark energy's pressure and density, what is called its equation of state parameter. If this value drops below -1 then the universe will eventually be pulled apart. Cosmologists have called this the "phantom barrier." In previous models with viscosity the universe could not evolve beyond this limit.

In the Desconzi-Kephart-Scherrer formulation, however, this barrier does not exist. Instead, it provides a natural way for the equation of state parameter to fall below -1. "In previous models with viscosity the Big Rip was not possible," said Scherrer. "In this new model, viscosity actually drives the universe toward this extreme end state."

According to the scientists, the results of their pen-and-paper analyses of this new formulation for relativistic viscosity are quite promising but a much deeper analysis must be carried out to determine its viability. The only way to do this is to use powerful computers to analyze the complex equations numerically. In this fashion the scientists can make predictions that can be compared with experiment and observation.

The research was supported by National Science Foundation grant 1305705 and Department of Energy grant DE-SC0011981.

http://www.bbc.com/news/health-33334245

Cuba stamps out mother-to-child HIV

Cuba has successfully eliminated mother-to-child transmission of both HIV and syphilis, the World Health Organization (WHO) says.

By Michelle Roberts Health editor, BBC News online

The head of the WHO, Dr Margaret Chan, called it one of the greatest public health achievements possible. It follows years of efforts to give pregnant women early access to prenatal care, testing and drugs to stop these diseases passing from mother to child. The WHO hopes other countries will be able to achieve the same.

Eliminating infections

Every year, globally, around 1.4 million women living with HIV become pregnant. Untreated, they have a 15-45% chance of transmitting the virus to their children during pregnancy, labour, delivery or breastfeeding.

That risk drops to about 1% if antiretroviral medicines are given to both mothers and their babies. And each year, nearly a million pregnant women worldwide are infected with syphilis. Again, early screening and treatment of these women can avoid complications for their unborn children.

In Cuba, according to the available official data, less than 2% of children whose mothers have HIV are born with the virus - the lowest rate possible with the available prevention methods.

Globally, seven in every 10 pregnant women living with HIV in low- and middle-income countries receive effective antiretroviral medicines to prevent transmission of the virus to their children.

Among the 22 countries that account for 90% of new HIV infections, eight have already reduced new HIV infections among children by more than 50% since 2009 (based on 2013 data) and another four are close to this mark, the WHO says. And by 2014, more than 40 countries were testing 95% or more of pregnant women in prenatal care for syphilis.

But experts say many countries must still do more to prevent and treat syphilis.

Dr Carissa Etienne, of the Pan American Health Organization, which has been working with the WHO, said: "Cuba's achievement today provides inspiration for other countries to advance towards elimination of mother-to-child transmission of HIV and syphilis."

http://www.eurekalert.org/pub_releases/2015-07/r-whe063015.php

Why human egg cells don't age well

Poorly-timed separation of paired chromosomes found to be at fault

When egg cells form with an incorrect number of chromosomes--a problem that increases with age--the result is usually a miscarriage or a genetic disease such as Down syndrome. Now, researchers at the RIKEN Center for Developmental Biology in Japan have used a novel imaging technique to pinpoint a significant event that leads to these types of age-related chromosomal errors. Published in Nature Communications, the study shows that as egg cells mature in older women, paired copies of matching chromosomes often separate from each other at the wrong time, leading to early division of chromosomes and their incorrect segregation into mature egg cells.

Most cells have two copies of each chromosome--one from each parent. Immature egg cells begin this way, but are transformed through a process called meiosis into mature egg cells that only have one copy of each chromosome. At the beginning of meiosis each chromosome copies itself and joins with its matching pair to form a group of four chromosomes that swap genetic material.

These groups of four chromosomes--called bivalents--then split apart into single pairs, and the cell divides. One part continues as the egg cell and the other part degrades. In the second stage of meiosis, the single pairs of chromosomes--two sister chromatids joined in the middle--separate and the egg cell divides again in the same way, leaving a single mature egg cell with one copy of each chromosome.

"What we found," explains team leader Tomoya Kitajima, "is that in older cells, the bivalents sometimes separate early, and this leads to division of sister chromatids in the first stage of meiosis, rather than in the second stage."

To determine the most common type of age-related segregation errors, the researchers first used a novel high resolution imaging technique to visualize chromosomes in live mouse egg cells throughout the whole first stage of meiosis. They found that chromosomes were always distributed correctly in young egg cells, but that a little less than 10% of older cells suffered from segregation errors. Closer examination of the chromosome-tracking data showed that the dominant type of error was predivision of sister chromatids, and not movement of intact chromosome pairs to only one of the new cells.

The tracking data also allowed researchers to go back in time and look at what was happening to chromosomes that eventually segregated incorrectly. They found that a large majority of them had been part of bivalents whose connection between paired chromosome copies had become hyperstretched and then snapped earlier in meiosis, leaving single pairs.

The researchers then confirmed that the number of singly paired chromosomes--also called univalents--was higher in older mouse and even human egg cells, indicating that age-related segregation errors could be tracked back to increased numbers of prematurely separated chromosome pairs. "We were surprised and pleased that the vast majority of errors are preceded by a single common event--bivalent separation," says Kitajima. "Now we can focus our efforts on developing an artificial tie to suppress premature separation and on understanding the molecular mechanism underlying the age-related reduction in bivalent cohesion that appears to precede it."

Sakakibara Y, Hashimoto S, Nakaoka Y, Kouznetsova A, Hoog C, and Kitajima TS (2015). Bivalent separation into univalents precedes age-related meiosis I errors in oocytes. Nature Communications. doi: 10.1038/ncomms8550.

http://www.eurekalert.org/pub_releases/2015-06/asoc-cfc063015.php

Citrus fruit consumption may be associated with increased melanoma risk

ASCO Perspective: Gary Schwartz, MD, ASCO Expert "This study adds to the growing discussion around food and cancer risk.

While the findings are intriguing, it's far too soon to recommend any broad changes to grapefruit or orange consumption. Until conclusive data are available, we should continue to be cautious about protecting our skin from sun exposure."

A new analysis of dietary patterns among more than 100,000 Americans suggests that frequent consumption of citrus -- namely whole grapefruit and orange juice -- may be associated with an increased risk of melanoma. Melanoma risk was 36% higher in people who consumed citrus fruit or juice at least 1.6 times daily compared to those who consumed them less than twice per week.

Consumption of grapefruit and oranges was not associated with an increased risk for any other non-skin cancers. This analysis, along with an accompanying editorial, "Dietary Advice for Melanoma: Not Ready for Prime Time," was published online today in the Journal of Clinical Oncology.

The study researchers argue that the apparent link between melanoma and citrus fruit consumption may be due to high levels of substances called furocoumarins found in citrus fruits. Prior research showed that furocoumarins make the skin more sensitive to sunlight, including to melanoma-causing ultraviolet (UV) rays.

"While our findings suggest that people who consume large amounts of whole grapefruit or orange juice may be at increased risk for melanoma, we need much more research before any concrete recommendations can be made," said lead study author Shaowei Wu, PhD, a postdoctoral research fellow at the Department of Dermatology, the Warren Alpert Medical School of Brown University in Providence, Rhode Island. "At this time, we don't advise that people cut back on citrus -- but those who consume a lot of grapefruit and/or orange juice should be particularly careful to avoid prolonged sun exposure."

The analysis included data on 63,810 women in the Nurses' Health Study (1984 - 2010) and 41,622 men in the Health Professionals Follow-Up Study (1986 - 2010). Questionnaires were mailed at various intervals to assess dietary intake (at least every four years) and collect information on medical history and lifestyle factors (every two years). For the purposes of the survey, a serving of citrus fruit was defined as the equivalent of half of a grapefruit, one orange, or a small (6 oz) glass of grapefruit or orange juice. People with a history of cancer were excluded from the analysis.

Over a follow-up period of up to 26 years, 1,840 (1.7%) study participants were diagnosed with melanoma. Higher overall citrus fruit consumption (the total number of servings of whole grapefruit, whole oranges, and juices from those fruits) was associated with increased risk of malignant melanoma in both men and women. The association was strongest for grapefruit, followed by orange juice. Conversely, and interestingly, consuming either grapefruit juice or whole oranges was not associated with melanoma risk.

Furthermore, the association between eating whole grapefruit and melanoma was independent of age and lifestyle factors, such as physical activity, cigarette smoking, alcohol and coffee intake, and use of vitamin C supplements. However, the association was more apparent among those who were more susceptible to sunburn as a child or adolescent and those who spent more time in direct sunlight.

The authors speculate that the levels of furocoumarins may be higher in whole fruit than in processed juices. They suspect that the significant effect of orange juice on melanoma risk can be explained by its consumption level, which was several times higher than any other citrus product. There was no significant association between other furocoumarin-rich foods, such as carrots and celery, and melanoma risk. "People often cook these vegetables, and heat treatment reduces the amount of furocoumarins in food," said Dr. Wu. Further research into furocoumarin levels in citrus fruit and juice and participants' blood samples is planned to confirm these hypotheses.

