http://www.eurekalert.org/pub_releases/2016-05/d-qc-ndp050216.php

Neuroscientists discover previously unknown function of cannabinoid receptor

Study could improve our insights into brain diseases

The cannabinoid type 2 receptor - also called "CB2 receptor" - is a special membrane protein. Its function is to receive chemical signals that control cellular activity. "Until now, this receptor was considered part of the immune system without function in nerve cells. However, our study shows that it also plays an important role in the signal processing of the brain," explains Professor Dietmar Schmitz, Speaker for the DZNE-Site Berlin and Director of the Neuroscience Research Center of the Charité (NWFZ/NeuroCure). Schmitz coordinated the current study, which involved Berlin colleagues and also scientists from the University of Bonn and from the "National Institute on Drug Abuse" of the US.

As the researchers demonstrated in an animal model, the CB2 receptor raises the excitation threshold of nerve cells in the hippocampus. "Operation of the brain critically depends on the fact that nerve impulses sometimes have an exciting impact on downstream cells and in other cases they have a suppressing effect," says Dr Vanessa Stempel, lead author of the current publication, who is now doing research in Cambridge, UK. "The CB2 receptor works like a set screw by which such communication processes can be adjusted."

Component of the "endocannabinoid system"

The CB2 receptor is part of the endocannabinoid system (ECS). This family of receptors and signaling substances exists in many organisms including humans. It is a biochemical control system which is involved in the regulation of numerous physiological processes. Its name refers to the fact that chemicals derived from the cannabis plant bind to receptors of the ECS. So far, there are two known types of these receptors: The CB2 receptor has no psychoactive effect. Hence, the mind-altering effects triggered by the consumption of cannabis are ascribed to the "cannabinoid type 1 receptor".

Potential therapeutic applications

The results of the current study could contribute to a better understanding of disease mechanisms and provide a starting point for novel medications. "Brain activity is disturbed in schizophrenia, depression, Alzheimer's disease and other neuropsychiatric disorders. Pharmaceuticals that bind to the CB2 receptor could possibly influence the activity of brain cells and thus become part of a therapy," Professor Schmitz concludes.

Cannabinoid type 2 receptors mediate a cell type-specific plasticity in the hippocampus", A. Vanessa Stempel, Alexander Stumpf, Hai-Ying Zhang, Tugba Özdogan, Ulrike Pannasch, Anne-Kathrin Theis, David-Marian Otte, Alexandra Wojtalla, Ildikó Rácz, Alexey Ponomarenko, Zheng-Xiong Xi, Andreas Zimmer, Dietmar Schmitz, Neuron, http://www.cell.com/neuron/fulltext/S0896-6273(16)30025-3 (DOI: 10.1016/j.neuron.2016.03.034)

http://www.eurekalert.org/pub_releases/2016-05/sdmc-oos050216.php

Origin of synaptic pruning process linked to learning, autism and schizophrenia identified

Findings may suggest new approaches to treatments

Brooklyn, NY - Research led by SUNY Downstate Medical Center has identified a brain receptor that appears to initiate adolescent synaptic pruning, a process believed necessary for learning, but one that appears to go awry in both autism and schizophrenia.

Sheryl Smith, PhD, professor of physiology and pharmacology at SUNY Downstate, explained, "Memories are formed at structures in the brain known as dendritic spines that communicate with other brain cells through synapses. The number of brain connections decreases by half after puberty, a finding shown in many brain areas and for many species, including humans and rodents."

This process is referred to as adolescent "synaptic pruning" and is thought to be important for normal learning in adulthood. Synaptic pruning is believed to remove unnecessary synaptic connections to make room for relevant new memories, but because it is disrupted in diseases such as autism and schizophrenia, there has recently been widespread interest in the subject.

Dr. Smith continued, "Our report is the first to identify the process which initiates synaptic pruning at puberty. Previous studies have shown that scavenging by the immune system cleans up the debris from these pruned connections, likely the final step in the pruning process.

"Working with a mouse model we have shown that, at puberty, there is an increase in inhibitory GABA receptors, which are targets for brain chemicals that quiet down nerve cells. We now report that these GABA receptors trigger synaptic pruning at puberty in the mouse hippocampus, a brain area involved in learning and memory." The report, published by eLife, "Synaptic pruning in the female hippocampus is triggered at puberty by extrasynaptic GABAA receptors on dendritic spines," (Afroz, S., Parato, J., Shen, H. and Smith, S.S.), is online at: http://dx.doi.org/10.7554/eLife.15106.

Dr. Smith adds that by reducing brain activity, these GABA receptors also reduce levels of a protein in the dendritic spine, kalirin-7, which stabilizes the scaffolding in the spine to maintain its structure. Mice that do not have these receptors maintain the same high level of brain connections throughout adolescence.

Dr. Smith points out that the mice with too many brain connections, which do not undergo synaptic pruning, are able to learn spatial locations, but are unable to re-

learn new locations after the initial learning, suggesting that too many brain connections may limit learning potential.

These findings may suggest new treatments targeting GABA receptors for "normalizing" synaptic pruning in diseases such as autism and schizophrenia, where synaptic pruning is abnormal. Research has suggested that children with autism may have an over-abundance of synapses in some parts of the brain. Other research suggests that prefrontal brain areas in persons with schizophrenia have fewer neural connections than the brains of those who do not have the condition.

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http://www.eurekalert.org/pub_releases/2016-05/ifri-doa050216.php

Discovery of a fundamental limit to the evolution of the genetic code

A study performed at IRB Barcelona offers an explanation as to why the genetic code, the dictionary used by organisms to translate genes into protein, stopped growing 3,000 million years ago.

Nature is constantly evolving--its limits determined only by variations that threaten the viability of species. Research into the origin and expansion of the genetic code* are fundamental to explain the evolution of life. In Science Advances, a team of biologists specialised in this field explain a limitation that put the brakes on the further development of the genetic code, which is the universal set of rules that all organisms on Earth use to translate genetic sequences of nucleic acids (DNA and RNA) into the amino acid sequences that comprise the proteins that undertake cell functions.

Headed by ICREA researcher Lluís Ribas de Pouplana at the Institute for Research in Biomedicine (IRB Barcelona) and in collaboration with Fyodor A. Kondrashov, at the Centre for Genomic Regulation (CRG) and Modesto Orozco, from IRB Barcelona, the team of scientists has demonstrated that the genetic code evolved to include a maximum of 20 amino acids and that it was unable to grow further because of a functional limitation of transfer RNAs--the molecules that serve as interpreters between the language of genes and that of proteins. This halt in the increase in the complexity of life happened more than 3,000 million years ago, before the separate evolution of bacteria, eukaryotes and archaebacteria, as all organisms use the same code to produce proteins from genetic information.

The authors of the study explain that the machinery that translates genes into proteins* is unable to recognise more than 20 amino acids because it would confuse them, which would lead to constant mutations in proteins and thus the erroneous translation of genetic information "with catastrophic consequences", in Ribas' words. "Protein synthesis based on the genetic code is the decisive feature of biological systems and it is crucial to ensure faithful translation of information," says the researcher.

A limitation imposed by shape

Saturation of the genetic code has its origin in transfer RNAs (tRNAs*), the molecules responsible for recognising genetic information and carrying the corresponding amino acid to the ribosome, the place where chain of amino acids are made into proteins following the information encoded in a given gene. However, the cavity of the ribosome into which the tRNAs have to fit means that these molecules have to adopt an L-shape, and there is very little possibility of variation between them.

"It would have been to the system's benefit to have made new amino acids because, in fact, we use more than the 20 amino acids we have, but the additional ones are incorporated through very complicated pathways that are not connected to the genetic code. And there came a point when Nature was unable to create new tRNAs that differed sufficiently from those already available without causing a problem with the identification of the correct amino acid. And this happened when 20 amino acids were reached," explains Ribas.

Application in synthetic biology

One of the goals of synthetic biology is to increase the genetic code and to modify it to build proteins with different amino acids in order to achieve novel functions. For this purpose, researchers use organisms such as bacteria in highly controlled conditions to make proteins of given characteristics.

"But this is really difficult to do and our work demonstrates that the conflict of identify between synthetic tRNAs designed in the lab and existing tRNAs has to be avoided if we are to achieve more effective biotechnological systems," concludes the researcher.

This study has been funded by the Ministry of the Economy and Competitiveness, the Generalitat de Catalunya, the European Research Council (ERC) and the Howard Hughes Medical Institute in the US.

Reference article:

Saturation of recognition elements blocks evolution of new tRNA identities

Adélaïde Saint-Léger, Carla Bello-Cabrera, Pablo D. Dans, Adrian Gabriel Torres, Eva Maria Novoa, Noelia Camacho, Modesto Orozco, Fyodor A. Kondrashov, and Lluís Ribas de Pouplana

Science Advances (29 April 2016). DOI: 10.1126/sciadv.1501860

http://www.bbc.com/news/health-36168717

Breast cancer: Scientists hail 'milestone' genetic find

Scientists say they now have a near-perfect picture of the genetic events that cause breast cancer.

By James Gallagher Health editor, BBC News website

The study, published in Nature, has been described as a "milestone" moment that could help unlock new ways of treating and preventing the disease.

The largest study of its kind unpicked practically all the errors that cause healthy breast tissue to go rogue. Cancer Research UK said the findings were an important stepping-stone to new drugs for treating cancer.

To understand the causes of the disease, scientists have to understand what goes wrong in our DNA that makes healthy tissue turn cancerous.

The international team looked at all 3 billion letters of people's genetic code - their entire blueprint of life - in 560 breast cancers.

They uncovered 93 sets of instructions, or genes, that if mutated, can cause tumours. Some have been discovered before, but scientists expect this to be the definitive list, barring a few rare mutations.

'Important information'

Prof Sir Mike Stratton, the director of the Sanger Institute in Cambridge which led the study, said it was a "milestone" in cancer research.

He told the BBC: "There are about 20,000 genes in the human genome. It turns out, now we have this complete view of breast cancer - there are 93 of those [genes] that if mutated will convert a normal breast cell into a breast cancer cell. That is an important piece of information.

"We hand that list over to the universities, the pharmaceuticals, the biotech companies to start developing new drugs because those mutated genes and their proteins are targets for new therapeutics.

"There are now many drugs that have been developed over the last 15 years against such targets which we know work." Targeted drugs such as Herceptin are already being used by patients with specific mutations.

Prof Stratton expects new drugs will still take at least a decade to reach patients and warns: "Cancers are devious beasts and they work out ways of developing resistance to new therapeutics so overall I'm optimistic, but it's a tempered optimism." There is also bad news in the data - 60% of the mutations driving cancer are found in just 10 genes.

At the other end of the spectrum, there are mutations so rare they are in just a tiny fraction of cancers meaning it is unlikely there will be any financial incentive to develop therapies. But why do those genes mutate in the first place?

Mutations leave unique scars - known as mutational signatures - on our DNA and that allowed the team to identify 12 types of damage that cause mutations in the breast. Some are related to family risk, but most are still unexplained.

One class of mutation seems to stem from the body attacking viruses by mutating their genetic code, but also suffering collateral damage in the process.

Whether any of these processes can be altered is still unknown in this nascent field, but researchers hope the findings could eventually lead to ways of reducing the risk of cancers.

Dr Serena Nik-Zainal, another researcher at the Sanger Institute, added: "In the future, we'd like to be able to profile individual cancer genomes so that we can identify the treatment most likely to be successful for a woman or man diagnosed with breast cancer. "It is a step closer to personalised health care for cancer."

