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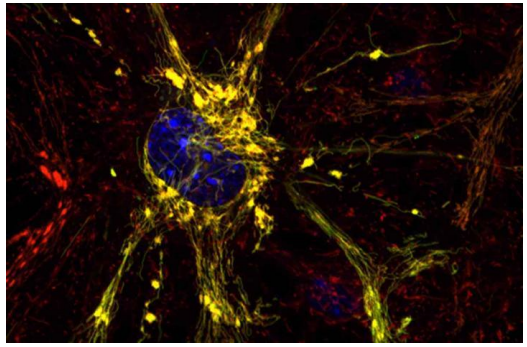
Possible strategy identified for Charcot-Marie-Tooth disease, other disorders

Research leads to development of compounds to correct mitochondrial dysfunction

Charcot-Marie-Tooth disease is an inherited disorder that leads to a gradual loss of motor neurons and, eventually, paralysis. The condition is caused by genetic mutations that disrupts cells' energy factories, called mitochondria. No drugs are available to slow or stop the progression of the disease, which affects nearly 3 million people worldwide.



Shown is a diseased neuron, with disease indicated by clumpy yellow mitochondria. Scientists at Washington University School of Medicine in St. Louis and Stanford University have designed small compounds that have the potential to correct mitochondrial dysfunction that leads to Charcot-Marie-Tooth disease and other conditions involving mitochondria, the cells' energy factories. **G. Dorn and A. Franco**

However, in research slated for fast-track advance online publication Oct. 24 in Nature, scientists at Washington University School of Medicine in St. Louis and Stanford University report that they have designed small compounds that have the potential to correct the mitochondrial dysfunction that leads to Charcot-Marie-Tooth and other conditions involving mitochondria. The team designed the compounds after its work in mouse cells revealed a new understanding of the 3-D structure of a key protein that is disabled in the mitochondria of patients with the disease.

"This mitochondrial protein has never been targeted before," said senior author Gerald W. Dorn II, MD, the Philip and Sima K. Needleman Professor of Medicine. "There are no drugs that work on this protein that is so important for mitochondrial function. We designed two compounds -- one that activates and one that inhibits the function of this protein. We are working on testing them in mice with mitochondrial defects."

Most people with Charcot-Marie-Tooth disease begin to see symptoms between ages 10 and 20. Patients with the condition have an average lifespan but slowly lose motor control, especially of the legs. Onset of symptoms before age 10 is associated with more severe disease, and such patients eventually may require crutches or a wheelchair.

The mitochondrial protein the researchers studied is called mitofusin 2. There's a lot of interest in this protein because scientists think it also may have roles in many diseases, including diabetes and heart disease, that generally aren't considered disorders of mitochondria. Mitofusin 2 governs whether two mitochondria are able to tether to each other and then fuse, exchanging genetic information, which is thought to be important for maintaining healthy mitochondria and, by extension, healthy tissues.

"In the past, scientists assumed mitofusin 2 was always active, always ready to tether to another mitofusin molecule and promote mitochondrial fusion," Dorn said. "Our study now shows this is incorrect. Mitofusin 2 folds and unfolds, giving it active and inactive forms that either encourage or discourage tethering and the resulting fusion of mitochondria."

Once Dorn and his colleagues, including co-author Daria Mochly-Rosen, PhD, of Stanford University, understood how mitofusin 2 changes shape, they were able to design small peptides that interact with the protein and drive it toward either an active or inactive state.

"We designed these molecules based on our new knowledge of mitofusin 2," Dorn said. "My colleague, Dr. Mochly-Rosen, is a genius at designing this kind of small peptide drug. She looks at amino acid sequences and sees things I don't see."

One of the small molecules, dubbed GoFuse, forces mitofusin 2 into its active, healthy state, which encourages tethering and the resulting

mitochondrial fusion. Conversely, the other small molecule, called TetherX, forces mitofusin 2 into its inactive state, which suppresses tethering and prevents fusion.

"The design of these peptide inhibitors was a challenge," Mochly-Rosen said. "But it is always exciting when a basic research discovery leads to the design of a new drug that may eventually help patients who currently have no treatment options."

Dorn said more work must be done to determine whether these small peptides will be effective in animal models of diseases. But the hope is that GoFuse, or a similar molecule, could encourage the mitochondrial tethering and fusion that is missing in Charcot-Marie-Tooth disease. If such tethering could be restored, it could prevent or delay the loss of motor neurons that gradually paralyzes many patients with this genetic disorder.

But the researchers see a potential use for the peptide inhibitors beyond Charcot-Marie-Tooth disease, such as reducing tissue damage that occurs when oxygen returns to the heart after a heart attack or to the brain after a stroke.

"Re-establishing oxygen flow is really important after a heart attack or stroke," Dorn said. "But you also get a huge wave of cell death when oxygen suddenly returns to tissues of the body, such as the heart or the brain."

The rush of oxygen back into tissues causes an influx of calcium into mitochondria that are tethered. Large amounts of calcium flowing into mitochondria causes water to rush in as well. Like an overfilled water balloon, the mitochondria burst, which kills the cell. But, Dorn speculated, if this type of tethering could be suppressed, it would prevent the sudden influx of calcium and protect mitochondria from being destroyed.

"These peptides are two sides of the same coin," Dorn said. "Mutations that disrupt tethering cause a neurodegenerative disease. We would like to encourage tethering in that case. But there are other situations where tethering is destructive, and we would like the ability to interrupt it briefly and then go back to normal. We've shown these peptides can influence mitochondrial tethering in cells grown in the lab, and now we are working to test them in mouse models of disease."

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Boosting levels of known antioxidant may help resist age-related decline

Natural decline in glutathione sets the stage for a wide range of age-related health problems

CORVALLIS, Ore. - Researchers at Oregon State University have found that a specific detoxification compound, glutathione, helps resist the toxic stresses of everyday life - but its levels decline with age and this sets the stage for a wide range of age-related health problems.

A new study, published in the journal Redox Biology, also highlighted a compound - N-acetyl-cysteine, or NAC - that is already used in high doses in medical detoxification emergencies. But the researchers said that at much lower levels NAC might help maintain glutathione levels and prevent the routine metabolic declines associated with aging.

In that context, the research not only offers some profound insights into why the health of animals declines with age, but specifically points to a compound that might help prevent some of the toxic processes involved.