According to the authors, this is the first large study to investigate the link between dietary furocoumarin and melanoma risk. Prior research has shown that tanning lotions containing psoralens (a group of naturally occurring furocoumarins) increase the risk for melanoma. Long-term use of oral psoralen as part of therapy for severe psoriasis can also increase risk of melanoma.

In an accompanying editorial, Marianne Berwick, PhD, MPH, professor of the Department of Internal Medicine and Dermatology at the University of New Mexico, acknowledges that this study was quite large and data were collected prospectively. However, she identified several important limitations of the study worth noting. This includes a study population of health professionals, which is not representative of the general population.

According to Dr. Berwick, this is a potentially important study because citrus consumption is widely promoted as an important part of the diet. Citrus has demonstrated benefit for coronary heart disease, cancer prevention, and overall health effects. "At this point in time, a public overreaction leading to avoidance of citrus products is to be avoided," said Dr. Berwick. "For people who would be considered at high risk, the best course might be to advise individuals to use multiple sources of fruit and juice in the diet and to use sun protection, particularly if one is sun sensitive. There is clearly a need for replication of the study findings in a different population prior to modifying current dietary advice to the public."

This research was supported by the U.S. National Cancer Institute, National Institutes of Health.

http://www.eurekalert.org/pub_releases/2015-07/uoa-waa070115.php

Warts and all: How St. John's Wort can make you sick

St John's Wort can produce the same adverse reactions as antidepressants, and serious side effects can occur when the two are taken together, according to new University of Adelaide research.

In a study published this month in the journal, Clinical and Experimental Pharmacology and Physiology, researchers compared the pattern of spontaneous reported adverse drug reactions to St John's Wort, a herbal treatment for depression, and fluoxetine, a commonly prescribed antidepressant. They found the adverse reactions were the same for people who took St John's Wort as it was for those who took fluoxetine.

University of Adelaide pharmacology PhD student Claire Hoban says St John's Wort, like all herbal medicines, is a drug. Importantly, it is a drug that can cause

serious side effects such as dangerous increases in body temperature and blood pressure.

"There is a common belief that because something is natural and can be purchased from a health food shop without a prescription, it's safe. However, people need to start thinking of St John's Wort, and other herbal medicines, as a drug and seek advice from a qualified healthcare practitioner to be sure they use it safely," says Mrs Hoban. "It's concerning to see such severe adverse reactions in our population, when people believe they are doing something proactive for their health with little risk.

"During 2000-2013, we found 84 reports of adverse reactions to St John's Wort and 447 to fluoxetine. While there were fewer confirmed cases of side effects for St John's Wort, we know that less people use St John's Wort and adverse reactions for herbal medicines largely go unreported because they are not considered drugs.

"Furthermore, we found that the reported reactions for St John's Wort were very similar to fluoxetine, which included anxiety, panic attacks, dizziness, vomiting, amnesia and aggression," she says.

Dr Ian Musgrave says the real danger is that people can access St John's Wort without a prescription so there is no control over the dosage or what drugs people are using it with.

"Most people taking St John's Wort will not have any adverse reactions; however, those who do take it should tell their doctor and pharmacist," says Dr Musgrave.

"It's important that doctors and pharmacists know about all the drugs their patients take, not just prescription drugs, because herbal medicines like St John's Wort can have serious reactions with some pharmacy medicines, like antidepressants, the contraceptive pill and some blood thinners.

"Based on this research, I'd also like to see bottles of St John's Wort containing improved warnings of the potential adverse reactions," he says.

http://www.eurekalert.org/pub_releases/2015-07/cifa-mpe062915.php

Mitochondria, plastids evolved together into this single-celled plankton's 'eye'

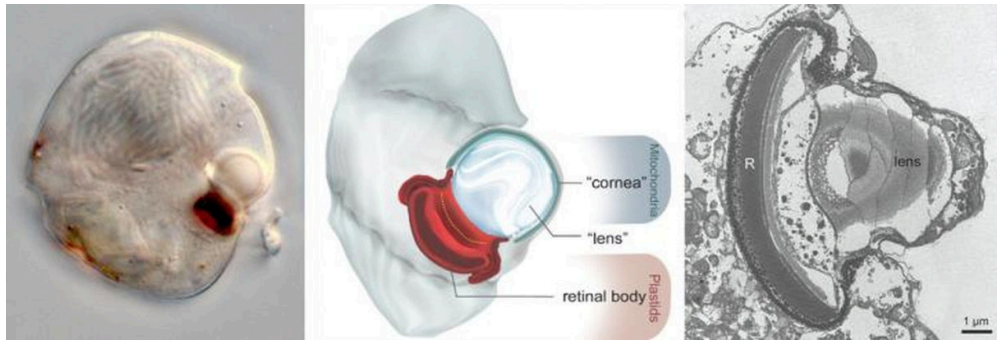
Scientists have peered into the eye-like structure of single-celled marine plankton called warnowiids and found it contains many of the components of a complex eye.

The single-cell marine plankton, a predatory microbe, bears a dark purple spot known as an ocelloid. It resembles the multicellular eye of animals so much that it was originally mistaken for part of an animal the warnowiids had eaten.

Canadian Institute for Advanced Research senior fellows Brian Leander and Patrick Keeling supervised lead author Greg Gavelis at the University of British Columbia and, in collaboration with senior fellow Curtis Suttle, showed that this eye-like structure contains a collection of sub-cellular organelles that look very much like the lens, cornea, iris and retina of multicellular eyes that can detect objects -- known as camera eyes -- that are found in humans and other larger animals.

The researchers gathered single cells of warnowiids off the coasts of B.C. and Japan, sequenced their genomes, and analyzed how the eyes are built using new methods in electron microscopy that allow the reconstruction of three dimensional structures at the subcellular level.

They found that a layer of interconnected mitochondria, organelles that supply energy to cells, surrounds a robust lens and makes up the warnowiids's equivalent of a cornea. In addition, a network of interconnected plastids that originated from an ancient symbiosis with red alga radiate from the retinal body.



Light micrograph (left), illustration (center) and transmission electron micrograph (right) show the eye-like structure in warnowiid dinoflagellates. **Hoppenrath and Leander**

Plastids have their own genome and are responsible for harvesting energy from light in photosynthetic plants and algae. The scientists determined that the retinal body contains a plastid genome suggesting components of the light-harvesting machinery may have been adapted to use in detecting light for sensory functions rather than to acquire energy.

Scientists still don't know exactly how warnowiids use the eye-like structure, but clues about the way they live have fuelled compelling speculation. warnowiids hunt other dinoflagellates, many of which are transparent. They have large nematocysts, which Leander describes as "little harpoons," for catching prey. And some have a piston -- a tentacle that can extend and retract very quickly -- with an unknown function that might be used for escape or feeding.

The team speculates that the eye-like structures help warnowiids detect their dinoflagellate prey and send chemical messages to communicate with other parts of the cell. Dinoflagellates have a uniquely large nucleus with tightly packed chromosomes that can change the polarization of light passing through them. One possibility could be that warnowiids can detect the light's orientation change as it passes through their transparent prey, showing them in which direction to hunt.

"The internal organization of the retinal body is reminiscent of the polarizing filters on the lenses of cameras and sunglasses," Leander says. "Hundreds of closely packed membranes lined up in parallel."

Definitive evidence for how ocelloids function remains elusive for now, because warnowiids are very hard to find and have never been grown in the lab. The team surmounted this problem by conducting their investigations on single cells isolated from nature. The work sheds shed new light on how very different organisms can evolve similar traits in response to their environments, a process known as convergent evolution. Eye-like structures have evolved independently many times in different kinds of animals and algae with varying abilities to detect the intensity of light, its direction, or objects.

"When we see such similar structural complexity at fundamentally different levels of organization in lineages that are very distantly related to each other, in this case warnowiids and animals, then you get a much deeper understanding of convergence," Leander says.

"The project was facilitated by combining the different expertise found in the labs of three CIFAR fellows and Tula Investigators," Leander says. These were the Suttle Lab centres on marine viruses, the Keeling Lab centres on comparative genomics, and the Leander Lab centres on evolutionary morphology. Keeling, Suttle and Leander are all part of the CIFAR program Integrated Microbial Biodiversity. The research will be published in the July 9 print issue of Nature.

http://www.eurekalert.org/pub_releases/2015-07/uoe-het062915.php

Humans evolved to be taller and faster-thinking, study suggests

People have evolved to be smarter and taller than their predecessors, a study of populations around the world suggests.

Those who are born to parents from diverse genetic backgrounds tend to be taller and have sharper thinking skills than others, the major international study has found.

Researchers analysed health and genetic information from more than 100 studies carried out around the world. These included details on more than 350,000 people from urban and rural communities.

The team found that greater genetic diversity is linked to increased height. It is also associated with better cognitive skills, as well as higher levels of education.

However, genetic diversity had no effect on factors such as high blood pressure or cholesterol levels, which affect a person's chances of developing heart disease, diabetes and other complex conditions.

Researchers from the University of Edinburgh examined individuals' entire genetic make-up. They pinpointed instances in which people had inherited identical copies of genes from both their mother and their father - an indicator that their ancestors were related. Where few instances of this occur in a person's genes, it indicates greater genetic diversity in their heritage and the two sides of their family are unlikely to be distantly related.