Dr Emma Smith, from Cancer Research UK, said: "This study brings us closer to getting a complete picture of the genetic changes at the heart of breast cancer and throws up intriguing clues about the key biological processes that go wrong in cells and drive the disease.

"Understanding these underlying processes has already led to more effective treatments for patients, so genetic studies on this scale could be an important stepping stone towards developing new drugs and boosting the number of people who survive cancer."

http://bit.ly/1TmcutV

Nearby Star Harbors Trio of Earth-Size Worlds

Astronomers speculate that the three planets orbiting the small, cool star TRAPPIST-1 could support life

By Charles Q. Choi, SPACE.com on May 3, 2016

On May 2, 2016, scientists announced the discovery of TRAPPIST-1, an alien solar system 40 light-years from Earth with a tiny, ultracool dwarf star and three small exoplanets that just might be habitable.

Three potentially habitable Earth-size planets have been discovered orbiting a dim, cold nearby star that is barely larger than Jupiter, researchers say.

"These kinds of tiny, cold stars may be the places we should first look for life elsewhere in the universe, because they may be the only places where we can detect life on distant Earth-sized planets with our current technology," study lead author Michaël Gillon, an astronomer at the University of Liège in Belgium, told Space.com.

Astronomers focused on a star originally named 2MASS J23062928-0502285 that was discovered using TRAPPIST (TRAnsiting Planets and PlanetesImals Small Telescope), a telescope in Chile. This dim cold red star, now known as TRAPPIST-1, is located in the constellation of Aquarius about 39 light-years from

Earth. In comparison, Alpha Centauri, the nearest star system, is about 4.3 light-years from Earth.

TRAPPIST-1 is 2,000 times less bright than the sun, a bit less than half as warm as the sun, about one-twelfth the sun's mass, and less than one-eighth the sun's width, making it only slightly larger in diameter than Jupiter. TRAPPIST-1 is a type of star known as an ultracool dwarf that is very common in the Milky Way, making up about 15 percent of the stars near the sun.

Scientists spotted the three planets by observing TRAPPIST-1 dimming at regular intervals as the worlds crossed in front of it. This is the first time that distant planets, called exoplanets, have been found around an ultracool dwarf, the researchers said.

"So far, the existence of such 'red worlds' orbiting ultracool dwarf stars was purely theoretical, but now we have not just one lonely planet around such a faint red star, but a complete system of three planets," study co-author Emmanuël Jehin, an astronomer at the University of Liège, said in a statement.

These three planets are each only about 10 percent larger in diameter than Earth. "The kind of planets we've found are very exciting from the perspective of searching for life in the universe beyond Earth," study co-author Adam Burgasser at the University of California, San Diego, said in a statement.

The two innermost planets are about 60 to 90 times closer to their star than the Earth to the sun, with orbits only 1.5 and 2.4 days long, respectively. The orbit of the third planet is currently less certain, ranging between 4.5 and 73 days long. The small size of the star and its planets' orbits means "the structure of this planetary system is much more similar in scale to the system of Jupiter's moons than to that of the solar system," Gillon said in the statement.

Although all three planets orbit very near their star, the inner two planets receive only four times and two times, respectively, the amount of radiation that Earth receives, since their star is much fainter than the sun. The third outer planet probably receives less radiation than Earth does, the researchers said.

Given how close TRAPPIST-1's trio of planets are to its star, the researchers suggest TRAPPIST-1's gravitational pull likely forced these worlds to become "tidally locked" to it. When a planet is tidally locked to its star, it will always show the same side to its star, just as the moon always shows the same face to Earth. This causes those worlds to each have one permanent dayside and one permanent nightside.

The third of TRAPPIST-1's planets, the one farthest from the star, may lie within the star's habitable zone — the area around a star where planets have surfaces warm enough to have liquid water, a key ingredient to life as it is known on Earth. The two planets closest to TRAPPIST-1 may have daysides that are too hot and nightsides that are too cold to host any kind of life as it is known on Earth, but the researchers suggest that the borders of the planets' day- and nightsides may be sweet spots temperate enough for life.

For the most part, exoplanet-hunting missions have focused on finding systems around sun-like stars emitting visible light, but these stars can be so bright, they can drown out key features of their planets, the researchers said. In contrast, cold dwarf stars emit mostly infrared light, and are so faint they would not overwhelm details of their planets. TRAPPIST was designed to look for planets around 60 nearby ultracool dwarfs. [7 Ways to Discover Alien Planets]

"The detection of these planets [around TRAPPIST-1] should intensify the search for more systems around ultracool dwarfs," Gillon said. "Exciting scientific adventures are now beginning."

Since the planets around TRAPPIST-1 are relatively nearby, scientists can in principle analyze the compositions of their atmospheres, "and further down the road, which is within our generation, assess if they are actually inhabited," study co-author Julien de Wit, a planetary scientist at Massachusetts Institute of Technology, said in a statement. "All of these things are achievable, and within reach now. This is a jackpot for the field."

The masses of these worlds remain unknown, but future research can pinpoint how much each of these planets gravitationally pulls at its siblings when they get close to each other, Gillon said. The strength of each planet's gravitational pull will help scientists deduce its mass, which in turn will help them estimate the planets' densities and, thus, compositions, he added.

"We can tell if the planets are probably rocky, or rich in ice like the moons of Jupiter, or rich in metal like Mercury," Gillon said.

The researchers noted that the Hubble Space Telescope and the forthcoming James Webb Space Telescope could help analyze the atmospheres of those planets for molecules linked with life, such as water, carbon dioxide and ozone.

"Now we have to investigate if they're habitable," de Wit said in the statement.

The scientists detailed their findings online today (May 2) in the journal Nature.

http://bbc.in/1QSwS4x

DNA secrets of Ice Age Europe unlocked

A study of DNA from ancient human bones has helped unlock the secrets of Europe's Ice Age inhabitants.

By Paul Rincon Science editor, BBC News website

Researchers analysed the genomes of 51 individuals who lived between 45,000 years ago and 7,000 years ago. The results reveal details about the biology of these early inhabitants, such as skin and eye colour, and how different populations were related. It also shows that Neanderthal ancestry in Europeans has been

shrinking over time, perhaps due to natural selection. The study in Nature journal shines a torchlight over some 40,000 years of prehistory, showing that ancient patterns of migration were just as complex as those in more recent times.

Some of the earliest arrivals on the continent contributed little to later populations. But between 37,000 years ago and 14,000 years ago, different groups of Europeans were descended from a single founder population. The fortunes of these human hunting groups were often linked to changes in the climate.

These 31,000-year-old skulls from Dolni Věstonice in the Czech Republic belong to people from the Gravettian culture **Martin Frouz and Jiří Svoboda**

Co-author Prof David Reich, from Harvard Medical School in Boston, US, said the 51 ancient individuals comprised "a pretty substantial fraction of the known human skeletons in this period". He told BBC News: "Because we've studied so many ancient humans from Europe from the beginning of the modern human occupation, we're able to form a picture of how populations transformed over time."

Prof Reich, Svante Paabo from the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and others found evidence that people belonging to one of Europe's most important Ice Age cultures - the Aurignacian - were displaced between 34,000 and 26,000 years ago by another group of humans called the Gravettians.

After 14,000 years ago, Europeans became more closely related to populations from the Middle East, the Caucasus and Turkey. This happens to coincide with the first major warming period at the end of the Ice Age and could reflect an expansion of people from the South-East. "We see multiple, huge movements of people displacing previous ones," said Prof Reich. "During this first four-fifths of modern human history in Europe, history is just as complicated as it is during the last fifth that we know so much more about."

Research on that last fifth of population history has revealed that mass movements of people in the Neolithic period (from 7,000 years ago) and the Bronze Age (5,000 years ago) transformed the genetic landscape of Europe.

Analysis of genes carried by Ice Age Europeans shows, among other things, that they had dark complexions and brown eyes. Only after 14,000 years ago did blue eyes begin to spread, and pale skin only appeared across much of the continent after 7,000 years ago - borne by early farmers from the Near East.

Early European populations possessed more Neanderthal ancestry than present-day people, consistent with the idea that much of the DNA we inherited from the Neanderthals had harmful effects. Scientists think this inheritance was progressively lost via natural selection. What seems clear is that most modern populations offer only hazy glimpses into the past, because their genetics are shaped by relatively recent patterns of migration.

Insights like those from this study have only been made possible by dramatic progress in the last two decades on techniques for analysing degraded DNA from ancient remains.

"A lot of amazing work was done [previously] to develop and use sophisticated methods to forensically piece apart patterns based on populations today," Prof Reich told BBC News. "But it's a little bit like trying to dissect the ingredients that go into the batter of a cake from the mixed up batter... how much flour, how much egg, how much sugar, how much butter.

"You could do it if you worked really hard and knew the chemistry. But what if you could go back to when they were adding in the butter, adding in the sugar, adding in the flour and measure how much was added in each time."

Meet the ancestors

The Aurignacians: A 35,000-year-old male from Goyet, Belgium, belonged to a distinctive branch of the Ice Age population. DNA was extracted from the upper arm bone of the hunter, who was associated with the Aurignacian archaeological culture.

The Gravettians: This ancestral group displaced the Aurignacians to dominate much of Europe from 34,000 to 26,000 years ago. Though they carried distinct genetic signatures, the Gravettians and Aurignacians were descended from the same ancient founder population.

The Magdalenians: The Aurignacian genetic signature disappeared from much of Europe when the Gravettians arrived. But it resurfaced 15,000 years later in the "Red Lady of El Mirón Cave" from northern Spain (pictured). This tall, robust woman was a member of the Magdalenian archaeological culture, which expanded north as the ice sheets melted.

The Villabruna cluster: From about 14,000 years ago, the gene pools of Europe and the Middle East draw closer together - perhaps reflecting an expansion of people from the south-east. This genetic cluster is named after a male hunter from Villabruna, Italy, who had dark skin and blue eyes.

http://www.eurekalert.org/pub_releases/2016-05/iu-iu042716.php

Indiana University researchers find Earth may be home to 1 trillion species

Largest-ever analysis of microbial data reveals an ecological law concluding 99.999 percent of species remain undiscovered

BLOOMINGTON, Ind. -- Earth could contain nearly 1 trillion species, with only one-thousandth of 1 percent now identified, according to a study from biologists at Indiana University.

The estimate, based on the intersection of large datasets and universal scaling laws, appears May 2 in the Proceedings of the National Academy of Sciences. The study's authors are Jay T. Lennon, associate professor in the IU Bloomington College of Arts and Sciences' Department of Biology, and Kenneth J. Locey, a postdoctoral fellow in the department.

The IU scientists combined microbial, plant and animal community datasets from government, academic and citizen science sources, resulting in the largest compilation of its kind. Altogether, these data represent over 5.6 million microscopic and nonmicroscopic species from 35,000 locations across all the world's oceans and continents, except Antarctica.

"Estimating the number of species on Earth is among the great challenges in biology," Lennon said. "Our study combines the largest available datasets with ecological models and new ecological rules for how biodiversity relates to abundance. This gave us a new and rigorous estimate for the number of microbial species on Earth. "Until recently, we've lacked the tools to truly estimate the number of microbial species in the natural environment," he added. "The advent of new genetic sequencing technology provides an unprecedentedly large pool of new information."

The work is funded by an effort of the National Science Foundation to transform, by 2020, understanding about the scope of life on Earth by filling major gaps in humanity's knowledge about the planet's biodiversity.

"This research offers a view of the extensive diversity of microbes on Earth," said Simon Malcomber, director of the NSF's Dimensions of Biodiversity program. "It also highlights how much of that diversity still remains to be discovered and described."