Decline of these detoxification pathways, scientists say, are causally linked to cardiovascular disease, diabetes and cancer, some of the primary causes of death in the developed world.

"We've known for some time of the importance of glutathione as a strong antioxidant," said Tory Hagen, lead author on the research and the Helen P. Rumbel Professor for Health Aging Research in the Linus Pauling Institute at OSU.

"What this study pointed out was the way that cells from younger animals are far more resistant to stress than those from older animals," said Hagen, also a professor of biochemistry in the OSU College of Science. "In young animal cells, stress doesn't cause such a rapid loss

of glutathione. The cells from older animals, on the other hand, were quickly depleted of glutathione and died twice as fast when subjected to stress.

"But pretreatment with NAC increased glutathione levels in the older cells and largely helped offset that level of cell death."

Glutathione, Hagen said, is such an important antioxidant that its existence appears to date back as far as oxygen-dependent, or aerobic life itself - about 1.5 billion years. It's a principal compound to detoxify environmental stresses, air pollutants, heavy metals, pharmaceuticals and many other toxic insults.

In this study, scientists tried to identify the resistance to toxins of young cells, compared to those of older cells. They used a toxic compound called menadione to stress the cells, and in the face of that stress the younger cells lost significantly less of their glutathione than older cells did. The glutathione levels of young rat cells never decreased to less than 35 percent of its initial level, whereas in older rat cells glutathione levels plummeted to 10 percent of their original level.

NAC, the researchers said, is known to boost the metabolic function of glutathione and increase its rate of synthesis. It's already used in emergency medicine to help patients in a toxic crisis, such as ingestion of poisonous levels of heavy metals. It's believed to be a very safe compound to use even at extremely high levels - and the scientists are hypothesizing that it might have significant value at much lower doses to maintain glutathione levels and improve health.

"I'm optimistic there could be a role for this compound in preventing the increased toxicity we face with aging, as our abilities to deal with toxins decline," Hagen said. "We might be able to improve the metabolic resilience that we're naturally losing with age."

Also of interest, Hagen said, is the wide range of apparent detoxification potential offered by glutathione. Higher levels of it - boosted by NAC - might help reduce the toxicity of some prescription drugs, cancer chemotherapies, and treat other health issues.

"Using NAC as a prophylactic, instead of an intervention, may allow glutathione levels to be maintained for detoxification in older adults," the researchers wrote in their conclusion.

This research was supported by the National Institutes of Health, the National Science Foundation and the Medical Research Foundation of Oregon.

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Rabies vaccine effective even after warm storage

Work could improve vaccination coverage in remote areas with limited refrigeration

PULLMAN, Wash. - A Washington State University-led research team determined rabies vaccines stored at warmer temperatures still protect against the disease in dogs.

The work, published in the journal Vaccine, could lead to improved vaccination coverage in hard to reach, rural areas in Africa and Asia where electricity for cooling is limited.

"Thermotolerant vaccines were a really important feature of the campaign to eliminate smallpox," said Felix Lankester, lead author and clinical assistant professor in the WSU Paul G. Allen School for Global Animal Health. "We hope it will have the same effect for eradicating rabies."

Recommendations by the World Health Organization are for vaccines to be transported and stored in a "cold chain" at between 2°C (35.6°F) and 8°C (46.4°F). Lankester and his colleagues found that Nobivac, a commonly used rabies vaccine, produces the same level of protective antibodies in dogs after being stored for six months at 25°C (77°F) and for three months at 30°C (86°F).

"The ability to distribute vaccines widely outside the cold chain will allow for more consistent coverage across communities," said Lankester. "It could be a quantum shift in how vaccines are delivered."

Eradicating one of the deadliest diseases

"Human rabies from dog bites has the highest fatality rate of any human infectious disease," said Guy Palmer, WSU's senior director of

global health. "But rabies is easily preventable with regular dog vaccinations.

felix-administering-vaccine-2015-web

Felix Lankester, left, WSU clinical assistant professor, takes a blood sample to test whether a rabies vaccine stored at warmer temperatures is effective against the disease.

Each year roughly 60,000 people, mostly children, die from rabies. Globally, more than 99 percent of human rabies deaths are caused by dog bites -- almost all in sub-Saharan Africa and Asia.

Millions of people are saved by costly post-exposure prophylaxis - a series of post-bite vaccinations, the first of which must be administered within the first 24 hours after a person is bitten by a rabid dog. But once symptoms appear, the disease is fatal.

Vaccinating 70 percent of the dog population will protect humans and wildlife, such as endangered African wild dogs, from the disease.

WSU, in collaboration with the Serengeti Health Initiative, has been working to control rabies in areas of northern Tanzania through annual mass dog rabies vaccination campaigns. But rabies continues to be prevalent, in part because of the challenges of transporting vaccines to remote areas where vulnerable people live in resource-poor communities.

"If a team-led vaccination campaign misses a village because it is very far or because rain washed out a bridge, then there will be pockets where vaccination coverage is low," said Lankester. "With a community-led initiative, we are hopeful we would improve the coverage levels."

Empowering communities to lead vaccination programs

Mass vaccination teams generally only visit communities once a year, if they can get there at all. When new dogs are born or move into the community, the level of protection against rabies drops. In community-led programs, thermotolerant vaccines could be stored in the community where local coordinators would vaccinate the entire dog population.

"Through community-led programs, coverage could be kept relativity consistently high, which would reduce the likelihood of rabies returning to a community," said Lankester. "These findings also give confidence to those working to control rabies that if vaccines are kept outside of the cold chain for a small time, they don't have to be thrown away."

In the next phase of the research, Lankester and his colleagues will test the effectiveness of using low-tech cooling options for storing rabies vaccines in rural communities.

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Coral 'Twilight Zone' Reveals New Type of Photosynthesis

Corals that inhabit "twilight zone" adapted to eke out enough light energy to survive

By Stephanie Pappas, Live Science Contributor

More than 200 feet (60 meters) below the ocean's surface, where the water is cold and only about 1 percent of the daylight above penetrates, is a dim, blue world filled with little-understood creatures. Now, researchers have discovered that the corals that inhabit this "twilight zone" have a never-before-seen adaptation that enables them to eke out enough light energy to survive.