It had been thought that close family ties would raise a person's risk of complex diseases but the researchers found this not to be the case. The only traits they found to be affected by genetic diversity are height and the ability to think quickly. The findings suggest that over time, evolution is favouring people with increased stature and sharper thinking skills but does not impact on their propensity for developing a serious illness. The study is published in the journal Nature and was funded by the Medical Research Council.

Dr Jim Wilson, of the University of Edinburgh's Usher Institute, said: "This study highlights the power of large-scale genetic analyses to uncover fundamental information about our evolutionary history."

Dr Peter Joshi, of the University of Edinburgh's Usher Institute, said: "Our research answers questions first posed by Darwin as to the benefits of genetic diversity. Our next step will be to hone in on the specific parts of the genome that most benefit from diversity."

http://www.eurekalert.org/pub_releases/2015-07/b-epm062915.php

End pharmacists' monopoly on selling certain drugs, argues expert

A 2-tier system of prescription or non-prescription, as in the US, drugs would be simpler

Evidence is lacking that having a category of drugs that can be sold only by pharmacists or under their supervision ("pharmacy medicines") has benefits, writes a pharmacy professor in The BMJ this week.

Professor Paul Rutter at the School of Pharmacy, University of Wolverhampton, calls for an end to pharmacists' monopoly on selling some drugs and thinks that a two tier system of prescription or non-prescription drugs, like in the US, would be simpler.

He mentions the recent case of the painkiller, oral diclofenac, that used to be available as a non-prescription drug sold exclusively under the direction of a pharmacist. In January 2015, the UK drugs regulator (MRHA) announced that it

would revert to a prescription-only drug "because of a small but notably increased risk of cardiovascular side effects." This implies that, even with this system of restricted availability, "doubt exists that pharmacists (and their staff) can supervise sales to consumers appropriately," writes Rutter.

Given this decision, should any drugs still be restricted to sale only with a pharmacist's supervision, he asks?

Some may argue that the pharmacy medicines category helps pharmacists in the community to help patients care for themselves, thereby reducing doctors' workloads, adds Rutter. "But does their four to six years of drug training mean that they should have a monopoly on selling some drugs?" he writes.

Furthermore, if pharmacy is to hold a monopoly on selling some medicines it needs to show value to consumers in terms of health outcomes, when compared with consumers purchasing these drugs without restriction, he argues.

He points out that in the UK in the past four years just three drugs were switched from prescription-only control to pharmacy medicine status, but 12 pharmacy medicines were switched to general retail sale.

Without credible evidence to support the pharmacy medicines monopoly - namely, that pharmacy intervention improves patient outcomes - "it is only a matter of time before a two tier system of prescription or non-prescription drugs becomes the standard model, as in the US," argues Rutter.

Such a system, he concludes, is easy to understand: access to medicines is obtained either with a prescription or from any retail outlet. "This is less confusing for consumers and increases accessibility, but it still allows pharmacies to sell drugs and gives them a chance to demonstrate their worth."

http://www.eurekalert.org/pub_releases/2015-07/tmsh-ne070115.php

New epigenetic mechanism revealed in brain cells

Findings argue against long-held belief that histones are highly stable proteins in non-dividing cells like nerve cells

For decades, researchers in the genetics field have theorized that the protein spools around which DNA is wound, histones, remain constant in the brain, never changing after development in the womb. Now, researchers from the Icahn School of Medicine at Mount Sinai have discovered that histones are steadily replaced in brain cells throughout life - a process which helps to switch genes on and off. This histone replacement, known as turnover, enables our genetic machinery to adapt to our environment by prompting gene expression, the conversion of genes into the proteins that comprise cellular structures and carry signals in the brain. This new concept, described in a study led by researchers in the Department of Pharmacology and Systems Therapeutics at the Icahn School of Medicine at Mount Sinai, and at the Laboratory of Chromatin Biology and Epigenetics, The Rockefeller University, was published today in the journal Neuron.

The study's findings argue against the long-held belief that histones, part of the chromatin structure that package and protect genetic material in chromosomes, are highly stable proteins in non-dividing cells like nerve cells. The study authors argue that aging histones are instead constantly replaced with new histones, rather than being created once and remaining attached to DNA throughout a person's life. The newfound mechanism is epigenetic, meaning it fine-tunes gene expression without changing the DNA code we inherit from our parents.

The study results revolve around the fact that, although some cell types, such as skin cells, constantly self-destruct and are replaced in an ongoing turnover that keeps tissues viable, others, such as nerve and heart cells, are programmed to perform specific functions with complex genetic memory involved, and do not often divide. With few exceptions, humans get one supply in the womb that must last a lifetime. Therefore, these cells must be highly adaptable, able to form new connections and behave differently depending on outside factors encountered. The research team found that histone turnover regulates how genes in the brain are turned on and off in response to various stimuli, thereby allowing neurons to form new synaptic connections.

"These are very exciting results, creating a new front in the field of chromatin biology," said Ian Maze, PhD, Assistant Professor of Pharmacology and Systems Therapeutics at the Icahn School of Medicine at Mount Sinai. "By identifying this new mechanism of epigenetic regulation, or changes to gene expression caused by external and environmental factors, this work provides a novel conceptual framework for further studies aimed at identifying the molecular underpinnings of neurodevelopmental disease and psychiatric illness."

Specifically, the study examined a specific type of histone called H3.3 in human and rodent brains. H3.3 is a version of the histone H3 with a small random genetic change in its code, and thus a small difference in its protein structure. Cells with this version of H3.3 frequently turn over their histones.

To study histone composition in mouse nerve cells and related turnover, researchers fed young, post-weaning rodents a special diet containing heavy labeled lysines, a process known as staple isotope labeling of amino acids in cell cultures and live mice. When examining the nerve cells, researchers explored whether the H3.3 variant was labeled with that stable isotope ("new" histones) or if they were free of the label ("older" histones). This was accomplished by isolating individual neurons from the mice and performing mass spectrometry. The prevalence of the labeled H3.3 demonstrated the fact that the older histones had been replaced with newer ones, indicating histone turnover.

In humans, researchers used a technique called 14C/12C bomb pulse dating to measure turnover. The technique is based on the fact that high levels of radioactive carbon (14C) were released into the atmosphere during the 1950s and 1960s, when open-air nuclear bomb testing occurred following the Second World War. Researchers can take samples from cells - in this case, purified H3.3 samples from brain cells of postmortem human brains, and determine present 14C/12C ratios from the time of death against past atmospheric levels from the time of the subject's birth. As with the rodent observations, the researchers found that H3.3 turnover occurs in the human brain throughout life.

Additionally, the researchers deliberately manipulated H3.3 dynamics in both embryonic and adult neurons, confirming the role of histone turnover in neuronal plasticity. The findings thus establish histone turnover as a critical, and new, regulator of cell-type specific transcription in the brain.

"Histone turnover, shown through our work with H3.3, is essential for the behavior of brain cells," said Dr. Maze. "Furthering our understanding of how the brain works, learns, forms new memories and reacts to changes in the environment can help us to find new ways to treat neurodegenerative diseases and mental illness."

http://www.eurekalert.org/pub_releases/2015-07/rb-hcr070115.php

How cortisol reinforces traumatic memories

Stress hormone takes effect while people retrieve and reconsolidate emotional memories

The stress hormone cortisol strengthens memories of scary experiences. However, it is effective not only while the memory is being formed for the first time, but also later when people look back at an experience while the memory reconsolidates. This has been published by cognition psychologists from the Ruhr-Universität Bochum in the journal "*Neuropsychopharmacology*". They suggest that the results might explain the persistence of strong emotional memories occurring in anxiety and Post-Traumatic Stress Disorder (PTSD).

Memories of emotional experiences usually fade over time

Strong memories of stressful experiences occur frequently, but they usually fade away over time. People suffering from anxiety or Post-Traumatic Stress Disorder, however, are affected by terrifying memories that haunt them again and again. It had been shown that the stress hormone cortisol has a strengthening impact on the consolidation of memories, i.e. the several-hour process in the course of which a memory is formed immediately after the experience.

Cortisol influences the reconsolidation of emotional memories

The researchers from Bochum have demonstrated that cortisol effects memories in humans also during the so-called reconsolidation, i.e. the consolidation of memories occurring after memory retrieval. The stress hormone can enhance this process. "The results may explain why certain undesirable memories don't fade, for example in anxiety and PTSD sufferers," says Prof Dr Oliver Wolf. If a person remembering a terrifying event has a high stress hormone level, the memory of that specific event will be strongly reconsolidated after each retrieval.

The experiment

On three consecutive days, the subjects took part in the study, carried out by Shira Meir Drexler, PhD student at the International Graduate School of Neuroscience in Bochum. On the first day, they learned an association between specific geometric shapes and an unpleasant electric shock. On the second day, some of the participants were given a cortisol pill, others a placebo. Subsequently, they were shown one of the geometric shapes associated with the electric shock. On the third day, the memory for the geometric shapes was tested. Participants who had taken cortisol remembered the fear-associated shape particularly well. This was evident in a heightened skin conductance, which is an established measure for emotional arousal.