Microbial species are all forms of life too small to be seen with the naked eye, including all single-celled organisms, such as bacteria and archaea, as well as certain fungi. Many earlier attempts to estimate the number of species on Earth simply ignored microorganisms or were informed by older datasets that were based on biased techniques or questionable extrapolations, Lennon said.

"Older estimates were based on efforts that dramatically under-sampled the diversity of microorganisms," he added. "Before high-throughput sequencing, scientists would characterize diversity based on 100 individuals, when we know that a gram of soil contains up to a billion organisms, and the total number on Earth is over 20 orders of magnitude greater."

The realization that microorganisms were significantly under-sampled caused an explosion in new microbial sampling efforts over the past several years, including the collection of human-related microorganisms by the National Institutes of Health's Human Microbiome Project; marine microorganisms by the Tara Oceans Expedition; and aquatic, terrestrial and host-related microorganisms by the Earth Microbiome Project.

These data sources -- and many others -- were compiled to create the inventory in the IU study, which pulls together 20,376 sampling efforts on bacteria, archaea and microscopic fungi and 14,862 sampling efforts on communities of trees, birds and mammals. All of these sources were either publically available or provided access to IU.

"A massive amount of data has been collected from these new surveys," said Locey, whose work included programming required to compile the inventory. "Yet few have actually tried to pull together all the data to test big questions.

"We suspected that aspects of biodiversity, like the number of species on Earth, would scale with the abundance of individual organisms," he added. "After analyzing a massive amount of data, we observed simple but powerful trends in how biodiversity changes across scales of abundance. One of these trends is among the most expansive patterns in biology, holding across all magnitudes of abundance in nature."

Scaling laws, like those discovered by the IU scientists, are known to accurately predict species numbers for plant and animal communities. For example, the number of species scales with the area of a landscape.

"Until now, we haven't known whether aspects of biodiversity scale with something as simple as the abundance of organisms," Locey said. "As it turns out,

the relationships are not only simple but powerful, resulting in the estimate of upwards of 1 trillion species."

The study's results also suggest that actually identifying every microbial species on Earth is an almost unimaginably huge challenge. To put the task in perspective, the Earth Microbiome Project -- a global multidisciplinary project to identify microscope organisms -- has so far cataloged less than 10 million species.

"Of those cataloged species, only about 10,000 have ever been grown in a lab, and fewer than 100,000 have classified sequences," Lennon said. "Our results show that this leaves 100,000 times more microorganisms awaiting discovery -- and 100 million to be fully explored. Microbial biodiversity, it appears, is greater than ever imagined."

This research was also supported in part by the U.S. Army Research Office.

http://bit.ly/1rqT3JZ

Dinosaurs Migrated Out of Europe as Ancient Supercontinent Broke Up

During the breakup of the supercontinent Pangea, dinosaurs migrated from Europe to other parts of the world.

By Lindsay Dodgson, Live Science Contributor | April 29, 2016 02:10pm ET

Between 230 million and 66 million years ago, dinosaurs plodded across the supercontinent Pangea, and migrated from Europe to other parts of the world. Now, by gathering and comparing all the data about their fossils, paleontologists have been able to visually map the dinosaurs' migration during the time they ruled the Earth. The researchers used "network theory" in a new way to see how different dinosaur fossils were connected.

"A network is just as you imagine it being; it's a series of points which are your entities that you want to investigate," said study lead author Alex Dunhill, a paleobiologist at the University of Leeds, in the United Kingdom. "And then you look at how they interact or are connected together, by simply drawing lines between them." The team chose continents as points and then drew connecting lines if the same types of dinosaurs were found on two or more continents.

"We can then use some really simple maths to look at how the level of connectivity and the strength of the connection changes through time," Dunhill told Live Science. "It's something that's used really commonly in computing."

For example, network theory is used all over the internet, which is basically one giant network itself. Things like Facebook friends and Twitter interactions can all be calculated and mapped by network theory.

Dinos on the move

The researchers looked at what happened when Pangea (sometimes spelled Pangaea) broke up into smaller continents in the Triassic period, which is when dinosaurs first evolved. By the end of the Cretaceous, about 65.5 million years ago, the continents had broken up and drifted, almost to the positions we know today. High sea levels during this era also meant that some land masses appeared to be completely isolated, the researchers said. Using the fossil data, the scientists mapped where the dinosaurs trekked as the supercontinent was becoming fractured.

"One thing we actually find is that even though the migration of dinosaur groups slows down, it doesn't completely stop," Dunhill said. "We're still getting the movement of dinosaur groups between major continental land masses, even when the continents appear to be really isolated."

In other words, dinosaur families cropped up on continents even when they were completely separate from their original areas. Dunhill said this conclusion had been reached in previous studies using different methods, so the researchers were sure they were looking at the correct historical movements.

Dinosaurs may have been able to move across continents, and between islands, by the formation of temporary land bridges, which could have formed because of fluctuating sea levels during the Cretaceous era, Dunhill said.

Great migration

To make the mapping exercise more manageable, the researchers separated the dinosaurs by type: the sauropodomorphs, which are huge, long-necked plant-eaters like the Diplodocus and Brachiosaurus; the theropods that include all the carnivorous dinosaurs like the Tyrannosaurus rex; and the ornithischians, which include all other plant-eaters, such as the Triceratops and Stegosaurus.

"One thing we found was that sauropodomorphs tend to be less mobile, particularly [compared to] the theropods," Dunhill said. "These were really big animals, and probably less likely to swim, and less likely to be able to get across sea waves than some of the other smaller dinosaurs."

The theropod family also includes birds, and although they probably weren't great at flying, Dunhill said they were probably mobile enough to be able to still disperse across narrow sea ways.

But figuring out whether the results show real patterns of dinosaur migrations — or whether the findings simply reflect limitations in the fossil record — has been challenging.

"The fossil record is incomplete and biased in quite a severe way, and the terrestrial vertebrate fossil record is incredibly patchy," Dunhill said. "The main problem we tried to overcome was working out if these were true biological patterns of dinosaur movement or just that we've got a varying quality of fossil records through time."

Europe has been sampled for fossils for more than 250 years, and North America and Asia have strong records of fossils. However, other parts of the world, such as Australia, Africa and Antarctica, have a poor history of digging up and documenting fossils, the researchers said.

To combat this, the researchers removed some of the areas where the fossil record isn't as strong from the analysis, and ran it again to see if the overall patterns changed through time. When they did this, they found that there was a decline in connectivity, meaning there were fewer connections between the dinosaur families across the world (thus they weren't as widespread). Using all the data showed more lines of connections, which showed the families were distributed further away, giving the impression that they travelled more distance.

Out of Europe

But what caused the dinosaurs to flee? Instead of a natural disaster happening in Europe that prompted the animals' migration, Dunhill said the dinosaurs' exit could have two possible explanations.

"There's a biological possible explanation where Europe had been isolated for a while, had a burst of speciation, and then re-connections occurred with the rest of the world," he said. "Then, these new groups of dinosaurs that have evolved in Europe have then radiated out and expanded their geographic ranges."

The other explanation, he admits, is a little less exciting.

"It may just be an artifact of this patchy fossil record, and that maybe Europe has a really good fossil record throughout all this time period and other areas don't," Dunhill said. "It's always really difficult to distinguish between the two."

Dunhill says that more data is needed to really know what the dinosaurs were up to during that period, but the next stages of the research will involve integrating dinosaur phylogeny into the networks, and looking at relationships between the different groups.

The study's findings were published April 25 in the Journal of Biogeography.

http://bit.ly/1UATAEX

Did Scientists Stumble on a Battery that Lasts Forever?

Researchers studying nanowires have found a battery material that can be recharged for years, even decades

By Emily Matchar

Imagine a battery that could be recharged for decades. No more getting rid of cell phones because of waning battery life.

No more landfills filled with lithium ion batteries.

This is one step closer to reality, thanks to work by researchers from the University of California at Irvine.

The discovery that could lead to ultra-long-life batteries happened by serendipity. A team of researchers led by Reginald Penner, chair of the university's chemistry department, had been studying nanowires, tiny conductive wires that show great promise for use in batteries.

The problem is nanowires are fragile and generally begin to fray and crack after a certain number of charging cycles.

One day, Mya Le Thai, a PhD candidate in Penner's lab, decided on a whim to switch the liquid electrolyte surrounding the nanowire assembly with a gel version.

"She started to cycle these gel capacitors, and that's when we got the surprise," Penner recalls. "She said, 'this thing has been cycling 10,000 cycles and it's still going.' She came back a few days later and said 'it's been cycling for 30,000 cycles.' That kept going on for a month."

The team realized they had something special on their hands. While they're still not certain why using a gel electrolyte seems to keep the nanowires from breaking down, they have a hypothesis.

The gel, Penner explains, is about as thick as peanut butter. The nanowires, which are hundreds of times thinner than human hair and made of manganese oxide, are 80 percent porous.

Over time, the thick gel slowly seeps into the pores in the nanowires and makes them softer. This softness reduces their fragility.

"After 5,000 cycles with normal liquid, [the nanowires] start to break," Penner says. "And then they start to fall off. None of that is happening in the gel."

Right now, the team is working to test this hypothesis. If it's correct, they'll continue to experiment with different types of materials and gels to see what works best.

Should the work hold up, the gel-wrapped nanowires could eventually be a component in ultra-long-lasting batteries.

This is likely several years down the road, Penner says, though he has been fielding calls from companies interested in his lab's creation.

"The big picture is that there may be a very simple way to stabilize nanowires of the type that we studied," Penner says. "If this turns out to be generally true, it would be a great advance for the community."

Since most household electronics have life spans limited by factors besides battery life, a battery that lasts for a decade or two could easily outlive the device it powers.

"If you could get 100,000 cycles out of a lithium ion battery it might mean you never need to buy two of them," Penner says. "We're talking about a lifetime of 20 years, maybe even longer than that."

http://www.eurekalert.org/pub_releases/2016-05/jhm-ssm050216.php

Study suggests medical errors now third leading cause of death in the US

Physicians advocate for changes in how deaths are reported to better reflect reality

Analyzing medical death rate data over an eight-year period, Johns Hopkins patient safety experts have calculated that more than 250,000 deaths per year are due to medical error in the U.S. Their figure, published May 3 in the BMJ, surpasses the U.S. Centers for Disease Control and Prevention's (CDC's) third leading cause of death -- respiratory disease, which kills close to 150,000 people per year.

The Johns Hopkins team says the CDC's way of collecting national health statistics fails to classify medical errors separately on the death certificate. The researchers are advocating for updated criteria for classifying deaths on death certificates.

"Incidence rates for deaths directly attributable to medical care gone awry haven't been recognized in any standardized method for collecting national statistics," says Martin Makary, M.D., M.P.H., professor of surgery at the Johns Hopkins University School of Medicine and an authority on health reform. "The medical coding system was designed to maximize billing for physician services, not to collect national health statistics, as it is currently being used."

In 1949, Makary says, the U.S. adopted an international form that used International Classification of Diseases (ICD) billing codes to tally causes of death.

"At that time, it was under-recognized that diagnostic errors, medical mistakes and the absence of safety nets could result in someone's death, and because of that, medical errors were unintentionally excluded from national health statistics," says Makary.

The researchers say that since that time, national mortality statistics have been tabulated using billing codes, which don't have a built-in way to recognize incidence rates of mortality due to medical care gone wrong.

In their study, the researchers examined four separate studies that analyzed medical death rate data from 2000 to 2008, including one by the U.S. Department of Health and Human Services' Office of the Inspector General and the Agency for Healthcare Research and Quality. Then, using hospital admission rates from 2013, they extrapolated that based on a total of 35,416,020 hospitalizations, 251,454 deaths stemmed from a medical error, which the researchers say now translates to 9.5 percent of all deaths each year in the U.S.