The photosynthetic algae that live on and power these corals have unusual cellular "machinery" that enables them to conduct photosynthesis more efficiently than species that live at shallower depths, the researchers reported Oct. 17 in the journal Frontiers in Marine Science.

"It's unlike anything we've seen on land, or anything we've even seen in the shallow reefs," said David Gruber, a marine biologist at the City University of New York and one of the researchers on the study.

Capturing a limited resource

On land and in the water, plants use cellular structures called light-harvesting complexes, or photosynthetic antennas, to capture photons (particles of light) and transfer them to the photosynthetic complexes

that convert light into usable energy. The photosynthetic antennas are made of various proteins and chlorophyll pigments. In dim forests on land, plants in the underbrush often evolve very large antenna complexes to wring every drop of light out of the sky, Gruber said.

Mesophotic reefs, also known as twilight reefs, exist in a perpetual state of dim blueness.

But that's not what the researchers found 213 feet (65 m) down in the northern Red Sea when they collected coral called Stylophora pistillata from reefs there. Inside the coral is symbiotic algae called Symbiodinium, which provide the coral oxygen and energy from photosynthesis in exchange for nutrients and protection. This makes for relatively easy living in shallow reefs, where sunlight is abundant. But below about 130 feet (40 m), the ocean gets dim. This is the "mesophotic" zone, where it's always twilight. At about 330 feet (100 m), only 1 percent of the sunlight above can reach down below. And only blue wavelengths of light can penetrate.

It might make sense for algae living in the mesophotic zone to build huge photosynthetic antennas. But that's not what Symbiodinium does. In fact, when Gruber and colleagues from the Hebrew University of Jerusalem and the University of Haifa, both in Israel, analyzed the deep-living algae, they found that the algae antenna structures were actually smaller than that of shallower Symbiodinium algae.

Extreme environment

Instead of building bigger antennas, the algae modified its light-gathering system. Plants like algae have two types of cellular machines for converting light into sugars: photosystem I and photosystem II. Symbiodinium relies more heavily on photosystem II but positions the cellular machinery close to the machinery of photosystem I. This makes it easier for the two systems to share energy. They also adjust the types of light-snatching proteins in their cellular membranes, the researchers said.

Diving to these coral habitats is hard for humans; commercial scuba divers don't usually go below about 130 feet. To get to the twilight zone of the Red Sea, the researchers, led by lead diver Shai Einbinder, donned tri-gas rebreather systems, which enable divers to go lower while facing a smaller risk of serious problems such as nitrogen narcosis (an altered state of consciousness that occurs when nitrogen enters the bloodstream at the increased pressures seen at extreme water depths). Still, divers stay down only a few minutes because they must ascend very slowly to equilibrate to the lower pressures at the surface and thus avoid decompression sickness, also known as "the bends", Gruber said.

Over the course of four years of diving, the scientists took some samples of deep-reef coral and transferred them to shallow environments, and took shallow corals and transferred them to deeper areas. They did this slowly, moving the corals only 16 feet (5 m) every two weeks. They found that the corals collected in water depths of about 10 feet could hang on to life at 213 feet. Corals from the deep, however, couldn't survive at shallow depths. They lacked the natural compounds that protect corals from the sun's damaging ultraviolet light.

"They didn't have the 'sunscreen,'" Gruber said. "The light was just burning them out." The researchers studied only one species of algae, and there are probably many more adaptations among the photosynthesizers of mesophilic reefs, Gruber said.

"I'm never unimpressed by the way nature evolved unique traits to allow life in some of the most seemingly unhospitable places," he said.

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Microbe hunters discover long-sought-after iron-munching microbe

A microbe that 'eats' both methane and iron: microbiologists have long suspected its existence, but were not able to find it - until now.

A microbe that 'eats' both methane and iron: microbiologists have long suspected its existence, but were not able to find it -- until now. Researchers at Radboud University and the Max Planck Institute for Marine Microbiology in Bremen discovered a microorganism that

couples the reduction of iron to methane oxidation, and could thus be relevant in controlling greenhouse gas emissions worldwide. Their results are published in the scientific journal PNAS on October 24, 2016.

The balance between methane-producing and -consuming processes has a major effect on the worldwide emission of this strong greenhouse gas into our atmosphere. The team of microbiologists and biogeochemists now discovered an archaeon -- the other branch of ancient prokaryotes besides bacteria -- of the order Methanosarcinales that uses iron to convert methane into carbon dioxide. During that process, reduced iron become available to other bacteria. Consequently, the microorganism initiates an energy cascade influencing the iron and methane cycle and thus methane emissions, describe first authors Katharina Ettwig and Baoli Zhu in the paper.

Application in wastewater treatment

Besides, these archaea have another trick up their sleeve. They can turn nitrate into ammonium: the favourite food of the famous anammox bacteria that turn ammonium into nitrogen gas without using oxygen. "This is relevant for wastewater treatment," says Boran Kartal, a microbiologist who recently moved from Radboud University to the Max Planck Institute in Bremen. "A bioreactor containing anaerobic methane and ammonium oxidizing microorganisms can be used to simultaneously convert ammonium, methane and oxidized nitrogen in wastewater into harmless nitrogen gas and carbon dioxide, which has much lower global warming potential." The same process could also be important in paddy fields, for example, which account for around 20 percent of human-related emissions of methane.

Closer than expected

While there have been numerous indications that such iron-dependent methane oxidizers existed, researchers have never been able to isolate them. Surprisingly, they were right in front of our doorstep: "After years of searching, we found them in our own sample collection," says microbiologist Mike Jetten of Radboud University with a smile. "We eventually discovered them in enrichment cultures from the Twentekanaal in The Netherlands that we've had in our lab for years. We obtained a large amount of biomass by feeding them with methane and nitrate." Kartal adds, "Based on the genetic blueprint of these microorganisms, we hypothesized that they could also convert particulate iron coupled to methane oxidation. When we tested our hypothesis in the lab, these organisms did the trick." In the next step, Kartal wants to look closer into the details of the process. "These findings fill one of the remaining gaps in our understanding of anaerobic methane oxidation. Now we want to further investigate which protein complexes are involved in the process."

Magical square of microbiology

Years ago, Jetten and his team drew up a table chart with available electron donors and acceptors, that should allow for the growth of -- still unknown -- microorganisms. A kind of magical square of microbiology. He expected that each box would fit a bacteria or achaeon, since evolution rarely leaves a niche unoccupied. His team has already discovered eight of the nine ghost microorganisms in the table chart: Methanosarcinales fills up the next-to-last box. "This is a really special finding," Jetten explains. "We hope to discover the last microorganism soon, but Australian and American researchers are snapping at our heels, so these are exciting times."