The study was financed by the DFG research group "Extinction Learning" (FOR 1581).

Bibliographic record

S.M. Drexler, C.J. Merz, T.C. Hamacher-Dang, M. Tegenthoff, O.T. Wolf (2015): Effects of cortisol on reconsolidation of reactivated fear memories, Neuropsychopharmacology, DOI: 10.1038/npp.2015.160

http://www.eurekalert.org/pub_releases/2015-07/lsoh-bov063015.php

Benefits of vitamin B12 supplements for older people questioned

Supplements offer no benefits for nervous system and brain function in older people with moderate vitamin B12 deficiency

Vitamin B12 supplements offer no benefits for neurological or cognitive function in older people with moderate vitamin B12 deficiency, according to a new study published in the American Journal of Clinical Nutrition.

Around one sixth of people in the UK aged over 75 have vitamin B12 deficiency, which when severe can lead to significant problems in the nervous system including muscle weakness, problems with walking, tiredness, and pins and needles, as well as depression and problems with memory and other important everyday cognitive functions. Vitamin B12 is found in everyday foods such as fish, meat, poultry, and dairy products.

There is clear evidence that individuals with severe vitamin B12 deficiency (with or without anaemia) benefit significantly from treatment. However, there is uncertainty about the relevance of vitamin B12 treatment in non-anaemic individuals with moderate vitamin B12 levels.

Previous studies have suggested that people with moderate vitamin B12 deficiency have poorer nerve and memory functions. The effects of daily supplementation with vitamin B12 to correct moderate deficiency on nervous system function were previously unknown.

Researchers led by Dr Alan Dangour at the London School of Hygiene & Tropical Medicine conducted a trial of 201 people aged over 75 years. Participants, who had moderate vitamin B12 deficiency and were not anaemic, received a tablet every day for one year containing either vitamin B12 or a placebo.[1] At the end of the study after 12 months of supplementation, participants undertook clinical tests to assess their nervous system function including measures of muscle strength, coordination, mobility, tests of cognitive function including memory, and of psychological health.

The researchers found no evidence of improved neurological or cognitive function among people who received vitamin B12 compared to those who received the placebo tablets.

Dr Alan Dangour, Reader in Food and Nutrition for Global Health at the London School of Hygiene & Tropical Medicine, said: "This is the first trial of the effect of vitamin B12 supplementation on neurological and cognitive function in older people with moderate vitamin B12 deficiency. Many people may be taking vitamin B12 supplements on a regular basis and it has been thought they would enhance function in older people. Our study found no evidence of benefit for nervous system or cognitive function from 12 months of supplementation among older people with moderate vitamin B12 deficiency.

"We advise older people concerned about their health and cognitive function to eat a diverse and healthy diet, keep cognitively active and when possible take regular physical activity."

The study was conducted by a team of researchers from the London School of Hygiene & Tropical Medicine, King's College London, UCL, and Oxford University.

Although the number of participants in the study was relatively small, the researchers report that it was sufficiently large to detect clinically relevant effects. The supplements contained a safe recommended dose of vitamin B12, although it is possible that the dose may have been too low to affect neurological or cognitive function, or that the supplements might be needed for several years to have an impact.

The study was funded by the Department of Health and the nutrition team at the Food Standards Agency who are now part of Public Health England. The funders had no role in the implementation, data collection, management, analysis, or interpretation of the study or in the publication of its findings.

Alan D Dangour, Elizabeth Allen, Robert Clarke, Diana Elbourne, Astrid E Fletcher, Louise Letley, Marcus Richards, Ken Whyte, Ricardo Uauy, Kerry Mills. Effects of vitamin B12 supplementation on neurological and cognitive function in older people: a randomized controlled trial. American Journal of Clinical Nutrition. DOI: 10.3945/ajcn.115.110775 Once published the paper will appear on this page: http://ajcn.nutrition.org/content/early/recent

[1]. Double-blind randomised controlled trial conducted 2008-2011. Supplements contained 1mg vitamin B12, which is greater than the minimum recommended daily intake required to correct vitamin B12 deficiency in older people. Participants had moderate vitamin B12 deficiency and were non-anaemic.

http://bit.ly/1Cd6ZM9

Chronic fatigue breakthrough offers hope for millions

Misunderstood and neglected for more than 25 years, there is suddenly new hope for people diagnosed with what was once cruelly called "yuppy flu"

HAVING a condition that no one understands is bad enough. Having one that many also doubt the existence of is worse. Yet that has been the unenviable fate of millions of people diagnosed with chronic fatigue syndrome.

CFS first entered the medical lexicon in 1988 to describe a cluster of symptoms without an obvious cause that doctors were seeing in the Lake Tahoe area of Nevada. The principal symptom was debilitating tiredness, but people also complained of sore throats, headaches, muscle pain and various other manifestations of general malaise.

The lack of a clear biological cause, the fuzziness of the symptoms and the fact that many of the people diagnosed were young professionals opened the door to a smear campaign. The media were quick to dub CFS "yuppie flu".

Although it has shaken off some of its more pejorative nicknames in recent years, CFS has struggled to lose the stigma. People with the syndrome still say they are not taken seriously, blamed for their illness, or accused of malingering. Treatments are often psychiatric, which are a great help to many but unintentionally add weight to the idea that CFS has no physical cause.

Over the years, medical groups have launched campaigns to have CFS taken more seriously. The latest was in February, when the US Institute of Medicine proposed making a clean break with the past by renaming it systemic exertion intolerance disease. This has not caught on as yet.

The unsatisfactory state of affairs is largely a reflection of the fact that we do not have a good biological explanation for CFS. That has not been for lack of trying, but even here the disease seems to be a magnet for controversy. A paper published in 2009 in *Science* claimed to have found an association between CFS and a mouse virus. The paper was later retracted after other teams failed to replicate the result.

Now there is hope of a breakthrough. Researchers in Norway have been trialling a drug normally used to knock out white blood cells in people with lymphoma and rheumatoid arthritis. Two thirds of the people who took it experienced major remission of CFS symptoms, essentially returning to normal life, with bursts of vitality unthinkable while they were ill (see "Antibody wipeout relieves symptoms of chronic fatigue syndrome").

The discovery – which sprang from a serendipitous observation – offers more than just the promise of a much-needed treatment. It also suggests that the symptoms are somehow caused by antibodies originally produced to fight off an infection. The researchers speculate that they might disrupt blood flow, leaving muscles drained of energy.

If correct, this brings the scientific story full circle. CFS was initially suspected to be a "post-viral" syndrome – the lingering after-effects of an infection with Epstein-Barr. More importantly, it could offer people diagnosed with CFS both physical relief and psychological closure.

There are wider implications too. Pain and fatigue without an obvious cause account for a large percentage of visits to the doctor, and usually have an unsatisfactory outcome. On top of that, there are many other conditions – Morgellons, for example – that struggle for credibility. If the CFS mystery is finally solved, that offers hope to countless others struggling with unexplained symptoms. It may take another serendipitous discovery, but science is good at those.

http://bit.ly/1qhtw0O

Antibody wipeout found to relieve chronic fatigue syndrome

There's now hope of a treatment for chronic fatigue syndrome

19:00 01 July 2015 by Andy Coghlan

"I was completely revitalised," says Karen. "Suddenly, I could be sociable again. I would go to work, go home, eat dinner and feel restless."

Karen (not her real name) experienced this relief from chronic fatigue syndrome while taking a drug that is usually used to treat the blood cancer lymphoma and rheumatoid arthritis (see "Karen's experience", below).

She was one of 18 people with CFS who reported improvements after taking rituximab as part of a small trial in Bergen, Norway. The results could lead to new treatments for the condition, which can leave people exhausted and housebound.

Finding a cause for CFS has been difficult. Four years ago, claims that a mouse virus was to blame proved to be unfounded, and some have suggested the disease is psychosomatic. The latest study implicates the immune system, at least in some cases. Rituximab wipes out most of the body's B-cells, which are the white blood cells that make antibodies.

Øystein Fluge and Olav Mella of the Haukeland University Hospital in Bergen noticed its effect on CFS symptoms in 2004, when they used the drug to treat lymphoma in a person who happened to also have CFS.

Several months later, the person's CFS symptoms had disappeared. A small, one-year trial in 2011 found that two-thirds of those who received rituximab experienced relief, compared with none of the control group.

The latest study, involving 29 people with CFS, shows that repeated rituximab infusions can keep symptoms at bay for years. "Eleven of the 18 responders were still in remission three years after beginning the treatment, and some have now had no symptoms for five years," says Fluge. "Suddenly, their limbs started to work again and their hands were no longer cold or sweaty."

"I am very intrigued by the rituximab story," says Nancy Klimas, an authority on CFS at Nova Southeastern University in Fort Lauderdale, Florida. "It's particularly exciting when people seem to have experienced very long periods of remission, and even speak of recovery," she says.

A crucial clue?

The researchers think the body's own antibodies are to blame in at least a proportion of people with CFS. Relief started four to six months after the first dose of rituximab, approximately the time it would take for existing antibodies to be cleared from the body. Participants relapsed after about a year - roughly how long B-cells take to regrow and start making new antibodies.