According to the CDC, in 2013, 611,105 people died of heart disease, 584,881 died of cancer and 149,205 died of chronic respiratory disease -- the top three causes of death in the U.S. The newly calculated figure for medical errors puts this cause of death behind cancer but ahead of respiratory disease.

"Top-ranked causes of death as reported by the CDC inform our country's research funding and public health priorities," says Makary. "Right now, cancer and heart disease get a ton of attention, but since medical errors don't appear on the list, the problem doesn't get the funding and attention it deserves."

The researchers caution that most of medical errors aren't due to inherently bad doctors, and that reporting these errors shouldn't be addressed by punishment or legal action. Rather, they say, most errors represent systemic problems, including poorly coordinated care, fragmented insurance networks, the absence or underuse of safety nets, and other protocols, in addition to unwarranted variation in physician practice patterns that lack accountability.

"Unwarranted variation is endemic in health care. Developing consensus protocols that streamline the delivery of medicine and reduce variability can improve quality and lower costs in health care. More research on preventing medical errors from occurring is needed to address the problem," says Makary.

Michael Daniel of Johns Hopkins is a co-author on the study.

http://www.eurekalert.org/pub_releases/2016-05/p-ewc042916.php

Early warning: Current Japanese encephalitis vaccine might not protect

Current vaccines may fail to protect individuals against an emerging strain of the virus

Japanese encephalitis virus (JEV) is the leading cause of viral encephalitis (infection of the brain) in Asia. There is no specific treatment for Japanese encephalitis (JE) which can cause death or serious long-term disability, and WHO recommends JEV vaccination in all areas where the disease is recognized as a public health priority. A study published in PLOS Neglected Tropical Diseases suggests that current vaccines may fail to protect individuals against an emerging strain of the virus.

An estimated 3 billion people live in 24 South-East Asian and Western Pacific countries where the virus is present. JE viruses come in different 'flavors': there are five different genotypes (G1-G5), defined by differences in the 'envelope' gene that codes for proteins covering the virus surface. Strain G5 was originally isolated from a patient and described in 1951, but then not seen again until found recently (in 2009) in China and subsequently in Korea.

No specific treatment exists against the JE virus, but a number of vaccines are used to protect local populations and travellers. All of the vaccines are based on

G3 virus strains and have been shown to work well against G1 through G4 strains. However, their efficiency against the previously rare but possibly re-emerging G5 strain is not clear.

Guodong Liang, from the Chinese Center for Disease Control and Prevention, in Beijing, China, and colleagues were the first to report the re-emergence of the G5 strain. In this study, they compared G3 and G5 viruses and tested whether the vaccine commonly used in China can protect against G5 viruses.

Geographic Distribution of Japanese Encephalitis Virus **CDC**

Having found the two strains similar in their ability to cause disease in mice, the researchers vaccinated mice and tested whether they were protected against a dose of virus that would be lethal to unvaccinated animals. They found that the (G3-based) vaccine protected all the mice against a lethal challenge with G3 virus, but only 50% of the mice infected with G5 virus survived.

Next, the researchers looked for inactivating (or neutralizing) antibodies in vaccinated two-year-old children. They examined blood samples from 26 children that had been collected both before and 28 days after JE vaccination. Following vaccination, they were able to detect neutralizing antibodies against G3 strains in all the children, but only 35% of them also had antibodies that could neutralize G5 strains.

Finally, the researchers asked whether people who had been infected with JEV naturally (presumably with strains other than G5) and developed encephalitis had antibodies that could neutralize either G3 or G5 strains. Analyzing samples from 45 clinically diagnosed JE patients, they found that while all of the patients had neutralizing antibodies against G3 strains, only 29 of the 45 patients (64%) had the ability to neutralize G5 strains. Most of the latter were older patients; less than half of the pediatric patients (those under age 15) had neutralizing antibodies against G5 virus.

These results suggest that the existing vaccines provide only partial protection against G5 JEV strains. Moreover, natural infection with a different strain might not protect against subsequent G5 infection, especially in children.

As the researchers discuss, whether the JE cases that occurred over recent years despite wide-spread vaccination programs in countries like China and Korea are caused by G5 strains is not known. Nor is it clear how much of a public health threat G5 strains are at present, or might become in the future. Nonetheless, the results reported represent early warning signs of a potential infectious disease crisis in South-East Asia, and further research on the G5 JEV strains and on vaccines that better protect against them seems warranted.

http://dx.plos.org/10.1371/journal.pntd.0004686

http://bit.ly/1q5yNN6

Which Came First on Earth—Habitability or Life?

One astronomer suggests that we cannot necessarily disentangle the two

By Shannon Hall on May 3, 2016

The hunt for life on other planets is due for a makeover. Although it is often confined to planets orbiting in the so-called habitable zone where proximity to their host stars makes temperatures just right for liquid water, many astronomers are beginning to think outside the “Goldilocks” box. Some wonder if previously overlooked mechanisms—including life itself—could broaden the habitable zone well beyond its current definition.

Colin Goldblatt, a planetary scientist at the University of Victoria in British Columbia, even argues that life’s ability to alter a planet’s climate poses a new paradox: A planet’s habitability could depend on whether life has already made itself at home there, a situation that would place habitability and life in a baffling chicken-or-egg scenario.

Goldblatt has been looking beyond Earth-like atmospheres to see how different concentrations of nitrogen and carbon dioxide might tweak a planet’s habitability. Higher concentrations of carbon dioxide, for example, could keep a planet that is relatively far from its host star toasty whereas lower concentrations could keep a close-in planet chilly. Nitrogen is more complicated because higher concentrations both scatter sunlight (helping cool a planet) and make greenhouse gases absorb light more efficiently (keeping it warmer).

At the fall 2015 American Geophysical Union meeting in San Francisco, Goldblatt argued these gases could help keep a planet habitable. He recently summarized his talk in a paper published to the preprint server arXiv.

“It's absolutely essential to keep in mind that habitability is not just where you are in a solar system,” says David Crisp, the lead research scientist for the Orbiting Carbon Observatory 2 at the NASA Jet Propulsion Laboratory (JPL). “It's a property of the planet that you're living on.”

Earth, for example, has a built-in temperature control system: the carbon–silicate cycle. Some 2.5 billion years ago the sun was so faint that the oceans should have

been frozen—but they were not. The simple explanation is that Earth likely boasted an atmosphere thick with greenhouse gases. Then as the sun's brightness grew, the planet counteracted the warming climate by scrubbing carbon dioxide from the air: Higher temperatures increased rainfall, which pulled the greenhouse gas from the atmosphere and carried it into the oceans, where plate tectonics eventually subducted it into Earth's mantle.

Today most of the world's carbon dioxide is safely stored beneath Earth's crust. Had the opposite occurred and the sun's brightness waned, the planet might have counteracted the cooling climate by pumping more carbon dioxide into the air. Cooler temperatures would have slowed precipitation and increased volcanic eruptions, spewing the greenhouse gas out of the Earth's mantle and back into the atmosphere.

This balancing act has stabilized Earth's climate for billions of years, letting the carbon dioxide swing up or down by more than 1,000 percent in order to keep the planet's temperature steady and thereby increase the size of its habitable zone. And it is not just due to geochemistry; the carbon–silicate cycle depends on biology as well. Carbon dioxide is removed from the ocean when sea creatures convert it into the calcium carbonate they use to build their shells.

After those creatures die they sink into the deep ocean where their shells are subducted into the mantle. For an example of this phenomenon, Goldblatt points to the White Cliffs of Dover. These limestone cliffs along the English coastline are composed of calcium carbonate that formed when the skeletal remains of planktonic algae sank to the bottom of the ocean during the Cretaceous period. It appears that levels of both carbon dioxide and nitrogen (which is similarly whipped between Earth's mantle and atmosphere) can be subject to a planet's biosphere. Life creates conditions that help sustain itself.

"The existence of a biosphere actually increases the span of a habitable zone in a given solar system," Crisp says. "The habitability of an environment is affected to a certain extent by whether or not it is inhabited by some life form." Although this is generally agreed on, Goldblatt takes it a step further by saying that we cannot disentangle a habitable planet from the presence of life itself.

"The thing that I want to push in this paper is a philosophical point—not a point of technical calculations," Goldblatt says. "You can't try to address whether a planet is suitable for life or not without considering whether there is already life on the planet." Whereas most astronomers search for worlds that are suited to host life around other stars, Goldblatt does not think a planet can be called "habitable." It is either inhabited, or it is not. If we find a lifeless Earth-like planet in the so-called habitable zone and we just plop an egg of life on that planet, there is no guarantee that life will take hold, Goldblatt says. "We have no idea what a planet at that [distance] without life would actually look like," he says. "It would look nothing at all like the Earth."

Although this paradox might make the search for life look bleak, Goldblatt is hopeful we will find life in the galaxy. He simply thinks that astronomers should not confine themselves to such a strict definition of the habitable zone around stars.

Life might exist within those bounds or it might exist well beyond them in ways that scientists have yet to imagine.

To demonstrate his point he told me a story about Carl Sagan. When Cassini first arrived at Saturn, the spacecraft beamed images back to Earth where Sagan and other scientists could watch them first appear in a room at JPL. Most scientists attempted to interpret the results immediately, but Sagan remained quiet. He knew that the theoretical postulating was over. It was time to let the data speak for itself. "When we went out in the solar system we found things that we never expected," Goldblatt says. "And when we go out to observe the atmospheres on planets, we're going to find things that we don't expect. We need to be ready to broaden our horizons."

http://bit.ly/1s2IqXs

Inheritable bacterium controls Aedes mosquitoes' ability to transmit Zika

Aedes mosquitoes carrying the bacterium Wolbachia are drastically less able to transmit Zika virus

Aedes mosquitoes carrying the bacterium Wolbachia--found inside the cells of 60 percent of all insect species--are drastically less able to transmit Zika virus, say researchers at Brazil's Oswaldo Cruz Foundation (FIOCRUZ) in a study published May 4 in Cell Host & Microbe.

This is the first report on the effect of Wolbachia bacteria on Zika virus. Originally inserted into Aedes eggs as part of the Eliminate Dengue Program, the bacterium is passed on from mother mosquitoes to offspring, so it is a sustainable control agent. The approach is already being piloted to control Dengue virus transmission and, with the proper resources and approvals, there's infrastructure in place to increase the scale of current trials to also help tackle the Zika epidemic.

Wolbachia bacteria were first identified in 2005 as a way to combat mosquito-borne infections. After four years, researchers were successful in their attempts to isolate the bacterium from fruit flies and get it inside Aedes mosquitoes' eggs, without using any genetic alteration. They expected Wolbachia to shorten mosquitoes' lifespans, but the bacterium provided an added bonus, in that it heavily reduced the Dengue virus replication in the mosquito. The bacterium, it

seems, has the same effect on Zika transmission. The same effect was previously seen on Chikungunya virus, also transmitted by Aedes mosquitoes.

"The idea has been to release Aedes mosquitoes with Wolbachia in the field over a period of a few months, so they mate with Aedes mosquitoes without Wolbachia living in the place and, over time, replace the mosquito population," says senior author Luciano Moreira of the Oswaldo Cruz Foundation. He is also actively involved in the Eliminate Dengue Program, a non-profit that is testing the approach in 40 locations around the world.

"Zika and Dengue belong in the same family of viruses, so with the outbreak in Brazil, the logical idea was to test the mosquitoes carrying Wolbachia by challenging them with Zika virus and see what would happen" he says.