Billions of years ago

The newly discovered process could also lead to new insights into the early history of our planet. Already billions of years ago, Methanosarcinales archaea might have abundantly thrived under the methane-rich atmosphere in the ferruginous (iron holding) Archaean oceans, 4 to 2.5 billion years ago. More information on the metabolism of this organism can therefore shed new light on the long-standing discussion of the role of iron metabolism on early earth.

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Cranberry disrupts harmful bacteria's ability to communicate, spread and become virulent

New study shows promise for blunting the spread of hard-to-fight bacterial infections

CARVER, Mass. - Scientists from McGill University and INRS-Institut Armand-Frappier in Canada recently released a novel investigation showing that cranberry extract successfully interrupted the communication between bacteria associated with problematic and pervasive infections. The authors of the data published in Nature's Scientific Reports, Eric Déziel, professor-investigator at INRS-Institut Armand-Frappier and Nathalie Tufenkji, professor at McGill University, state that not only do the results provide insights into how cranberry compounds may work, they also have implications for the development of alternative approaches to control infections.

Previously published work has shown that the American cranberry (Vaccinium macrocarpon L) contains compounds -- such as proanthocyanidins (PACs) -- that provide meaningful antioxidant, anti-adhesion and anti-microbial properties that help fend off illness. Given this, the scientific team hypothesized that cranberries may also have an anti-virulence potential. They wanted to know if these cranberry compounds could help manage bacterial infections. By feeding fruit flies -- a commonly used model for studying human infections -- cranberry extract, the team discovered that cranberry provided flies protection from a bacterial infection and they lived longer than their cranberry-free counterparts. In essence, the cranberry extract reduced the severity of the bacterial infection.

Study author, Dr. Tufenkji, elaborates on what this might mean for humans, as opposed to flies, "This means that cranberries could be part of the arsenal used to manage infections and potentially minimize the dependence on antibiotics for the global public."

To further explain cranberries' impact on bacteria, Dr. Déziel said, "Cranberry PACs interrupt the ability for bacteria to communicate with each other, spread and become virulent -- a process known as quorum sensing. The cranberry extract successfully interferes with the chain of events associated with the spread and severity of chronic bacterial infections."

Added to the evidence of cranberry's role in preventing recurrent urinary tract infections by blocking bacteria from sticking to cell walls, the current study suggests that PACs may help control the virulence or spread of potentially dangerous bacterial infections around the world.

The complete study can be accessed here: Cranberry-derived proanthocyanidins impair virulence and inhibit quorum sensing of Pseudomonas aeruginosa.

This investigation was supported by unrestricted support from the Natural Sciences and Engineering Research Council of Canada, the Wisconsin Cranberry Board and the Cranberry Institute. The cranberry extract was provided by Ocean Spray Cranberries, Inc.

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Calcium induces chronic lung infections

Researchers have now discovered that calcium induces the switch from acute to chronic infection.

The bacterium Pseudomonas aeruginosa is a life-threatening pathogen in hospitals. About ten percent of all nosocomial infections, in particular pneumonia, are caused by this pathogen. Researchers from the University of Basel's Biozentrum, have now discovered that calcium induces the switch from acute to chronic infection. In Nature Microbiology the researchers have also reported why antibiotics are less effective in fighting the pathogen in its chronic state.

One of the most serious pathogens is the bacterium Pseudomonas aeruginosa, which frequently causes hospital infections and is notoriously difficult to treat owing to its multi-resistance to antibiotics. Although P. aeruginosa is responsible for a range of different infections in humans, it is the leading cause of chronic lung infections in immune-compromised patients.

Calcium induces acute to chronic virulence switch

In an early, acute stage of pneumonia, the pathogen employs a wide arsenal of weapons -- so-called virulence factors -- to invade the host and evade its immune system. During disease progression, the

bacterium adapts its strategy by switching from acute to chronic virulence. It stops the production of virulence factors, such as bacterial injection apparatus and toxins and, instead, produces a protective matrix and reduces its growth rate. The environmental signals directing this transition were so far unknown. The team led by Prof. Urs Jenal, infection biologist at the Biozentrum of the University of Basel, has now identified calcium as a signal that specifically triggers the switch to chronic virulence.

"In Pseudomonas a central signaling pathway senses environmental information and ultimately determines whether the pathogen will undergo the acute to chronic virulence switch," explains Jenal. "Although the components of this pathway are well-known, none of the external signals modulating the switch are defined." The researchers have now discovered that a receptor located in the bacterial cell envelope monitors the calcium concentration in the environment and transmits this signal into the cell. Elevated calcium levels trigger the switch to a chronic program: The bacteria protect themselves within a biofilm structure, reduce their growth rate and by that increase their drug tolerance and persistence.

Cystic fibrosis patients harbor calcium sensitive bacteria

Finally, the researchers were able to demonstrate the clinical relevance of their findings. Patients suffering from cystic fibrosis develop lifelong chronic infections by P. aeruginosa, which permanently damage their lung tissue. "Most of the isolates from airways of CF patients have retained their calcium sensitivity," emphasizes Jenal. "We believe that this allows these bacteria to constantly adapt their virulence in response to the often changing conditions in the airways. One of the characteristics of cystic fibrosis is deregulated calcium homeostasis. We assume that elevated calcium levels in patients promote the switch from an acute to a chronic state of infection. This is of advantage for the pathogen, as it may ensure its long-term survival in the respiratory tract. At the same time, treatment of chronically infected patients becomes more challenging."

Materials provided by Universität Basel. Note: Content may be edited for style and length.
Journal Reference:

Ursula N. Broder, Tina Jaeger, Urs Jenal. LadS is a calcium-responsive kinase that induces acute-to-chronic virulence switch in Pseudomonas aeruginosa. Nature Microbiology, 2016; 2: 16184 DOI: 10.1038/nmicrobiol.2016.184

http://bit.ly/2eXwpo0

After blindness, the adult brain can learn to see again

More than 40 million people worldwide are blind, and many of them reach this condition after many years of slow and progressive retinal degeneration.