"We think the pattern of responses and relapses involves some mechanism with these antibodies," says Fluge.

An infection may trigger the body to produce antibodies that then turn against a person's own tissues, he says. His team suspect that these antibodies may stop blood from circulating properly, preventing people from getting enough oxygen, explaining their extreme fatigue.

The researchers caution that their theory is just speculation for now, but they do have some very preliminary evidence. "We think the antibodies target the blood vessel system, because patients have very low anaerobic pressure, and produce waste lactate earlier, which stops muscles working," says Mella.

If this theory turns out to be true, it would explain why people with CFS suffer muscle fatigue but show no signs of muscular abnormalities.

Clinicians who have focused on treating the disease psychiatrically have also welcomed the findings. "This uncontrolled treatment study of rituximab shows promising indications of effectiveness," says Fred Friedberg of Stony Brook University in New York.

"There is now a strong case to be made for a larger trial," says Simon Wessely of King's College London, who has treated people using cognitive behavioural

therapy. "The belief that [CFS] is all in the mind has been around since the beginning," he says. "It's tragic that it might take a study like this to take sufferers seriously."

A 150-person study is now under way, and includes a control group. While the 2011 study included a placebo, the most recent trial did not, leaving it potentially vulnerable to the placebo effect.

But Karen, for one, is convinced that the benefits of rituximab were genuine. "They were absolutely 100-per-cent real," she says. "There are some things you just can't fake."

Journal reference: PLoS One, DOI: 10.1371/journal.pone.0129898

Karen's experience

How were you before you tried rituximab?

I was really bad. I was unable to work as a teacher, I couldn't manage it any more. I just didn't have any energy. I couldn't focus, and it was painful in the joints and muscles. When I went to post a letter, it felt like I'd run a marathon.

You were unknowingly in the placebo group for the earlier trial in 2011. What was that like?

I waited, and was hoping, but nothing happened. Of course I was disappointed it didn't show any effect. I thought okay, probably I got the placebo. I wanted to finish my university degree and have a social life and job, and I couldn't.

What was it like receiving the drug in this latest study?

This time, I knew I was going to get the medicine. I was very excited, but also terrified – what if it didn't work? There's no other treatment so it was my only chance.

I got an effect quite early on. I was suddenly getting bursts of energy for maybe a half-hour or so. Then gradually I felt better. Suddenly, it was okay to keep my body upright. I restarted my master's degree and did it in half a year – I got an A. Then I started working full time. I was completely revitalised.

http://www.eurekalert.org/pub_releases/2015-07/sfeb-tci070115.php

The clock is ticking: New method reveals exact time of death after 10 days

A new method for calculating the exact time of death, even after as much as 10 days, has been developed by a group of researchers at the University of Salzburg.

Currently, there are no reliable ways to determine the time since death after approximately 36 hours. Initial results suggest that this method can be applied in forensics to estimate the time elapsed since death in humans. By observing how muscle proteins and enzymes degrade in pigs, scientists at the University of Salzburg have developed a new way of estimating time since death that functions up to at least 240 hours after death.

During the course of the study, they found that some of the proteins analysed (e.g. tropomyosin and actinin) showed no form of degradation until after 240 hours. "It is highly likely that all muscle proteins undergo detectable changes at a certain point in time, and this would extend the currently analysed timeframe even further," says Dr Peter Steinbacher, who is leading the research. .

Specific degradation products of proteins appear at a specific time after death. By studying the timing of their appearance, the researchers were able to calculate time since death.

The researchers have already started running experiments on human samples and initial results are promising: "We were able to detect similar changes and exactly the same degradation products in human muscle tissue as we had in our pig study", says Steinbacher.

The use of muscle tissue in post-mortem studies is a novel approach which presents several advantages: first, muscle tissue is the most abundant tissue of the human body and can therefore be sampled easily. Secondly, proteins in muscle tissue are well known. Thirdly, this method is simple and can deliver results within a day.

http://www.medscape.com/viewarticle/846942

Time to Become Familiar With Babesiosis?

Babesiosis is an infection that few people have encountered but may soon have a higher profile

Paul G. Auwaerter, MD

I am Paul Auwaerter with the Division of Infectious Diseases at Johns Hopkins University School of Medicine.

Babesiosis is an infection that few people have encountered unless they happen to live in the coastal areas of New England where the disease has historically been present[1] However, babesiosis may soon have a higher profile, in part because of considerations about whether to screen the US blood supply more carefully for *Babesia*.

The story begins with the *Babesia* parasite, which behaves like malaria and infects red blood cells, potentially becoming a source of febrile illness. The parasite is transmitted by the black-legged deer tick—*Ixodes scapularis*—the same vector that transmits Lyme disease. Babesiosis is much less common than Lyme disease, of which there are more than 30,000 cases annually. However, babesiosis is becoming more prominent: 1762 cases were described in 2013.[1,2] Although babesiosis is a nationally reportable disease, only 27 states have decided to

conduct passive surveillance. There are also some emerging foci of infection as this disease spreads geographically, even into Pennsylvania and Maryland.

Less well known is the fact that babesiosis is the single most common transfusion-related infection. There were 63 cases from 2004 to 2008, and more than 200 transfusion-related cases of *Babesia* have been reported since 2000.[2] In part, this is because many people who are infected by the parasite remain entirely asymptomatic and unaware that they have been bitten by a tick and that they have the parasite in their red blood cells.

Blood banks are not currently conducting uniform surveillance for *Babesia*, although some states (such as Connecticut and Rhode Island) have screened their blood supplies. The US Food and Drug Administration (FDA) recently convened a panel to explore this interesting question.[3] This is a regional disease, but it might have national significance because people travel and can donate blood in a state where the disease is not endemic. The FDA panel recommended a zero-tolerance policy, with national antibody screening of the blood supply for *Babesia microti* as well as selected molecular testing in endemic states.

Mixed modeling studies have suggested that screening would be extremely costly—more than $1 million [per quality-adjusted-life-year (QALY)] in endemic states in one study,[4] whereas another study indicated that screening would be cost-effective, at less than $50,000/QALY.[5]

It remains to be seen whether the FDA adopts the panel's recommendation. If so, then infectious disease practitioners, family medicine practitioners, and internists may find their frequent blood donors suddenly flagged for being positive for *Babesia* antibodies. Such antibodies can persist in a subset of patients for years after they have cleared the infection.[6] It does not mean that they still are infectious, [and the antibodies may be the result of cross-reactivity or false positive reactions]. These questions will come up, and the organism will have a much higher profile, if universal screening is adopted.

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A New Vaccine to Protect Against Shingles

Study looks at the efficacy of a new vaccine to protect against shingles

Hi. My name is Paul Offit, and I am talking to you today from the Vaccine Education Center at the Children's Hospital of Philadelphia. I thought it would be interesting to talk about a new study[1] that was just published in the May 28, 2015, issue of the *New England Journal of Medicine* that looked at the efficacy of a new vaccine to protect against shingles.

This vaccine is made in a manner that is different from the current vaccine. The current vaccine is made by taking the chickenpox vaccine and using about 14 times the dose. It is a live, weakened form of the varicella virus. This new vaccine is different. It is a subunit vaccine. The investigators took the glycoprotein E of varicella-zoster virus. They used 50 µg of that and added two adjuvants. One was 50 µg of monophosphoryl lipid A, which is detoxified lipid A. It is actually the same adjuvant that is used in the current Cervarix vaccine, which is a vaccine made to protect against human papillomavirus. They also took 50 µg of another adjuvant, called QS-21, which is a derivative of saponin.

The investigators tested this vaccine prospectively in 15,000 older adults who were stratified by age: 50-59 years of age, 60-69 years of age, and older than 70 years. They looked at the acquisition of shingles in these three groups over about a 3-year period. They found that in the placebo group, there were about 210 cases of shingles, whereas the vaccine group only had six. That is an efficacy of about 97%. That efficacy was found in all three groups. That is *phenomenally* good and it is actually much better than the current vaccine.

There are two issues that still need to be resolved. The first is: What is the long-term protection or longer-term protection beyond 3 years in these groups? I think those data will be generated over time. The second issue, and probably the more difficult one, is: To what extent will we be able to extend the use of an adjuvant like QS-21 in the United States? Right now in the United States, there are only two adjuvants that are licensed for use. One is the aluminum salts and the second is monophosphoryl lipid A. Although the adjuvant QS-21 has been used in other countries, it hasn't been used routinely in this country. So we will see. These are certainly very promising data.

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Long-term memories are maintained by prion-like proteins

Further evidence of a system in the brain that persistently maintains memories for long periods of time

NEW YORK, NY - Research from Eric Kandel's lab at Columbia University Medical Center (CUMC) has uncovered further evidence of a system in the brain that persistently maintains memories for long periods of time. And paradoxically, it works in the same way as mechanisms that cause mad cow disease, kuru, and other degenerative brain diseases.