Moreira's team gave Brazilian field mosquitoes and Wolbachia-infected mosquitoes Zika virus by feeding them human blood infected by two recent strains of the virus that is circulating in Brazil. After two weeks, the researchers saw that mosquitoes carrying Wolbachia had fewer viral particles in their bodies and saliva.

The tests showed that the virus present in the mosquito saliva was not active--meaning that, after biting, the mosquito would not be able to transmit Zika virus. The reason for this drop in viral reproduction is unknown, but one theory is that because Wolbachia lives inside of the mosquito's cells, if the virus goes inside the cell to replicate, then there is an internal competition for resources. Surprisingly, this drop held true no matter how many Wolbachia the mosquito carried.

"Wolbachia showed to be as effective on Zika as the most important Dengue experiments we did," Moreira says. He cautions that the strategy is not 100 percent effective nor will it eliminate the virus. "We know that there will not be only one solution for Zika--we have to do this alongside different approaches, like vaccines or insecticides, besides the public measures to control Aedes breeding sites."

He is currently discussing the Wolbachia approach with the Brazilian Ministry of Health, hoping to raise the resources and public support to test its effect on Zika in the field.

This work was supported by FAPEMIG, CNPq, CAPES, the Brazilian Ministry of Health (DECIT/SVS), and a grant to Monash University from the Foundation for the National Institutes of Health through the Vector-Based Transmission of Control: Discovery Research (VCTR) program of the Grand Challenges in Global Health Initiatives of the Bill and Melinda Gates Foundation.

Cell Host & Microbe, Dutra et al.: "Wolbachia blocks currently circulating Zika virus isolates in Brazilian Aedes aegypti mosquitoes" http://www.cell.com/cell-host-microbe/fulltext/S1931-3128(16)30157-3

http://www.eurekalert.org/pub_releases/2016-05/aaft-rsj050216.php

Robotic surgery just got more autonomous

Supervised autonomous robot can successfully perform soft tissue surgery

Putting surgery one step closer into the realm of self-driving cars and intelligent machines, researchers show for the first time that a supervised autonomous robot can successfully perform soft tissue surgery. The robot outperformed expert surgeons and current robot-assisted surgical techniques in open bowel surgery in pigs.

By taking human intervention out of the equation, autonomous robots could potentially reduce complications and improve the safety and efficacy of soft tissue surgeries, about 45 million of which are performed in the U.S. each year.

Robot-assisted surgery currently relies on the surgeon to manually control it, and outcomes can vary depending on the individual's training and experience. Efforts in automating surgery have made headway for hard tissues, such as in bone cutting, but have proven challenging for soft tissues, which are malleable and mobile and, thus, more unpredictable.

Azad Shademan and colleagues designed and programmed Smart Tissue Autonomous Robot (STAR) to perform complex surgical tasks. Equipped with a robotic arm and surgical tools, STAR combines smart imaging technologies and fluorescent markers to navigate and adapt to the complexities of soft tissue.

The researchers tested their robot against manual surgery by expert surgeons, laparoscopy, and robot-assisted surgery with the da Vinci Surgical System. Under supervision, STAR proved superior to all approaches in suturing and reconnecting bowel segments, known as intestinal anastomosis, both ex vivo and in vivo in pigs. The animals survived the operation with no complications.

The researchers say that with further development, autonomous robotic surgery may one day take human error out of the operating room, improving care for patients undergoing bowel surgery, tumor removal, and other soft tissue surgery.

http://www.eurekalert.org/pub_releases/2016-05/uonc-wrt050416.php

Women ratchet themselves up the social ladder, 1 high heel at a time

What high heels reveal about the deep human urge for status

Fashion seems to embrace two opposite goals--fitting in with the crowd and standing out from it. Now new research reveals that the choice to fit in or stand out depends on who exactly the crowd is - and the size of their high heels. That is, women adjust their fashion to look similar to the rich but different from the poor.

Kurt Gray, a co-author at the University of North Carolina at Chapel Hill, and his colleagues investigated thousands of shoe purchases made by women who move

to different cities, showing that women adopt the local trends when moving to wealthier cities but ignore them when moving to lower socioeconomic (SES) cities.

"In other words, women want to look like the rich girls, and different from the poor girls," said Gray, an assistant professor of psychology in UNC College of Arts and Sciences.

To examine trends of conformity and individuality, Gray and his colleagues at Carnegie Mellon University and Yale University teamed up with a large-online fashion retailer. They examined five years of shoe purchases--16,236 in total--of 2007 women who moved between one of 180 U.S. cities. Because fashion choices are hard to quantify, they used a straightforward number: the size of high heels.

When moving to richer locations, women embrace local trends, when moving to poor locations, women ignore them. **Gilt**

Their analyses revealed that heel sizes changed when women moved, but not uniformly. When women moved to higher SES zip codes such as New York City or Los Angeles, the heel size closely matched the heel size that other women in that zip code had bought--showing a desire for conformity. But when women moved to lower SES zip codes, the heel size closely matched the heel size of their own past purchase--showing a desire to keep their individuality.

The team of researchers, who included Jeff Galak, Nina Strohminger, Igor Elbert and Gray, label this phenomenon "trickle down conformity," because fashion preferences trickle down from the top but seldom up from the bottom. As Gray explained, "Walmart watches the styles on the runways in Milan, but Milan never watches the styles at Walmart."

The explanation for this lopsided conformity is the deep human urge for status. "From the beginning of time, people have thirsted for respect and social standing, and have aligned themselves with the powerful and distanced themselves from the powerless," said Gray. "So it makes sense that they do the same with heel sizes."

There is also reason to believe that this "aspirational fashion" is getting more prevalent. Inequality is increasing in America, and research reveals that the bigger the gap between rich and poor, the more people want to look rich. Such aspirations fuel the fortunes of fashion sites that provide high-status goods for low prices.

This study examined only women, but there is no reason to believe it applies only to them. "Men do the same thing when they purchase clothes, electronics or cars," said Gray, "When you move from Wichita to LA, you look around and sell your Chevy for a BMW, but when you move from Los Angeles to Wichita, Kansas, you look around, and then just keep the BMW."

This research builds off the past work of Gray and Strohminger, which examined what color combinations make outfits the most fashionable. "We often think of fashion as something frivolous, but it's an industry worth $1.7 trillion annually, and clothing often helps define ourselves," said Gray.

With their current study, Gray and colleagues reveal that fashion industry isn't only about making money, but letting people look like they belong with money.

http://www.eurekalert.org/pub_releases/2016-05/jhm-yil050316.php

Yeast infection linked to mental illness

Candida infections also more common among those with memory loss

In a study prompted in part by suggestions from people with mental illness, Johns Hopkins researchers found that a history of Candida yeast infections was more common in a group of men with schizophrenia or bipolar disorder than in those without these disorders, and that women with schizophrenia or bipolar disorder who tested positive for Candida performed worse on a standard memory test than women with schizophrenia or bipolar disorder who had no evidence of past infection.

The researchers caution that their findings, described online on May 4 in npj Schizophrenia -- a new publication from Nature Publishing Group -- do not establish a cause-and-effect relationship between mental illness and yeast infections but may support a more detailed examination into the role of lifestyle, immune system weaknesses and gut-brain connections as contributing factors to the risk of psychiatric disorders and memory impairment.

"It's far too early to single out Candida infection as a cause of mental illness or vice versa," says Emily Severance, Ph.D., assistant professor of pediatrics and member of the Stanley Division of Developmental Neurovirology at the Johns Hopkins University School of Medicine. "However, most Candida infections can be treated in their early stages, and clinicians should make it a point to look out for these infections in their patients with mental illness." She adds that Candida

infections can also be prevented by decreased sugar intake and other dietary modifications, avoidance of unnecessary antibiotics, and improvement of hygiene.

Candida albicans is a yeastlike fungus naturally found in small amounts in human digestive tracts, but its overgrowth in warm, moist environments causes burning, itching symptoms, thrush (rashes in the throat or mouth) in infants and those with weakened immune systems, and sexually transmittable genital yeast infections in men and women. In its more serious forms, it can enter the bloodstream. In most people, the body's own healthy bacteria and functioning immune system prevent its overgrowth.

Severance says she and her team focused on a possible association between Candida susceptibility and mental illness in the wake of new evidence suggesting that schizophrenia may be related to problems with the immune system, and because some people with weakened immune systems are more susceptible to fungal infections.

Also, she says, patients and parents of patients had shared personal stories and testimonials with the researchers about their experience with yeast infections, and these discussions prompted the investigation into possible links between mental illness and the microbiome -- the body's natural collection of bacteria. The researchers, she adds, chose to focus on Candida because it is one of the most common types of yeast in the body.

For the study, colleagues from the Sheppard Pratt Health System took blood samples from a group of 808 people between the ages of 18 and 65. This group was composed of 277 controls without a history of mental disorder, 261 individuals with schizophrenia and 270 people with bipolar disorder. The researchers used the blood samples to quantify the amount of IgG class antibodies to Candida, which indicates a past infection with the yeast. After accounting for factors like age, race, medications and socioeconomic status, which could skew the results, they looked for patterns that suggested links between mental illness and infection rates.

Significantly, the team says, it found no connection between the presence of Candida antibodies and mental illness overall in the total group. But when the investigators looked only at men, they found 26 percent of those with schizophrenia had Candida antibodies, compared to 14 percent of the control males. There wasn't any difference found in infection rate between women with schizophrenia (31.3 percent) and controls (29.4 percent). The higher infection rate percentages in women over men likely reflects an increased susceptibility for this type of infection in all women.

Men with bipolar disorder had clear increases in Candida as well, with a 26.4 percent infection rate, compared to only 14 percent in male controls. But, after accounting for additional variables related to lifestyle, the researchers found that the association between men with bipolar disorder and Candida infection could likely be attributed to homelessness. However, the link between men with schizophrenia and Candida infection persisted and could not be explained by homelessness or other environmental factors. Many people who are homeless are subjected to unpredictable changes in stress, sanitation and diet, which can lead to infections like those caused by Candida.

Severance says the data add support to the idea that environmental exposures related to lifestyle and immune system factors may be linked to schizophrenia and bipolar disorder, and that those factors may be different for each illness. Similarly, specific mental illnesses and related symptoms may be very different in men versus women.

This Johns Hopkins research group, led by Robert Yolken, M.D., director of the Stanley Division of Developmental Neurovirology, had previously shown that toxoplasmosis infection could trigger schizophrenia, and this could lead to neurocognitive problems. The organism that causes toxoplasmosis is a parasite that uses cats as its primary host, but it can also infect humans and other mammals.

To determine whether infection with Candida affected any neurological responses, all participants in the new study took a 30-minute assessment of cognitive tasks to measure immediate memory, delayed memory, attention skills, use of language and visual-spatial skills.

Each of the five skills tests are scored based on an adjusted 100-point system. Results showed that control men and women with and without prior Candida infection had no measureable differences in scores in the five neurological responses. However, the researchers noticed that women with schizophrenia and bipolar disorder who had a history of Candida infection had lower scores on the memory portions of this test compared to those women with no prior infection. For example, women with schizophrenia and the highest Candida antibody levels scored about an average of 11 points lower on the test for immediate memory than the controls, from a score of 68.5 without infection to 57.4 with infection. And the women with schizophrenia and the highest Candida antibody levels scored almost 15 points lower on the test for delayed memory, from a score of 71.4 without infection to 56.2 with infection. The effect of Candida infection in women with bipolar disorder on memory test scores was smaller than that seen in women with schizophrenia but was still measureable.