The development of sophisticated prostheses or new light-responsive elements, aiming to replace the disrupted retinal function and to feed restored visual signals to the brain, has provided new hope. However, very little is known about whether the brain of blind people retains residual capacity to process restored or artificial visual inputs. A new study publishing 25 October in the open-access journal PLOS Biology by Elisa Castaldi and Maria Concetta Morrone from the University of Pisa, Italy, and colleagues investigates the brain's capability to process visual information after many years of total blindness, by studying patients affected by Retinitis Pigmentosa, a hereditary illness of the retina that gradually leads to complete blindness.

The perceptual and brain responses of a group of patients were assessed before and after the implantation of a prosthetic implant that senses visual signals and transmits them to the brain by stimulating axons of retinal ganglion cells. Using functional magnetic resonance imaging, the researchers found that patients learned to recognize unusual visual stimuli, such as flashes of light, and that this ability correlated with increased brain activity. However, this change in brain activity, observed at both the thalamic and cortical level, took extensive training over a long period of time to become established: the more the patient practiced, the more their brain responded to visual stimuli, and the better they perceived the visual stimuli using the implant. In other words, the brain needs to learn to see again.

The results are important as they show that after the implantation of a prosthetic device the brain undergoes plastic changes to re-learn how to make use of the new artificial and probably aberrant visual signals. They demonstrate a residual plasticity of the sensory circuitry of the adult brain after many years of deprivation, which can be exploited in the development of new prosthetic implants.

Citation: Castaldi E, Cicchini GM, Cinelli L, Biagi L, Rizzo S, Morrone MC (2016) Visual BOLD Response in Late Blind Subjects with Argus II Retinal Prosthesis. PLoS Biol 14(10): e1002569. doi:10.1371/journal.pbio.1002569 http://dx.doi.org/10.1371/journal.pbio.1002569

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Sleep loss tied to changes of the gut microbiota in humans

Curtailing sleep alters the abundance of bacterial gut species that have previously been linked to compromised human metabolic health, results from a new clinical study suggests.

Results from a new clinical study conducted at Uppsala University suggest that curtailing sleep alters the abundance of bacterial gut species that have previously been linked to compromised human metabolic health. The new article is published in the journal Molecular Metabolism.

Changes in the composition and diversity of the gut microbiota have been associated with diseases such as obesity and type-2 diabetes in humans. These diseases have also been linked with chronic sleep loss. However, it is not known whether sleep loss alters the gut microbiota in humans. With this in mind, Christian Benedict, associate professor of neuroscience, and Jonathan Cedernaes, M.D., Ph.D, both from Uppsala University, collaborated with researchers from the German Institute of Human Nutrition Potsdam-Rehbruecke. In their study, the researchers sought to investigate in nine healthy normal-weight male participants whether restricting sleep to about four hours per night for two consecutive days as compared with conditions of normal sleep (about 8 hours of sleep opportunity) may alter the gut microbiota in humans.

"Overall we did not find evidence that suggests that the diversity of the gut microbiota was altered by sleep restriction. This was somewhat expected given the short-term nature of the intervention and the relatively small sample size. In more specific analyses of groups of bacteria, we did however observe microbiota changes that parallel some of the microbiota changes observed when for instance obese subjects have been compared with normal-weight subjects in other studies, such as an increased ratio of Firmicutes to Bacteroidetes. Longer and larger clinical sleep interventions will be needed to investigate to what extent alterations of the gut microbiota may mediate negative health consequences attributed to sleep loss, such as weight gain and insulin resistance," says senior author Jonathan Cedernaes.

"We also found that participants were over 20 percent less sensitive to the effects of the hormone insulin following sleep loss. Insulin is a pancreatic hormone needed to bring down blood glucose levels. This decreased insulin sensitivity was however unrelated to alterations in gut microbiota following sleep loss. This suggests that changes in microbiota may not, at least in the short-term, represent a central mechanism through which one or several nights of curtailed sleep reduce insulin sensitivity in humans," says first author Christian Benedict.

"The gut microbiota is very rich and its functional role far from completely characterized. Future studies will hopefully be able to ascertain how the composition and functional role of the gut microbiota is able to modulate at the individual level how sensitive we humans are to negative metabolic, but also cognitive, effects of sleep loss," concludes senior author Jonathan Cedernaes.

http://bit.ly/2eNRQYf

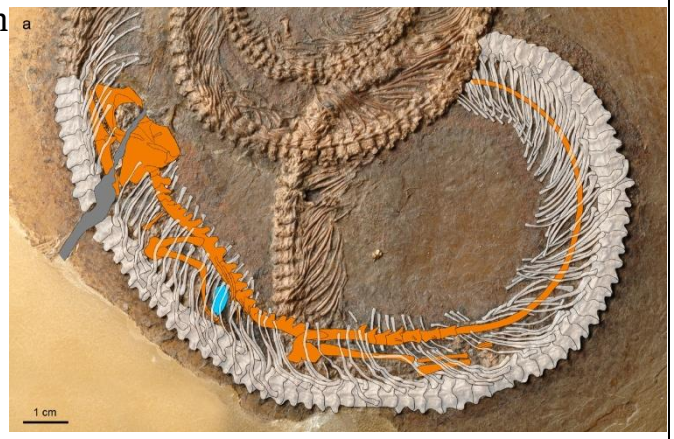
The Turducken of Fossils

A rare specimen shows a prehistoric chain of chowing down

- **By Brian Switek on October 24, 2016**

There are so many questions to ask about prehistoric creatures. How a species evolved, why they went extinct, what they looked like in life, what they sounded like... not to mention who ate whom. Look at paleoart and it's clear that we're often obsessed by the details of what was on the menu of long gone species.

This isn't as easy to work out as you might think. It's often possible to narrow down the range of what an animal ate based on its anatomy and what else was alive at the time, but, more often than not, we lack the bite marks, gut contents, and fossil feces to give us the specifics we yearn to know. That's what makes a fossil from the 48 million year old strata of Germany an exceptional insight into food webs long gone. The specimen, described by paleontologists Krister Smith and Agustín Scanferla, was found in the famous Messel Pit. This spot has given up beautifully-preserved remains of birds, primates, reptiles, and more, including this fortuitous find. It's a juvenile of an Eocene snake named *Palaeopython fischeri* with two surprises inside.