In four papers published in Neuron and Cell Reports, Dr. Kandel's laboratory show how prion-like proteins - similar to the prions behind mad cow disease in cattle and Creutzfeld-Jakob disease in humans - are critical for maintaining long-term memories in mice, and probably in other mammals. The lead authors of the four papers are Luana Fioriti, Joseph Stephan, Luca Colnaghi and Bettina Drisaldi.

When long-term memories are created in the brain, new connections are made between neurons to store the memory. But those physical connections must be maintained for a memory to persist, or else they will disintegrate and the memory will disappear within days. Many researchers have searched for molecules that maintain long-term memory, but their identity has remained elusive.

These memory molecules are a normal version of prion proteins, according to research led by Nobel laureate Eric Kandel, MD, who is University Professor & Kavli Professor of Brain Science, co-director of Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute, director of the Kavli Institute for Brain Science, and senior investigator, Howard Hughes Medical Institute, at CUMC.

Prions--derived from the words protein infectious particles--are a unique class of proteins. Unlike other proteins, they are not only able to self-propagate but also to induce other proteins to take on their alternative shape. When prions form in a cell, notably in a neuron, they cause damage by grouping together in sticky aggregates that disrupt cellular processes. Prion aggregates are highly stable and accumulate in infected tissue, causing tissue damage and cell death. The dying cell releases the prion proteins, which are then taken up by other cells - and are thus considered infectious. These abnormal proteins are known to cause mad cow disease (bovine spongiform encephalopathy). They also have been linked to a variety of neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's.

In contrast, functional prion proteins can play a physiological role in the cell and do not contribute to disease. Kausik Si and Dr. Kandel first identified functional prions in the giant sea slug (Aplysia) and found they contribute to the maintenance of memory storage. More recently, the Kandel laboratory searched for and found a similar protein in mice, called CPEB3.

In one of many experiments described in the paper by Luana Fioriti, the researchers challenged mice to repeatedly navigate a maze, allowing the animals to create a long-term memory. But when the researchers knocked out the animal's CPEB3 gene two weeks after the memory was made, the memory disappeared.

The researchers then discovered how CPEB3 works inside the neurons to maintain long-term memories. "Like disease-causing prions, functional prions come in two varieties, a soluble form and a form that creates aggregates," said. Kandel. "When we learn something and form long-term memories, new synaptic connections are made, the soluble prions in those synapses are converted into aggregated prions. The aggregated prions turn on protein synthesis necessary to maintain the memory."

As long as these aggregates are present, Kandel says, long-term memories persist. Prion aggregates renew themselves by continually recruiting newly made soluble prions into the aggregates. "This ongoing maintenance is crucial," said Dr. Kandel. "It's how you remember, for example, your first love for the rest of your life."

A similar protein exists in humans, suggesting that the same mechanism is at work in the human brain, but more research is needed. "It's possible that it has the same role in memory, but until this has been examined, we won't know," said Dr. Kandel.

"There are probably other regulatory components involved," he added. "Long-term memory is a complicated process, so I doubt this is the only important factor.

The Neuron paper is titled, "The Persistence of Hippocampal-based Memory Requires Protein Synthesis Mediated by the Prion-like Protein CPEB3." The complete list of authors is: Eric Kandel, Luana Fioriti, Cory Myers, Yan-You Huang, Xiang Li, Joseph Stephan, Pierre Trifilieff, Stelios Kosmidis, Bettina Drisaldi, and Elias Pavlopoulos (all at CUMC).

This work was supported by grants from the Howard Hughes Medical Institute and the National Institutes of Health (R01 GM070934-06).

http://www.eurekalert.org/pub_releases/2015-07/pp-hsc070215.php

Hard soft coral: New genus and species of 'living fossil' octocoral related to blue coral

Discovery of a very unusual new species of octocoral from a shallow coral reef in Okinawa, Japan

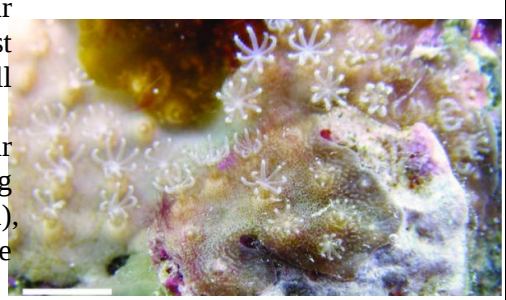
Research conducted in Okinawa, Japan, by graduate student Yu Miyazaki and associate professor James Davis Reimer from the University of the Ryukyus has found a very unusual new species of octocoral from a shallow coral reef in Okinawa, Japan. The new species can be considered a "living fossil", and is

related in many ways to the unusual blue coral. The study was published in the open access journal ZooKeys.

Unlike scleractinians, most octocorals lack a hard skeleton, and therefore many have the common name "soft coral". One exception is the endangered genus Heliopora, known as blue coral, which is found in tropical locations in the Pacific Ocean.

Blue coral forms a massive skeleton of aragonite calcium-carbonate. Due to this unique feature, blue corals have long been placed within their own special order inside the octocorals.

This new species, named Nanipora kamurai, also has an aragonite calcium-carbonate skeleton, and molecular analyses show the two groups are most closely related to each other among all octocorals.



As fossils show that blue coral and their relatives were globally distributed during the Cretaceous period 145 ± 4 to 66 mya), Heliopora and this new species can be considered "living fossils".

This is Nanipora kamurai found in Zamami Island Okinawa, Japan. Yu Miyazaki

In the past, another octocoral species with an aragonite skeleton, Epiphaxum, was discovered in 1977. Since 1977, several recent and fossil Epiphaxum specimens from the deep sea have been recorded.

Although this new species seems to be morphologically close to Epiphaxum, it is classified in a separate genus inside the same family (Lithotelestidae) due to many structural differences.

Perhaps most surprisingly, Nanipora kamurai was found from a very shallow coral reef of <1 m depth. "Most living fossils from the ocean seem to come from deeper, more stable environments" stated Miyazaki, "suggesting that there are important discoveries on coral reefs even in shallow areas still awaiting us."

"The diverse and pristine reefs of Zamami Island, which was recently included in a new national park, need to be investigated even more", he added.

The discovery of this species undoubtedly will give new insight on octocoral taxonomy.

Miyazaki Y, Reimer JD (2015) A new genus and species of octocoral with aragonite calcium-carbonate skeleton (Octocorallia, Helioporacea) from Okinawa, Japan. ZooKeys 511: 1-23. doi: 10.3897/zookeys.511.9432

http://www.bbc.com/news/science-environment-33369045

New Horizons: Pluto shows its spots to Nasa probe

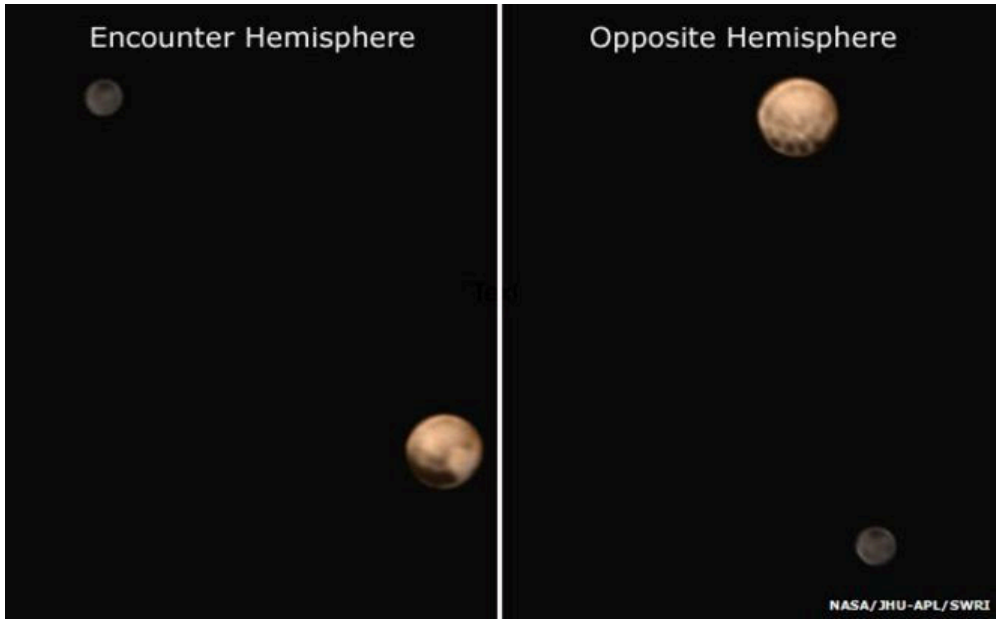
The science team on the American New Horizons mission to Pluto has released two colour views of the dwarf planet and its biggest moon, Charon.

By Jonathan Amos BBC Science Correspondent

They were made by combining pictures from the probe's high-resolution, "black and white" camera, Lorri, and its lower-resolution, colour imager known as Ralph. The difference in hue between Pluto and Charon is clear.

But what catches the eye are four dark spots on the 2,300km-wide dwarf planet. Each spot is about 500km across. Quite why they should be so similar in size and spacing is not clear. Their dominant placing is on the hemisphere that New Horizons will not see during its close flyby on 14 July. However, there should be ample opportunity to study them in the days leading up to the encounter.