"Although we cannot demonstrate a direct link between Candida infection and physiological brain processes, our data show that some factor associated with Candida infection, and possibly the organism itself, plays a role in affecting the memory of women with schizophrenia and bipolar disorder, and this is an avenue

that needs to be further explored," says Severance. "Because Candida is a natural component of the human body microbiome, yeast overgrowth or infection in the digestive tract, for example, may disrupt the gut-brain axis. This disruption in conjunction with an abnormally functioning immune system could collectively disturb those brain processes that are important for memory." Severance says they plan to take their studies of the gut-brain connection into mouse models to test for a cause-and effect-relationship with Candida and memory deficits.

The researchers emphasized that the current study design had limitations. For example, they were unable to tell where in the body the infection was located and whether or not participants had a current or past infection of Candida. The researchers were also not able to account for every possible lifestyle variable that might contribute to these results. The researchers in the Stanley Division of Developmental Neurovirology are investigating whether pathogens, such as bacteria or viruses, may contribute or trigger certain mental disorders.

According to the National Institute of Mental Health, about 1 percent of people in the U.S. have schizophrenia and about 2 percent have bipolar disorder. Although these diseases have a genetic component, there is evidence that they may also be triggered by environmental factors and stress.

Additional authors on the study include Kristin Gressitt of Johns Hopkins Medicine; Catherine Stallings, Emily Katsafanas, Lucy Schweinfurth, Christina Savage, Maria Adamos, Kevin Sweeney, Andrea Origoni, Sunil Khushalani and Faith Dickerson of Sheppard Pratt Health System; and F. Markus Leweke of Heidelberg University.

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A better bone replacement: 3-D printed bone with just the right mix of ingredients

Blend of natural and man-made materials works best, study in mice shows

To make a good framework for filling in missing bone, mix at least 30 percent pulverized natural bone with some special man-made plastic and create the needed shape with a 3-D printer. That's the recipe for success reported by researchers at The Johns Hopkins University in a paper published April 18 online in ACS Biomaterials Science & Engineering.

Each year, the Johns Hopkins scientists say, birth defects, trauma or surgery leave an estimated 200,000 people in need of replacement bones in the head or face. Historically, the best treatment required surgeons to remove part of a patient's fibula (a leg bone that doesn't bear much weight), cut it into the general shape needed and implant it in the right location. But, according to Warren Grayson, Ph.D., associate professor of biomedical engineering at the Johns Hopkins University School of Medicine and the report's senior author, the procedure not only creates leg trauma but also falls short because the relatively straight fibula can't be shaped to fit the subtle curves of the face very well.

That has led investigators to 3-D printing, or so-called additive manufacturing, which creates three-dimensional objects from a digital computer file by piling on successive, ultrathin layers of materials. The process excels at making extremely precise structures -- including anatomically accurate ones -- from plastic, but "cells placed on plastic scaffolds need some instructional cues to become bone cells," says Grayson. "The ideal scaffold is another piece of bone, but natural bones can't usually be reshaped very precisely." In their experiments, Grayson and his team set out to make a composite material that would combine the strength and printability of plastic with the biological "information" contained in natural bone.

They began with polycaprolactone, or PCL, a biodegradable polyester used in making polyurethane that has been approved by the FDA for other clinical uses. "PCL melts at 80 to 100 degrees Celsius (176 to 212 Fahrenheit) -- a lot lower than most plastics -- so it's a good one to mix with biological materials that can be damaged at higher temperatures," says Ethan Nyberg, a graduate student on Grayson's team. PCL is also quite strong, but the team knew from previous studies that it doesn't support the formation of new bone well. So they mixed it with increasing amounts of "bone powder," made by pulverizing the porous bone inside cow knees after stripping it of cells.

"Bone powder contains structural proteins native to the body plus pro-bone growth factors that help immature stem cells mature into bone cells," says Grayson. "It also adds roughness to the PCL, which helps the cells grip and reinforces the message of the growth factors."

The first test for the composite materials was printability, Grayson says. Five, 30 and 70 percent bone powder blends performed well, but 85 percent bone powder had too little PCL "glue" to maintain clear lattice shapes and was dropped from future experiments. "It was like a chocolate chip cookie with too many chocolate chips," says Nyberg.

To find out whether the scaffolds encourage bone formation, the researchers added human fat-derived stem cells taken during a liposuction procedure to scaffolds immersed in a nutritional broth lacking pro-bone ingredients.

After three weeks, cells grown on 70 percent bone powder scaffolds showed gene activity hundreds of times higher in three genes indicative of bone formation,

compared to cells grown on pure PCL scaffolds. Cells on 30 percent bone powder scaffolds showed large but less impressive increases in the same genes.

After the scientists added the key ingredient beta-glycerophosphate to the cells' broth to enable their enzymes to deposit calcium, the primary mineral in bone, the cells on 30 percent scaffolds produced about 30 percent more calcium per cell, while those on 70 percent scaffolds produced more than twice as much calcium per cell, compared to those on pure PCL scaffolds.

Finally, the team tested their scaffolds in mice with relatively large holes in their skull bones made experimentally. Without intervention, the bone wounds were too large to heal. Mice that got scaffold implants laden with stem cells had new bone growth within the hole over the 12 weeks of the experiment. And CT scans showed that at least 50 percent more bone grew in scaffolds containing 30 or 70 percent bone powder, compared to those with pure PCL. "In the broth experiments, the 70 percent scaffold encouraged bone formation much better than the 30 percent scaffold," says Grayson, "but the 30 percent scaffold is stronger. Since there wasn't a difference between the two scaffolds in healing the mouse skulls, we are investigating further to figure out which blend is best overall."

Although the use of "decellularized" cow bone has been FDA-approved for clinical use, in future studies, the researchers say, they hope to test bone powder made from human bone since it is more widely used clinically. They also want to experiment with the designs of the scaffolds' interior to make it less geometric and more natural. And they plan to test additives that encourage new blood vessels to infiltrate the scaffolds, which will be necessary for thicker bone implants to survive.

Other authors of the report include Ben Hung, Bilal Naved, Miguel Dias, Christina Holmes, Jennifer Elisseeff and Amir Dorafshar of the Johns Hopkins University School of Medicine.

This work was supported by the National Institute of Dental and Craniofacial Research (F31 DE024922), the Russell Military Scholar Award, the Department of Defense, the Maryland Stem Cell Research Fund and the American Maxillofacial Surgery Society Research Grant Award.

http://www.eurekalert.org/pub_releases/2016-05/pfan-dcf050516.php

Doctors call for single-payer health reform, cite need to move beyond Affordable Care Act

American Journal of Public Health publishes physicians' call for sweeping single-payer reform with detailed proposal signed by over 2,200 doctors nationwide

In a dramatic show of physician support for deeper health reform - and for making a decisive break with the private insurance model of financing medical care - 2,231 physicians called today [Thursday, May 5] for the creation of a publicly financed, single-payer national health program that would cover all Americans for all medically necessary care.

Single-payer health reform, often called "Medicare for All," has been a hotly debated topic in the presidential primaries, thanks in part to it being a prominent plank in the platform of Sen. Bernie Sanders. The new physicians' proposal is strictly nonpartisan, however.

The proposal, which was drafted by a blue-ribbon panel of 39 leading physicians, is announced today in an editorial titled "Moving Forward from the Affordable Care Act to a Single-Payer System" published in the American Journal of Public Health. The editorial links to the full proposal titled "Beyond the Affordable Care Act: A Physicians' Proposal for Single-Payer Health Care Reform" and the names of all the signers, and it appeals for additional physicians to add their names as endorsers. The proposal currently has signers from 48 states and the District of Columbia.

"Our nation is at a crossroads," said Dr. Adam Gaffney, a Boston-based pulmonary disease and critical care specialist, lead author of the editorial and co-chair of the Working Group that produced the proposal.

"Despite the passage of the Affordable Care Act six years ago, 30 million Americans remain uninsured, an even greater number are underinsured, financial barriers to care like co-pays and deductibles are rising, bureaucracy is growing, provider networks are narrowing, and medical costs are continuing to climb.

"Caring relationships are increasingly taking a back seat to the financial prerogatives of insurance firms, corporate providers, and Big Pharma," Gaffney said. "Our patients are suffering and our profession is being degraded and disfigured by these mercenary interests."

Dr. Steffie Woolhandler, a co-author of the editorial and proposal who is a professor of public health at the City University of New York's Hunter College and lecturer at Harvard Medical School, commented: "We can continue down this harmful path - or even worse, take an alternative, 'free-market' route that would compound our problems - or we can embrace the long-overdue remedy that we know will work: the creation of a publicly financed, nonprofit, single-payer system that covers everybody. Today we're saying we must quickly make that shift. Lives are literally at stake."

Dr. Marcia Angell, a co-author of the editorial and proposal, co-chair of the working group, member of the faculty of global health and social medicine at Harvard Medical School and former editor-in-chief of the New England Journal of Medicine, said: "We can no longer afford to waste the vast resources we do on the administrative costs, executive salaries, and profiteering of the private

insurance system. We get too little for our money. It's time to put those resources into real health care for everyone."

Under the national health program (NHP) outlined by the physicians:

Patients could choose to go to any doctor and hospital. Most hospitals and clinics would remain privately owned and operated, receiving a budget from the NHP to cover all operating costs. Physicians could continue to practice on a fee-for-service basis, or receive salaries from group practices, hospitals or clinics.

The program would be paid for by combining current sources of government health spending into a single fund with modest new taxes that would be fully offset by reductions in premiums and out-of-pocket spending. Co-pays and deductibles would be eliminated.

The single-payer program would save about $500 billion annually by eliminating the high overhead and profits of insurance firms, and the massive paperwork they inflict on hospitals and doctors.

The administrative savings of the streamlined system would fully offset the costs of covering the uninsured and upgraded coverage for everyone else, e.g. full coverage of prescription drugs, dental care and long-term care. Savings would also be redirected to currently underfunded health priorities, particularly public health.

The "single payer" would be in a strong position to negotiate lower prices for medications and other medical supplies, yielding additional savings and reining in costs.

Surveys show strong, rising support for single-payer national health insurance among physicians. A 2008 survey of physicians found that 59 percent supported "legislation to establish national health insurance," up from 49 percent five years earlier.

"Moving Forward From the Affordable Care Act to a Single-Payer System," by Adam Gaffney, M.D.; Steffie Woolhandler, M.D., M.P.H.; David U. Himmelstein, M.D.; Marcia Angell, M.D. American Journal of Public Health, June 2016, Vol. 106, No. 6, online first May 5, 2016, 1 p.m. Eastern. Includes link to full Physicians' Proposal. Article available at this link: http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2015.303157

The full, six-page Physicians' Proposal with reference citations and 2,231 signatures (titled "Beyond the Affordable Care Act: A Physicians' Proposal for Single-Payer Health Care Reform," written by a 39-member Working Group on Single-Payer Program Design) is also accessible at the following link: http://www.pnhp.org/nhi

http://www.eurekalert.org/pub_releases/2016-05/e-olc050516.php

Older lung cancer patients experience excellent survival following surgery

Newly combined data offer longer-term perspective on an increasingly growing population

Patients aged 65 years and older are living longer after lung cancer surgery, and with older people representing a rapidly growing proportion of patients diagnosed with lung cancer, this improved survival is especially significant, according to an article posted online today by The Annals of Thoracic Surgery.

Key findings in this study show that 5-year survival for older lung cancer surgery patients is favorable; surgeons will be able to better individualize care for older lung cancer patients based on newly and uniquely linked data, and the prevalence of lung cancer is expected to increase as the population continues to age.

The researchers combined data from lung cancer patients in The Society of Thoracic Surgeons (STS) General Thoracic Surgery Database (GTSD) with claims data from the Centers for Medicare & Medicaid Services (CMS).