The remains of the lizard highlighted inside the body of the snake. Credit: Smith and Scanferla, 2016.

Within the snake there is an ancient relative of basilisk lizards - *Geiseltaliellus maarius* - and within the lizard are the remains of an insect. This is as close as paleontologists are likely to get to a fossil turducken.

The lizard species is the most common in the Messel deposits, and a previously-found specimen had what appeared to be plant fragments in its gut. Finding a lizard with insect parts inside adds evidence that these reptiles were not strict herbivores.

More than that, *Geiseltaliellus* is thought to have been a tree-dwelling lizard, so perhaps *Palaeopython* slithered around in the trees of the time. On top of that, Krister and Scanferla point out, a lizard in the belly of a juvenile serpent fits with the general picture of snakes like *Palaeopython* feeding on lizards as juveniles before shifting to bulkier prey as they get older. Testing that idea relies on finding additional, older snakes with gut contents - a tall order given how capricious the fossil record can be - but if there's a place where such a fossil might be found, it's Messel.

Smith, K., Scanferla, A. 2016. Fossil snake preserving three trophic levels and evidence for an ontogenetic dietary shifts. Palaeobiodiversity and Palaeoenvironments. *doi: 10.1007/s12549-016-0244-1*

http://bit.ly/2dXTEMK

New research reveals accidental making of 'Patient Zero' myth during 1980s AIDS crisis

A new study proves that a flight attendant who became notorious as the human epicentre of the US AIDS crisis of the 1980s - and the first person to be labeled the 'Patient Zero' of any epidemic - was simply one of many thousands infected in the years before HIV was recognized.

Research by a historian from the University of Cambridge and the genetic testing of decades-old blood samples by a team of US scientists has demonstrated that Gaétan Dugas, a French-Canadian gay man posthumously blamed by the media for spreading HIV across North America, was not the epidemic's 'Patient Zero'.

In fact, work by Dr Richard McKay, a Wellcome Trust Research Fellow from Cambridge's Department of History and Philosophy of Science, reveals how the very term 'Patient Zero' - still used today in press coverage of outbreaks from Ebola to swine flu to describe the

first known case - was created inadvertently in the earliest years of investigating AIDS.

Before he died, Dugas provided investigators with a significant amount of personal information to assist with studies into whether AIDS was caused by a sexually transmitted agent. McKay's research suggests that this, combined with confusion between a letter and a number, contributed to the invention of 'Patient Zero' and the global defamation of Dugas.

Dr McKay's work has added important contextual information to the latest study, led by Dr Michael Worobey from the University of Arizona and published today in the journal Nature, which has compared a new analysis of Dugas's blood with eight other archived serum samples dating back to the late 1970s.

"Gaétan Dugas is one of the most demonised patients in history, and one of a long line of individuals and groups vilified in the belief that they somehow fuelled epidemics with malicious intent," says McKay.

While his wider research traces this impulse to blame back several centuries, for the Nature paper McKay located the immediate roots of the term "Patient Zero" in an early 'cluster study' of US AIDS patients.

Mistaken for zero

Reports emerged in early 1982 of historical sexual links between several gay men with AIDS in Los Angeles, and investigators from the Centers for Disease Control (CDC) undertook a study to interview these men for the names of their sexual contacts.

They uncovered more links across southern California, but one connection was named several times despite not residing in the state: Case 057, a widely travelled airline employee. Investigators found that his sexual contacts included men in New York City, and some of his sexual partners developed symptoms of AIDS after he did.

CDC investigators employed a coding system to identify the study's patients, numbering each city's cases linked to the cluster in the sequence their symptoms appeared (LA 1, LA 2, NY 1, NY 2, etc.). However, within the CDC, Case 057 became known as 'Out(side)-of-California' - his new nickname abbreviated with the letter 'O.'

Because other cases were numbered, it was here that the accidental coining of a new term took place. "Some researchers discussing the investigation began interpreting the ambiguous oval as a digit, and referring to Patient O as Patient 0," says McKay. "'Zero' is a capacious word. It can mean nothing. But it can also mean the absolute beginning."

The LA study expanded, due in no small part to information provided by Case 057. Over 65% of men in the cluster reported more than 1,000 partners in their lifetimes, over 75% more than 50 in the past year. But most could offer only a handful of names of those partners.

As well as donating plasma for analysis, Case 057 managed to provide 72 names of the roughly 750 partners he'd had in the previous three years. Also, his distinctive name may have been easier for other men to remember, says McKay. "The fact that Dugas provided the most names, and had a more memorable name himself, likely contributed to his perceived centrality in this sexual network."

By the time the expanded study was published in 1984, the same year Dugas died of his illness, the cluster showed dozens of cases connecting several North American cities. Near the very centre of an accompanying diagram is a floating case that links both coasts, the itinerant Dugas. Case 057, the 'Out-of-California' case, had been rechristened simply as "Patient 0" - causing much speculation in the media.

'Casting' an epidemic

The journalist Randy Shilts would use the LA cluster study as an important thread in his bestselling book on the AIDS crisis, And the Band Played On. During the book's research, he became fascinated by the study's 'Patient 0'.

Motivated to find out more about this man, Shilts eventually learned his name in 1986. The journalist tracked down his friends and

colleagues for interviews, and, as "Patient Zero," made him one of the more memorable villains in his book.

To call attention to the crisis, Shilts set out to "humanise the disease", says McKay, who discovered that an early outline for the book actually listed 'The Epidemic' itself among the cast of characters. "To Shilts, Dugas as Patient Zero came to represent the disease itself."

The 1982 study had initially suggested to investigators that the period between infection and the appearance of AIDS symptoms might be several months. By the time Shilts's book was published in 1987, however, it was known that an infected individual might not display symptoms for several years, and that the study was unlikely to have revealed a network of infection. Yet Shilts uncritically resurrected the story of the Los Angeles cluster study and its 'Patient 0,' with long-standing consequences.

The journalist's decision provoked immediate criticism from AIDS activists in lesbian and gay communities across North America and the UK. Some of their works of protest are cited in the Nature study, and explored in greater detail in McKay's own forthcoming book and in a 2014 article he published in the Bulletin of the History of Medicine.

"In many ways, the historical evidence has been pointing to the fallacy of Patient Zero for decades," explains McKay. "We now have additional phylogenetic evidence that helps to consolidate this position."