"It's a real puzzle - we don't know what the spots are, and we can't wait to find out," said New Horizons principal investigator, Alan Stern, of the Southwest Research Institute. "Also puzzling is the longstanding and dramatic difference in the colours and appearance of Pluto compared to its darker and greyer moon Charon."



If, as scientists think, Pluto and Charon are the products of a collision between two primitive bodies in the early Solar System, one might expect them to look more similar. New Horizon's flyby data will hopefully provide the answer.

The US space agency (Nasa) mission is now closing in on Pluto and its five moons. The moment of closest approach on the 14th will take place at 11:49 GMT, when the probe is just 12,500km above the surface.

It is moving too fast - at 13.7km/s - to go into orbit, and it will simply scream past the dwarf and its satellites, gathering as much data as it can.

No pictures will be sent back to Earth on the day itself; the spacecraft will be too busy executing its pre-programmed observation campaign. Instead, the first images from the flyby should be presented on the following day, on 15 July.

Controllers have decided not to alter the course of the probe. They had been looking for icy debris in the vicinity of Pluto that might pose a collision hazard, but could find nothing obvious. New Horizons was commanded to make a thruster burn earlier this week, to speed it up ever so slightly. This will ensure the spacecraft reaches a precise point in space and time to carry out the pre-programmed observation sequence.

The probe must spin around to take pictures of all the different targets, and if its navigation is off by even a small amount it will be looking in the wrong direction at the critical moment. On Thursday, New Horizons was just under 15 million km from Pluto, but 4.7 billion km from Earth. The vast distance to the probe's home world means a radio signal takes about 4.5 hours from sending to receipt.

http://www.eurekalert.org/pub_releases/2015-07/tl-tlr070115.php

First trial of gene therapy for cystic fibrosis to show beneficial effect on lung function

Replaces defective gene response for cystic fibrosis by using inhaled molecules of DNA to deliver a normal working copy

For the first time gene therapy for cystic fibrosis has shown a significant benefit in lung function compared with placebo, in a phase 2 randomised trial published in The Lancet Respiratory Medicine journal. The technique replaces the defective gene response for cystic fibrosis by using inhaled molecules of DNA to deliver a normal working copy of the gene to lung cells.

"Patients who received the gene therapy showed a significant, if modest, benefit in tests of lung function compared with the placebo group and there were no safety concerns," said senior author Professor Eric Alton from the National Heart and Lung Institute at Imperial College London. "Whilst the effect was inconsistent, with some patients responding better than others, the results are encouraging." [1]

Cystic fibrosis is a rare inherited disease caused by mutations in a single gene called cystic fibrosis transmembrane conductance regulator (CFTR) and affects 1 in every 2500 newborns in the UK and over 90000 people worldwide. Scientists have discovered around 2000 CFTR mutations so far. These mutations make the lining of the lungs secrete unusually thick mucus. This leads to recurrent life-threatening lung infections, which result in lung damage that causes 90% of deaths in people with cystic fibrosis.

Since the discovery of the genetic basis for cystic fibrosis in 1989, scientists have developed a variety of viral and non-viral vector systems for delivering a corrected CFTR gene back into lung cells. Despite expectations of a rapid breakthrough, no cystic fibrosis gene therapy trial so far has been able to show long-term clinical improvement.

Coordinated by the UK Cystic Fibrosis Gene Therapy Consortium [2], the two-year study involved 136 CF patients aged 12 years or older from across the UK. Participants were randomly assigned to either 5ml of nebulised (inhaled) pGM169/GL67A (gene therapy) or saline (placebo) at monthly intervals over 1 year. Lung function was evaluated using a common clinical measure of the volume of air forcibly exhaled in one second (FEV1).

After a year of treatment, in the 62 patients who received the gene therapy, FEV1 was 3.7% greater compared to placebo [3]. This was a result of stabilisation of respiratory function rather than an improvement. However, the effects were inconsistent, with some patients responding better than others. In particular, in the half of patients with the worst lung function at the start of the study, there was a doubling of the treatment effect, with changes in FEV1 of 6.4%.

Overall, the gene therapy was well tolerated and patients in the treatment and placebo groups experienced similar rates of adverse events.

According to senior co-author Professor Stephen Hyde from the Gene Medicine Research Group at the University of Oxford, "Stabilisation of lung disease in itself is a worthwhile goal. We are actively pursuing further studies of non-viral gene therapy looking at different doses and combinations with other treatments, and more efficient vectors." [1]

Senior co-author Dr Alastair Innes from Western General Hospital, Edinburgh, UK adds, "Publication of this trial is a landmark for cystic fibrosis patients and we are particularly grateful to the many patients across the UK who gave their time and effort to participate and make this collaborative venture a success." [1]

This study was funded by a partnership between the UK Medical Research Council (MRC) and the National Institute for Health Research (NIHR).

[1] Quotes direct from authors and cannot be found in text of Article.

[2] The UK Cystic Fibrosis Gene Therapy Consortium is a group of scientists and clinicians from Imperial College London, the Universities of Oxford and Edinburgh, the Royal Brompton and Harefield NHS Foundation Trust and NHS Lothian who have worked together for over fifteen years to develop gene therapy for CF supported by the Cystic Fibrosis Trust http://www.cfgenetherapy.org.uk/index.php

[3] *The 95% confidence interval for the effect size is 0.1% to 7.3%. Thus, although the best estimate of the effect size is 3.7%, the data are consistent with the true effect size lying anywhere in the range 0.1% to 7.3%. This interval straddles values from no effect to clear clinical relevance.*

http://www.bbc.com/news/health-33362472

Sniffing could provide autism test

The way children sniff different aromas could form the basis of a test for autism, suggest researchers in Israel.

By James Gallagher Health editor, BBC News website

People spend longer inhaling the delightful aroma of a bouquet of roses than the foul stench of rotting fish. The results of tests on 36 children, in the journal Current Biology, showed that there appeared to be no such difference in children with autism.

The National Autistic Society said smell could eventually become an additional tool for testing for autism. Behaviour, social interactions and communication skills are all affected by autism and the disorder affects one in every 160 children globally. It often takes until a child is at least two before it can be diagnosed.

'Somewhat surprising'

The children in the trial at the Weizmann Institute of Science took part in a 10-minute experiment. A red tube sent either pleasant or unpleasant odours up the nose while the green tube recorded changes in breathing patterns.

One of the researchers, PhD student Liron Rozenkrantz, said children normally altered the depth of their sniffing to the odours. She told the BBC: "Children with autism didn't show this modulation at all - they took the same sniff for the smell of shampoo as they did for rotten fish. "This is striking and somewhat surprising."

The team developed a computer program that could detect autism in the group of children with 81% accuracy. They also showed that the more severe the symptoms of autism, the longer the children inhaled the unpleasant smells.

Early testing

The earlier autism is diagnosed, the sooner children can get access to behavioural or educational interventions. The team at the Weizmann Institute of Science said that one of the advantages of a sniffing test was that it did not rely on the child being able to communicate so it may be useful at a very early age.

Miss Rozenkrantz added: "But before we can use it as a diagnostic test, we need to know at what age children start to develop a sniff response in the general population. "Are you born with it? Do you develop it later in life? No-one has looked at it yet. "I think what we have an interesting place to start, but we do have a way to go."

The researchers said smells had a role in social interaction and that this may explain the link with autism.

Dr Judith Brown, from the UK's National Autistic Society, said: "Getting a diagnosis is a crucial step to unlocking vital support services which can make a huge difference to people on the autism spectrum and their families.

"We believe that the possibility of developing a single and universal diagnostic test for autism is unlikely. "However, in future, if these initial findings are confirmed and fully understood, differences relating to processing smell may offer an additional tool in the necessarily multi-faceted process of diagnosing autism."

http://www.eurekalert.org/pub_releases/2015-07/du-owm070115.php

Old World monkey had tiny, complex brain

Findings suggest that brain complexity can evolve before brain size in primates

DURHAM, N.C. -- The brain hidden inside the oldest known Old World monkey skull has been visualized for the first time. The creature's tiny but remarkably wrinkled brain supports the idea that brain complexity can evolve before brain size in the primate family tree.

The ancient monkey, known scientifically as Victoriapithecus, first made headlines in 1997 when its fossilized skull was discovered on an island in Kenya's Lake Victoria, where it lived 15 million years ago.

Now, thanks to high-resolution X-ray imaging, researchers have peered inside its cranial cavity and created a three-dimensional computer model of what the animal's brain likely looked like. Micro-CT scans of the creature's skull show that Victoriapithecus had a tiny brain relative to its body.

Co-authors Fred Spoor of the Max Planck Institute for Evolutionary Anthropology and Lauren Gonzales of Duke University calculated its brain volume to be about 36 cubic centimeters, which is less than half the volume of monkeys of the same body size living today.

If similar-sized monkeys have brains the size of oranges, the brain of this particular male was more akin to a plum.