"The new data linkage between STS and CMS provides a more complete picture of what happens to a large subset of patients beyond the 30 days represented in the STS National Database," said Dr. Fernandez. "We now know more about long-term survival after our interventions, which is important to patients. This information can be included in the shared decision-making process when discussing treatment options with patients."

The GTSD data included 37,009 records for patients 65 years of age and older who underwent lung cancer surgery between 2002 and 2012. When merged with CMS data, the records of 26,055 patients were successfully linked, providing access to vital information related to long-term patient outcomes. This included hospital readmission rates, reinterventions (a second procedure), and long-term survival.

According to the National Cancer Institute, the 5-year survival of all patients diagnosed with lung cancer in the United States is approximately 17%. Fewer than half of all patients who undergo surgery for lung cancer survive as long as 5 years.

In examining the STS-CMS linked data, researchers found that the median survival following lung cancer surgery for pathologic Stage I (early stage) was 6.7 years, almost 2 years longer than the benchmark 5-year survival rate. In addition, the study showed that the 5-year survival rate for selected older patients with advanced lung cancer who were treated with surgical therapy was 29.9% for Stage III and 26.7% for Stage IV.

"This greater than expected survival in older patients selected for operative therapy is noteworthy," said Dr. Fernandez, "especially considering that the prevalence of lung cancer is expected to increase as the population continues to grow older and more people survive into old age."

According to the US Census Bureau, the elderly population in the United States is projected to almost double, from the most current estimate of 43 million in 2012 to 80 million by the year 2050.

Dr. Fernandez said that because clinical decision-making in older patients can be fairly complex, the long-term patient outcome information from the STS-CMS linked data certainly will prove beneficial. "This research effort is important because it will assist in recommending effective, optimal treatments tailored specifically to older patients with lung cancer," he said. "And it is available during a time when we expect to be seeing more of these patients."

http://www.eurekalert.org/pub_releases/2016-05/epfd-iwb050516.php

Intestinal worms boost immune system in a surprising way

Lymph nodes contain more immune cells when the host is infected with an intestinal worm

In order to fight invading pathogens, the immune system uses "outposts" throughout the body, called lymph nodes. These are small, centimeter-long organs that filter fluids, get rid of waste materials, and trap pathogens, e.g. bacteria or viruses. Lymph nodes are packed with immune cells, and are know to grow in size, or 'swell', when they detect invading pathogens. But now, EPFL scientists have unexpectedly discovered that lymph nodes also contain more immune cells when the host is infected with a more complex invader: an intestinal worm. The discovery is published in Cell Reports , and has significant implications for our understanding of how the immune system responds to infections.

The discovery was made by the lab of Nicola Harris at EPFL. Her postdoc and first author Lalit Kumar Dubey noticed that the lymph nodes of mice that had been infected with the intestinal worm Heligmosomoides polygyrus bakeri had massively grown in size. This worm is an excellent tool for studying how the worm interacts with its host, and is therefore used as a standard throughout labs working in the field.

Lymph nodes have microscopic compartments called "follicles", where they store a specific type of immune cells, the B-cells. Stored in the follicles, B-cells pump out antibodies into the bloodstream to attack invading pathogens.

The researchers found that the mouse lymph nodes were actually producing more follicles, suggesting they were producing more B-cells in response to the worm infection. Of course, this is not a simple event. Like many biological processes, it involves an entire sequence of molecular signals that result in the formation of new cells and tissue.

The EPFL scientists were able to reconstruct the molecular sequence, which is fairly complex: when the mouse is infected with the intestinal worm, a "cytokine" molecule is produced. This cytokine then stimulates B-cells in the lymph nodes to produce a molecule called a lymphotoxin. The lymphotoxin then interacts with the cells that form the foundation of the actual lymph node - the so-called "stromal cells". The stromal cells then produce another cytokine, which stimulates the production of new follicles in the lymph node.

Until now, formation of new B-cell follicles in the lymph nodes was thought to only happen just after birth. This study provides the first detailed evidence to show that this phenomenon can take place in an adult mammal. The researchers also showed that formation of new follicles is important for fighting infection as it encourages the production of more antibodies.

Unlike bacterial or viral infections, worm infections are enormously complex. "Worms are large creatures that produce a host of their own molecules upon infection," says Nicola Harris. "Some of these molecules stimulate the host's immune system while some others suppress it. The field is investigating every one of these molecules, but it is slow work."

It must be noted that the new production of B-cell follicles has only been confirmed in worm infections. "We are currently looking at this effect with bacterial infections in mice," says Nicola Harris. "Nonetheless, we are pursuing a deeper understanding of this process to see if it is involved in producing adequate antibodies in response to vaccines."

This work was lead by Nicola Harris's lab at EPFL's Global Health Institute, and included contributions from the Institute of Immunobiology of Kantonsspital St. Gallen and the Center for Immunity and Infection at the University of Lausanne. It was funded by the Leenaards Foundation (prize for Translational Medical Research).

Dubey LK, Lebon L, Mosconi I, Yang C-Y, Scandella E, Ludewig B, Luther SA, Harris NL. Lymphotoxin-Dependent B Cell-FRC crosstalk promotes de novo follicle formation and antibody production following intestinal helminth infection. Cell Reports 05 May 2016. DOI: 10.1016/j.celrep.2016.04.023

http://www.eurekalert.org/pub_releases/2016-05/bumc-rin050316.php

Researchers identify new pathway leading to Alzheimer's disease

Studies may provide insight into novel therapeutic approaches targeting formation of tau pathology that drives degeneration

Boston - A newly discovered pathway leading to neurodegeneration in Alzheimer's disease (AD) may unlock the door to new approaches for treating the disease.

The findings, published in the journal Cell Reports, focuses on the tau protein, whose abnormal aggregation (clumping) has long been known to drive the nerve damage in AD. New research shows that the tau protein directs the formation of stress granules, which are molecular complexes that allow nerve cells to adapt to stresses, such as injury. The tau-stress granule complex is usually short lived, but in the setting of chronic stress, tau persistently forms into a cluster, leading to the degeneration of nerve cells seen in AD.

Boston University School of Medicine (BUSM) researcher Benjamin Wolozin, MD, PhD, explains, "Scientists have known for a long time that during disease,

tau protein gets modified, changes its location in nerve cells and then aggregates." In healthy nerve cells, tau resides in a part of the nerve cell termed the axon, the long, slender part of the cell that carries electrical impulses away from the neuron's body. Wolozin's group showed that moving tau from the axon to the nerve cell body helps the nerve cells respond to stress (such as injury). "The nerve cells do this in order to stimulate the formation of stress granules, which help the cell to adapt under stressful conditions. Stress granules instruct the cell to divert energy toward making protective proteins and away from making specialized proteins, which are less necessary during stress."

"Surprisingly," says Wolozin, professor of pharmacology and neurology, "the association of tau with stress granules also caused tau to cluster." Most stresses are short term, resolve quickly and are therefore not a problem. "But some stresses are chronic, such as vascular disease or the accumulation of beta-amyloid--a protein that accumulates outside the neuron in Alzheimer's disease." Chronic stress leads to excessive, persistent accumulation of stress granules containing aggregated tau, which ultimately damages nerve cells, causing degeneration.

According to Wolozin with this finding comes hope. His team found that reducing the amount of one of the key stress granule proteins, TIA1, prevented tau aggregation and nerve cell degeneration. "While still in its early stages, this work points to entirely new approaches to treating Alzheimer's disease." Wolozin and his team are now planning to test their research findings in animal models of Alzheimer's disease.

Funding for this study was provided by the BrightFocus Foundation, the Alzheimer Association, the Cure Alzheimer's fund and the National Institute of Health.

Note a Conflict of Interest:

Benjamin Wolozin is Co-Founder of Aquinnah Pharmaceuticals Inc.

http://www.eurekalert.org/pub_releases/2016-05/cp-ops042816.php

Our personal skin microbiome is surprisingly stable

Personal milieu of skin microbes remains highly stable over time

Despite regular washing and contact with bacteria-laden objects, our personal milieu of skin microbes remains highly stable over time, reports a metagenomics study published May 5 in Cell. The authors say this knowledge could be applied to better understand a wide range of human skin disorders through the development of prebiotic, probiotic, and microbial transplantation approaches.

Human skin is an ecosystem composed of a wide range of habitats for bacteria, fungi, and viruses. While most of these microbes are harmless or beneficial, some have been linked to skin disorders such as acne, psoriasis, and eczema. Studying the variability of microbial communities across skin sites has been key to understanding, for instance, why eczema tends to affect moist sites such as the bends of the arms and legs, while psoriasis commonly occurs on dry, exposed sites such as the elbows and knees. However, it has not been clear how microbial communities found across skin sites change over time and how these changes may affect human health.

In a recent metagenomic study, senior study authors Heidi Kong of the National Cancer Institute and Julie Segre of the National Human Genome Research Institute found that bacterial, fungal, and viral communities not only show a strong preference for inhabiting specific skin sites, but also serve as microbial fingerprints that are highly unique to individuals. In the new study, they expanded upon this work by examining the longitudinal stability of these skin microbial communities. The researchers took skin samples from 12 healthy individuals at three successive time points, spanning from 1 month to 2 years, and performed metagenomic shotgun sequencing across 17 skin sites.

Surprisingly, skin microbial communities remained highly stable over time, despite typical exposure to external perturbations such as routine contact with other individuals, clothing, and environments. Rather than acquiring prevalent microbes from the environment, individuals retained their own unique microbial signatures. However, the stability of skin microbial communities varied across individuals and microbial strains, with some showing more changes than others.

In addition, some skin sites contained more variable microbial communities than others. For example, oily skin sites such as the back and external auditory canal contained the most stable bacterial and fungal communities, and even highly exposed, dry sites such as the palm showed remarkable stability over time. By contrast, sites with high microbial diversity, such as the feet and moist sites, were the least stable over time, perhaps due to factors such as personal hygiene or exposure to more variable environments.

One limitation of the study is that it focused on a small number of healthy adults. In future studies, Kong and Segre plan to use what they've learned about healthy skin microbes to study patients with eczema and primary immune deficiencies. "Future studies can use the knowledge of the relative stability of the skin microbial communities in healthy adults to understand how various exposures or disease state may alter these skin microbes," Segre says. "For example, studies in acne patients could explore whether specific strains bloom during adolescent acne flares or change with medications such as antibiotics."

This work was primarily supported by NHGRI and NCI Intramural Research Programs and a Chanel/CE.R.I.E.S. research award.

Cell, Oh and Byrd et al.: "Temporal Stability of the Human Skin Microbiome" http://www.cell.com/cell/fulltext/S0092-8674(16)30399-3

http://www.eurekalert.org/pub_releases/2016-05/dumc-aat050216.php

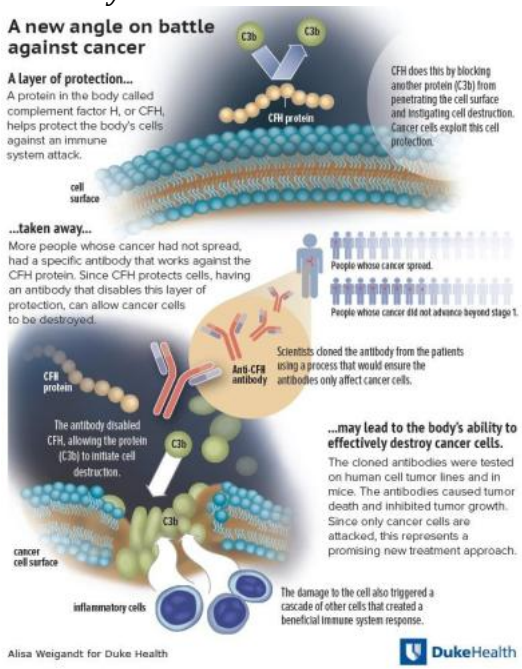
Antibody appears to attack cancer cells, leaving other cells unscathed

A research team from Duke Health has developed an antibody from the body's own immune system that preferentially attacks cancer cells.