McKay describes the very phrase 'Patient Zero' as "infectious." "Long before the AIDS epidemic there was interest in locating the earliest known cases of disease outbreaks. Yet the phrases 'first case,' 'primary case,' and 'index case' didn't carry the same punch.

"With the CDC's accidental coining of this term, and Shilts's well-honed storytelling instincts, you can see the consolidation of an 'infectious' formula that would become central to the way many would make sense of later epidemics."

Blaming 'others'

Now, almost 30 years since Shilts's book, analysis of the HIV-1 genome taken from Dugas's 1983 blood sample, contextualised through McKay's historical research, has shown that he was not even a base case for HIV strains at the time, and that a trail of error and hype led to his condemnation as the so-called Patient Zero.

The researchers say it may be naïve to expect Patient Zero's legendary status, or the popular impulse to attribute blame for disease outbreaks, to ever disappear.

"Blaming 'others' - whether the foreign, the poor, or the wicked - has often served to establish a notional safe distance between the majority and groups or individuals identified as threats," says McKay.

"In many ways, the US AIDS crisis was no different - as the vilification of Patient Zero shows. It is important to remember that, in the 1970s, as now, the epidemic was driven by individuals going about their lives unaware they were contracting, and sometimes transmitting, a deadly infection.

"We hope this research will give researchers, journalists and the public pause before using the term Patient Zero. The phrase carries many meanings and a freighted history, and has seldom pointed to what its users have intended."

http://bit.ly/2elK9bf

Worms against the wheeze

Asthmatics could breathe easier in the future with help from an unlikely quarter -- parasitic hookworms

Asthmatics could breathe easier in the future with help from an unlikely quarter -- parasitic hookworms.

Australian Institute of Tropical Health and Medicine (AITHM) researchers, at James Cook University (JCU) in Cairns, Australia, have identified a protein secreted by hookworms that suppresses asthma in mice.

In vitro tests on cells from people with asthma indicate the protein is also a promising candidate as a treatment for humans with allergies such as asthma.

This work builds on previous AITHM research into possible treatments for inflammatory bowel disease (IBD), including clinical trials that established experimental hookworm infection as an effective anti-inflammatory treatment for people with coeliac disease.

'After our initial success with IBD, asthma was our next logical goal,' JCU immunologist Dr Severine Navarro said.

'Although IBD and asthma are very different conditions, what they have in common is a defect in the regulation of the immune system, which results in overwhelming inflammatory processes.

'To survive and remain undetected in the human gut, parasitic worms regulate their human host's immune response. We aim to use that to control the inappropriate inflammation that characterizes autoimmune diseases and allergy,' Dr Navarro said.

The asthma study, published today (Wednesday 26 October, US ET) in Science Translational Medicine, tested a recombinant form of the protein on both mice and human cells. Mice treated with the worm protein showed an extensive suppression of inflammatory responses after exposure to an allergen.

The protein, AIP-2, was also tested in vitro on human cells - from people allergic to dust mites, a common asthma trigger.

'Our previous work on inflammatory bowel disease established that hookworm proteins can change T cells from pro-inflammatory to anti-inflammatory,' Dr Navarro said. 'The good news is that this doesn't just protect the gut, it also protects other organs, such as the airways, where asthma develops.'

Professor Alex Loukas, head of JCU's Centre for Biodiscovery and Molecular Development of Therapeutics, said AIP-2 showed great promise as a potential treatment for allergies, which affect nearly a billion people worldwide, costing over $9 billion per year in Australia alone.

'This study also represents an important step forward in our exploitation of the therapeutic potential of hookworm proteins,' Professor Loukas said. 'In our initial work on IBD we infected some very committed trial participants with actual hookworms. We have since established that the protective properties of hookworms lie in their oral secretions. More recently, we've isolated AIP-2, one of the most abundant proteins in that secretion mixture.

'In the asthma study, we used a recombinant form of AIP-2, which is to say we're now able to reproduce it in large quantities. We treated the mice with it by injection and also intranasal.

'This is an exciting development for us, because it means we're another step closer to being able to put a pill-based treatment into clinical trials, not just for asthma but also for other inflammatory and autoimmune diseases.'

http://bit.ly/2elJCpF

Mulberry extract activates brown fat, shows promise as obesity treatment

New research in The FASEB Journal suggests that rutin extracted from mulberries acts as an activator of brown adipose tissue (BAT) to mimic cold which regulates energy metabolism by enhancing BAT activity

Good news for those who want to activate their brown fat (or BAT, brown adipose tissue) without having to be cold: New research, published in The FASEB Journal, suggests that a natural compound in mulberries, called "rutin," can activate the BAT in our bodies to increase metabolism and facilitate weight loss.

"The beneficial effects of rutin on BAT-mediated metabolic improvement have evoked a substantial interest in the potential treatment for obesity and its related diseases, such as diabetes," said Wan-Zhu Jin, Ph.D., a researcher involved in the work from the Institute of Zoology at the Chinese Academy of Sciences in Beijing, China. "In line with this idea, discovery of more safe and effective BAT activators is desired to deal with obesity and its related diseases."

To make their discovery, Jin and colleagues used both genetically obese mice and mice with diet-induced obesity as models. These mice

were fed a regular diet, and supplemental rutin (1 mg/ml) was added to their drinking water. Rutin treatment significantly reduced adiposity, increased energy expenditure, and improved glucose homeostasis in both the genetically obese mice and the mice with diet-induced obesity. Specifically, the researchers found that rutin directly binds to and stabilizes SIRT1 (NAD-dependent deacetylase sirtuin-1), leading to hypoacetylation of PGC1α protein, which stimulates Tfam transactivation and eventually augments mitochondrial number and UCP1 activity in BAT. Rutin functions as a cold mimetic through activating a SIRT1-PGC1α-Tfam signaling cascade and increasing mitochondrial number and UCP1 activity in BAT. Rutin also induced brown-like (beige) adipocyte formation in subcutaneous adipose tissue in both obesity mouse models.

"Unlike hibernating animals, we humans have only a small spot of brown fat, and yet its importance in human metabolism has only recently come into view," said Thoru Pederson, Ph.D., Editor-in-Chief of The FASEB Journal. "In this study, the philosophy of ancient Chinese medicine's exploitation of plant materials has conjoined in the modern era with a very able physiology research team to evoke a promising lead."