The brain hidden inside the oldest known Old World monkey skull has been visualized for the first time. The ancient monkey, known as Victoriapithecus, first made headlines in 1997 when its 15 million-year-old skull was discovered on an island in Kenya's Lake Victoria. Now, thanks to high-resolution X-ray imaging, researchers have peered inside its cranial cavity and created a three-dimensional computer model of what the animal's brain likely looked like. Its tiny but remarkably wrinkled brain supports the idea that brain complexity can evolve before brain size in the primate family tree. The creature's fossilized skull is now

part of the permanent collection of the National Museums of Kenya in Nairobi. **Photo courtesy of Fred Spoor of the Max Planck Institute for Evolutionary Anthropology.**

"When Lauren finished analyzing the scans she called me and said, 'You won't believe what the brain looks like,'" said co-author Brenda Benefit of New Mexico State University, who first discovered the skull with NMSU co-author Monte McCrossin.

Despite its puny proportions, the animal's brain was surprisingly complex.

The CT scans revealed numerous distinctive wrinkles and folds, and the olfactory bulb -- the part of the brain used to perceive and analyze smells -- was three times larger than expected.

"It probably had a better sense of smell than many monkeys and apes living today," Gonzales said. "In living higher primates you find the opposite: the brain is very big, and the olfactory bulb is very small, presumably because as their vision got better their sense of smell got worse."

"But instead of a tradeoff between smell and sight, Victoriapithecus might have retained both capabilities," Gonzales said.

The findings, published in the July 3 issue of Nature Communications, are important because they offer new clues to how primate brains changed over time, and during a period from which there are very few fossils.

"This is the oldest skull researchers have found for Old World monkeys, so it's one of the only clues we have to their early brain evolution," Benefit said.

In the absence of fossil evidence, previous researchers have disagreed over whether primate brains got bigger first, and then more folded and complex, or vice versa.

"In the part of the primate family tree that includes apes and humans, the thinking is that brains got bigger and then they get more folded and complex," Gonzales said. "But this study is some of the hardest proof that in monkeys, the order of events was reversed -- complexity came first and bigger brains came later."

The findings also lend support to claims that the small brain of the human ancestor Homo floresiensis, whose 18,000-year-old skull was discovered on a remote Indonesian island in 2003, isn't as remarkable as it might seem. In spite of their pint-sized brains, Homo floresiensis was able to make fire and use stone tools to kill and butcher large animals.

"Brain size and brain complexity can evolve independently; they don't have to evolve together at the same time," Benefit said.

The work was funded by the Max Planck Society and University College London. The skull was originally discovered with support from the National Science foundation (9505778).

CITATION: "Cerebral Complexity Preceded Enlarged Brain Size and Reduced Olfactory Bulbs in Old World Monkeys," L. Gonzales, B. Benefit, M. McCrossin and F. Spoor. Nature Communications, July 2015. DOI: 10.1038/ncomms8580.

http://www.bbc.com/news/science-environment-33380677

Peeking into the brain's filing system

Aspects of a single memory can be scattered throughout the outer "cortex" of the brain

By Jonathan Webb Science reporter, BBC News

Storing information so that you can easily find it again is a challenge. From purposefully messy desks to indexed filing cabinets, we all have our preferred systems. How does it happen inside our brains?

Somewhere within the dense, damp and intricate 1.5kg of tissue that we carry in our skulls, all of our experiences are processed, stored, and - sometimes more readily than others - retrieved again when we need them.

It's what neuroscientists call "episodic memory" and for years, they have loosely agreed on a model for how it works. Gathering detailed data to flesh out that model is difficult. But the picture is beginning to get clearer and more complete.

A key component is the small, looping structure called the hippocampus, buried quite deep beneath the brain's wrinkled outer layer. It is only a few centimetres in length but is very well connected to other parts of the brain. People with damage to their hippocampus have profound memory problems and this has made it a major focus of memory research since the 1950s.

Quick learning

It was in the hippocampus, and some of its neighbouring brain regions, that scientists from the University of Leicester got a glimpse of new memories being formed, in a study published this week. They used a rare opportunity to record the fizz and crackle of single human brain cells at work, in epilepsy patients undergoing brain surgery.

Individual neurons that went crazy for particular celebrities, like Clint Eastwood, could be "trained" to respond to, for example, the Statue of Liberty as well - as soon as the patients were given a picture of Clint in front of the statue.

It seemed that single brain cells, in the hippocampus, had been caught in the act of forming a new association. And they do it very fast.

But that outer wrapping of the brain - the cortex - is also important. It is much bigger than the hippocampus and does myriad jobs, from sensing the world to moving our limbs. When we have a particular experience, like a trip to the beach, different patches of the cortex are called up to help us process different elements: recognising a friend, hearing the seagulls, feeling the breeze.

So traces of that experience are rather scattered across the cortex. To remember it, the brain needs some sort of index to find them all again. And that, neuroscientists generally agree, is where the hippocampus comes in.

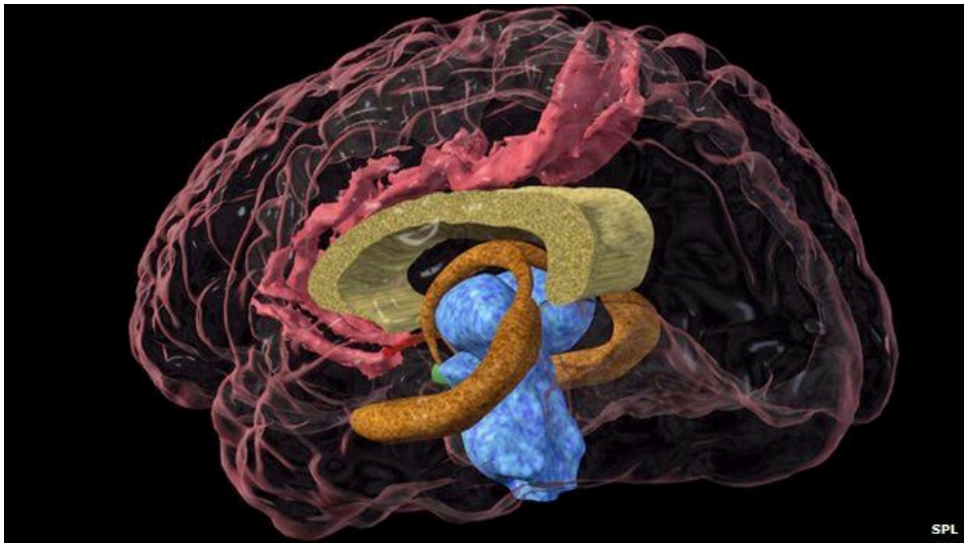
"Think of the [cortex] as a huge library and the hippocampus as its librarian," wrote the prominent Hungarian neuroscientist Gyorgy Buszaki in his 2006 book Rhythms of the Brain.

The elements of our day at the beach might litter the cortex like specific books along miles of shelving; the hippocampus is able to link them together and - if all goes well - pull them off the shelf when we want to reminisce.

Completing patterns

Another brand new study, out this week in the journal Nature Communications, looks inside the brain using fMRI imaging to see this filing system in action.

By getting people to learn and remember imaginary scenarios while inside a brain scanner, Dr Aidan Horner and his colleagues at University College London collected the first firm evidence for "pattern completion" in the human hippocampus.



The hippocampus (darker brown) is centrally located and very well connected

Pattern completion is the mechanism behind a phenomenon we all recognise, when one particular aspect of a memory - the smell of salt in the air, perhaps - brings all the other aspects flooding back.

"If you have an event that involves the Eiffel tower, your friend and, say, a pink balloon… I can show you a picture of the Eiffel tower, and you remember not only your friend, but also the pink balloon," Dr Horner told the BBC.

While his volunteers had just this sort of experience inside the scanner, Dr Horner saw interplay between different parts of the cortex, associated with different parts of a memory, and the hippocampus.

The brain activity flowed in a way that showed "pattern completion" was indeed underway - and the cortex and the hippocampus were working just like the library and the librarian in Prof Buzsaki's analogy.

"If I cue you with the location, and I get you to explicitly retrieve the person, what we also see is activation in the region that's associated with the object for that event," Dr Horner explained. "So even though it's task-irrelevant, you don't have to retrieve it, it seems that we still bring that object to mind.

"And the extent to which we see that activation in the 'object' region correlates with the hippocampal response. So that suggests that it's the hippocampus that's doing the pattern completion, retrieving all these elements. "It's able to act as an index, I suppose, by linking these things together - and doing it very very quickly, that's the key thing."

If the cortex were left to make its own connections between the fragments of a memory, he added, it would be far too slow. "That's clearly not a system we want, if we're going to remember a specific event that happens once in a lifetime."

Dr Horner said the findings also dovetail nicely with the single-neuron, celebrity-spotting results from the Leicester study. "We can look across the cortex and the hippocampus, and we can relate it to recollection. But what they can do is say look, these cells [in the hippocampus] have learned really quickly. "So that's the sort of underlying neural basis of what we're looking at, at a slightly broader scale."

Science, it seems, is finally managing to unpick the way our brains record our lives. It is a remarkable, beautiful, fallible system. Building some sort of memory storage like this is regarded as one of the next key challenges for researchers trying to build intelligent machines. Our own memories, for all their flaws, are a hard act to follow.