DURHAM, N.C. -- The antibody works by targeting a natural defense mechanism that cancer tumors exploit.

Cells in the body essentially use a home security system that relies on certain proteins to protect the cell surface and keep it safe. These proteins help the cell avoid injury and even death from unwanted activation of the immune system.

In a paper published online May 5, 2016 in Cell Reports, the Duke team describes the workings of a cancer-fighting antibody they discovered, developed and tested in cell lines and animal models. The antibody dismantles a specific part of a cancer cell's defense system and then employs several mechanisms of attack.



A research team from Duke Health has developed an antibody from the body's own immune system that preferentially attacks cancer cells. The antibody works by targeting a natural defense mechanism that cancer tumors exploit. Cells in the body essentially use a home security system that relies on certain proteins to protect the cell surface and keep it safe. These proteins help the cell avoid injury and even death from unwanted activation of the immune system. **Alisa Weigandt for Duke Health**

"This is the first completely human-derived antibody developed as an anti-cancer therapy, which is very different from other immunotherapy approaches," said senior author Edward F. Patz, Jr., M.D., the James and Alice Chen Professor of Radiology and professor in the Department of Pharmacology and Cancer Biology at Duke.

Patz and colleagues -- including principals from the Duke Human Vaccine Institute who have been advancing the development of antibodies for an HIV vaccine -- started with the observation that some lung cancer patients have early-stage tumors that never progress to advanced disease.

One of the features that separated these patients from those who had more lethal tumors was the presence of antibodies against a protein called complement factor H, or CFH, which protects cells from an immune system attack.

CFH works by preventing activation of an important immune response. It inhibits the deposit of a complement C3b protein on the cell surface. Complement C3b initiates the degradation of the cell membrane, which eventually leads to cell death.

Once the antibody for CFH was identified, Patz and colleagues sought to explore how this immune response could be optimized as a cancer therapy. Critical to that effort was finding a way to produce antibodies that recognized the exact same part of CFH as the autoantibodies made by the early-stage cancer patients, thus assuring that the antibodies would have a particular affinity for cancer cells.

Patz and colleagues pooled the white blood cells from CFH antibody-producing cancer patients and then isolated and cloned the antibody genes from single immune cells that make the specific antibodies.

This was an efficient process that enabled the researchers to produce mature antibodies that recognized the same region of CFH targeted by the original patient's immune systems -- therefore leading to the attack of cancer cells, not healthy cells.

The researchers then tested the antibodies in multiple cancer cell lines, including lung, gastric and breast cancers in lab dishes, and in tumors in living mice. They found that the antibodies caused tumor cell death without any obvious side effects. The antibodies also appeared to trigger an additional adaptive immune response when the damaged cells sent signals to recruit an army of lymphocytes, creating a potentially more lethal systemic attack.

"We believe it might be this additional cellular response that could potentially have the most profound impact on cancer outcomes long-term," Patz said, noting that further tests would be required to understand the full potential of the approach. "This could represent a whole new approach to treating cancer, and it's exciting because the antibody selectively kills tumor cells, so we don't have significant side effects to achieve tumor control," Patz said. "We believe we can modulate the immune response and let the body's own immune system take over to either kill the tumor or keep it from growing."

In addition to Patz, study authors include Ryan T. Bushey; M. Anthony Moody; Nathan Nicely; Barton F. Haynes; S. Munir Alam; Stephen T. Keir; Rex C. Bentley; Kingshuk Roy Choudhury; Elizabeth B. Gottlin; Michael J. Campa; and Hua-Xin Liao.

The study received funding from the LUNGevity Foundation, the Department of Defense (W81XWH-13-1-0189), the National Institutes of Health (UL1TR001117), and the Duke Translational Research Institute.

http://www.eurekalert.org/pub_releases/2016-05/cp-etz042916.php

Evidence that Zika causes neural stem cells to self-destruct

Human neural stem cells infected by zika trigger an innate immune response leading to cell death

A new addition in the growing number of studies using brain organoids to understand how the Zika virus leads to microcephaly reveals that human neural stem cells infected by the virus subsequently trigger an innate immune response that leads to cell death.

On May 6 in Cell Stem Cell, University of California San Diego School of Medicine researchers report that if this immune response is blocked, it helps neural stem cells survive Zika infection.

Zika contributes to cell self-destruction by activating an infected brain cell's innate immune receptor TLR3, which has long been known to coax cells into producing antiviral proteins as a first line of defense against microbial invaders. Graduate student Jason Dang, whose research interest is in how TLR3 responds to different viruses, stumbled upon this connection when he decided to test TLR3 levels in Zika-infected brain organoids developed in the lab of Tariq Rana at UC San Diego's Biomedical Sciences Graduate Program.

"We were wondering how strong the evidence was, and we were excited when we saw that when we inhibit TLR3 in the Zika-infected brain organoids, the reduction in their size was less dramatic," says Rana, a professor of pediatrics and senior author on the paper.

"I was still not convinced, so we used a chemical to enhance TLR3 activation and observed that the brain tissue started to shrink a lot faster."

Previous work in Zika-infected brain organoids helped establish the connection between viral infection and the death of neural stem cells, but Rana's team adds in a new piece about the role of the immune system.

Inhibition of TLR3 may help neurons infected by Zika survive and continue to function as well as their uninfected counterparts, thus providing a target for therapeutic development.

"A part of my lab works on other viruses and we always look at macrophages and other external immune cells--we never would have thought to look at this system," Rana says. "There are many other viruses that cause central nervous system damage, and now I want to go back and look at those as well."

This work was supported in part by grants from the National Institutes of Health.

Cell Stem Cell, Dang and Tiwari et al.: "Zika Virus Depletes Neural Progenitors in Human Cerebral Organoids through Activation of the Innate Immune Receptor TLR3" http://www.cell.com/cell-stem-cell/fulltext/S1934-5909(16)30057-1

http://www.livescience.com/54680-intelligent-alien-life-probability-high.html

The Universe Has Probably Hosted Many Alien Civilizations: Study

Many other planets throughout the universe probably hosted intelligent life long before Earth did, a new study suggests.

By Mike Wall, Space.com Senior Writer

The probability of a civilization developing on a potentially habitable alien planet would have to be less than one in 10 billion trillion — or one part in 10 to the 22nd power — for humanity to be the first technologically advanced species the cosmos has ever known, according to the study.

"To me, this implies that other intelligent, technology-producing species very likely have evolved before us," said lead author Adam Frank, a professor of physics and astronomy at the University of Rochester in New York.

"Think of it this way: Before our result, you'd be considered a pessimist if you imagined the probability of evolving a civilization on a habitable planet was, say, one in a trillion," Frank said in a statement. "But even that guess — one chance in a trillion — implies that what has happened here on Earth with humanity has in fact happened about 10 billion other times over cosmic history."

In 1961, astronomer Frank Drake devised a formula to estimate the number of extraterrestrial civilizations that may exist today in the Milky Way.

Adam Frank and co-author Woodruff Sullivan of the University of Washington were interested in the odds that intelligent aliens have ever existed anywhere in the universe. So they tweaked the famous Drake equation, coming up with an "archaeological version" that doesn't take into account how long alien civilizations may last.

Frank and Sullivan also incorporated observations from NASA's Kepler space telescope and other instruments, which suggest that about 20 percent of all stars host planets in the life-friendly, "habitable zone," where liquid water could exist on a world's surface.

The researchers then calculated the probability that Earth was the universe's first-ever abode for intelligent life, after taking into account the number of stars in the observable universe (about 20 billion trillion, according to a recent estimate).

"From a fundamental perspective, the question is, 'Has it ever happened anywhere before?'" Frank said. "Our result is the first time anyone has been able to set any empirical answer for that question, and it is astonishingly likely that we are not the only time and place that an advanced civilization has evolved."

But this doesn't mean that there are lots of intelligent aliens out there, just waiting to be contacted, the researchers stressed.

"The universe is more than 13 billion years old," Sullivan said in the same statement. "That means that even if there have been 1,000 civilizations in our own galaxy, if they live only as long as we have been around — roughly 10,000 years — then all of them are likely already extinct. And others won't evolve until we are long gone. For us to have much chance of success in finding another 'contemporary' active technological civilization, on average they must last much longer than our present lifetime."

(The 10,000-year figure cited by Sullivan refers to humanity's development of agriculture and other "rudimentary" technologies; mankind has been capable of sending radio waves and other electromagnetic signals out into the cosmos for just a century or so.)

The new study has been published in the journal Astrobiology; you can read it for free here.

http://bit.ly/24EOFpA

Ice core reveals how lush Antarctica changed to icy desert

Antarctica was once covered with tropical forests. Now researchers have fully charted the slow transition from tropical paradise to icy wasteland, thanks to a single marine sediment core.

By Andy Coghlan

The core shows for the first time that temperate forests were a key transitional stage before falling temperatures turned the continent into a white wasteland.

The ice core was taken from the sea floor off Wilkes Land in East Antarctica as part of the Integrated Ocean Drilling Programme. Pollen grains found inside show how vegetation on the continent changed between the early Eocene, around 54 million years ago and into the Miocene, 12 million years ago.

"The core from Wilkes Land is the first to give the entire story from the Eocene all the way through," says Ulrich Salzmann of Northumbria University in Newcastle upon Tyne, UK, who presented preliminary results at the European Geosciences Union meeting in Vienna last month. "It seems that vegetation had disappeared completely by 12 million years ago."

Vanishing monkey puzzles

The core's story starts in much warmer climes, around 16 °C, in the Eocene between 53.8 and 47.9 million years ago. Back then, the climate was subtropical, the verdant landscape dominated by palms and trees such the monkey puzzle.

By the early Oligocene around 31 to 33 million years ago, the palms and monkey puzzles had disappeared. They gave way to more temperate species, including Huon pines, trees known as living fossils that still thrive in New Zealand and Tasmania today.

Podocarpus conifers began to abound, as did Nothofagus, or southern beeches, which are also still common in New Zealand and Tasmania.

For trees, the transition from the Oligocene to the Miocene 23 million years back was the beginning of the end. Podocarpus trees and southern beeches remained, but their territory was increasingly being invaded by mosses and other plants that are the hallmarks of tundra. The temperatures dropped to around 6°C by this period.

Tundra takeover

"Tundra starts to take over," says Salzmann. "The vegetation moves down to the lowlands and the tundra becomes dominant. The landscape became very similar to that seen today in Tierra del Fuego in Patagonia."

But the end for all greenery came around 12.5 million years ago, when even the tundra disappeared. "Then, the glaciers took over and turned Antarctica into a white desert," says Salzmann. "Wilkes Land must have been the last refuge of woody vegetation."

"It's a super-exciting find, and opens the door to this new look at Earth's history in the Antarctic," says Jörg Pross, a paleoclimatologist at the University of Heidelberg in Germany. "Obviously, this is particularly important in light of anthropogenic climate change, with Antarctica warming up quickly and its ice sheets becoming potentially unstable."

But he says that even though Saltzmann's core is a great start, it is like trying to use a single core from Europe to say what the entire climate was like, from southern Spain up to Norway. "To get a grip of what happened, more drill cores around Antarctica are needed," says Pross.