Details: Xiaoxue Yuan, Gang Wei, Yilin You, Yuanyuan Huang, Hyuek Jong Lee, Meng Dong, Jun Lin, Tao Hu, Hanlin Zhang, Chuanhai Zhang, Huiqiao Zhou, Rongcai Ye, Xiaolong Qi, Baiqiang Zhai, Weidong Huang, Shunai Liu, Wen Xie, Qingsong Liu, Xiaomeng Liu, Chengbi Cui, Donghao Li, Jicheng Zhan, Jun Cheng, Zengqiang Yuan, and Wanzhu Jin. Rutin ameliorates obesity through brown fat activation. FASEB J. doi:10.1096/fj.201600459RR ; http://www.fasebj.org/content/early/2016/10/19/fj.201600459RR.abstract

http://bit.ly/2elMMK9

Iron supplements in the fight against lead

Lead is a toxic heavy metal that was added to petrol for use in cars until as recently as 25 years ago.

It is particularly harmful to the developing brains of infants, children and teenagers, and the damage it does is irreversible.

The situation becomes significantly worse if people are exposed to a high level of lead at the same time as they are suffering from iron deficiency. In the small intestine, lead and iron bind to the same transport protein, which absorbs the metals into the bloodstream. If someone consumes too little iron with their food, the transporter increases its activity, and can carry lead into the bloodstream instead, leading to increased levels of the toxic heavy metal in the body and brain.

450 Moroccan schoolchildren examined

A team of researchers led by ETH professor Michael B. Zimmermann from the Laboratory of Human Nutrition have now shown in a study that fortifying food with iron produces a striking reduction in blood lead concentration in children exposed to high levels of the metal.

This is the result of a trial involving over 450 children carried out by Zimmermann's former doctoral student Raschida Bouhouch and colleagues in southern Morocco. It is the first controlled prospective study to investigate the connection between iron deficiency and lead poisoning and to demonstrate that iron fortification can reduce blood lead levels. The study came about within the framework of a North-South project conducted by ETH Zurich and the University and University Hospital of Marrakesh.

Mining in the surrounding area meant that children of preschool and school age were exposed to an increased quantity of lead. At the same time, the level of iron in their blood was relatively low, placing them in a high-risk group.

Biscuits with iron

Depending on their weight, the children were given several white-flour biscuits on a daily basis for a period of four and a half months. The biscuits were fortified with different iron preparations: some received biscuits containing a specific quantity of iron sulphate, while others received biscuits with sodium iron EDTA or sodium EDTA without iron. To test the effect of the iron supplements, some children received only placebo biscuits containing no additional iron.

EDTA, which stands for ethylene diamine tetraacetic acid, forms stable complexes with iron, aiding its uptake into the bloodstream

from the intestines, but it is not absorbed itself. EDTA can also bind to lead in the intestines, reducing its absorption. In Europe, the compound is approved as food additive E385 in emulsified sauces and foods preserved in tins and jars. Sodium iron EDTA has already been used for iron fortification in foodstuffs for many years.

The researchers measured the children's blood lead concentration and iron status before and after the trial, as well as conducting tests to determine how well the children could solve cognitive tasks.

A positive effect on lead concentration

The researchers were delighted to find that the biscuits fortified with iron did indeed reduce the level of lead in the blood - specifically, by a third with sodium iron EDTA complexes and by a quarter with EDTA and iron sulphate.

Before the study began, the children's blood contained on average 4.3 micrograms of lead per decilitre. Biscuits with added sodium iron EDTA facilitated a reduction in blood lead concentration to 2.9 micrograms per decilitre. The biscuits also brought about an improvement in the children's iron status. On the other hand, the reduction in lead concentration had no effect on cognitive performance, as the researchers discovered during the corresponding tests.

Nevertheless, Zimmermann is very happy with the study's results: "The finding - that you can reduce blood lead concentration in exposed individuals with just a short intervention - is hugely significant for public health services," says the ETH professor.

Although, contrary to the researchers' expectations, the children's blood lead concentration before supplementation with iron was in line with the worldwide average at 4.3 micrograms per decilitre of blood, it was still possible to achieve a considerable reduction by administering the biscuits.

Zimmermann attributes the lack of improvement in cognitive performance to the fact that lead leaves behind lasting damage that cannot be reversed by administering iron. "Nevertheless, it definitely makes sense to use iron fortification to prevent brain damage in exposed sectors of the population," says the nutrition specialist. Iron supplementation may even provides foetuses in the womb with effective protection against subsequent brain damage.

As the base level of lead in the schoolchildren in the study corresponds to the worldwide average, Zimmermann says the results offer good transferability to other regions and population groups.

The tool of choice: NaFeEDTA

Based on these findings, he recommends using sodium iron EDTA to fortify foodstuffs in areas where lead poisoning and iron deficiency are common, and iron fortification is already used in food. "This is the most effective way to reduce the level of lead in the bloodstream." Although it is more expensive than iron sulphate, it also works better.

Lead contamination of food and water is still a serious problem in mining and heavy industry areas in Africa, India and China, but the issue is not yet resolved even in industrialised Western countries. The discussion has flared up in Flint, Michigan (USA), where the drinking water is contaminated with lead because inhabitants are supplied with water that flows through lead pipes. The pipes should have been replaced a long time ago.

Raschida R Bouhouch, Sana El-Fadeli, Maria Andersson, Abdelmounaim Aboussad, Laila Chabaa, Christophe Zeder, Maria Kippler, Jeannine Baumgartner, Azzedine Sedki, and Michael B Zimmermann. Effects of wheat-flour biscuits fortified with iron and EDTA, alone and in combination, on blood lead concentration, iron status, and cognition in children: a double-blind randomized controlled trial. American Journal of Clinical Nutrition. Published 12 October 2016, 10.3945/ajcn.115.129346

http://bit.ly/2f18wMi

Natural compound reduces signs of aging in healthy mice

Safety of NMN being tested in small clinical trial in Japan

Much of human health hinges on how well the body manufactures and uses energy. For reasons that remain unclear, cells' ability to produce energy declines with age, prompting scientists to suspect that the steady loss of efficiency in the body's energy supply chain is a key driver of the aging process.

Now, scientists at Washington University School of Medicine in St. Louis have shown that supplementing healthy mice with a natural compound called NMN can compensate for this loss of energy production, reducing typical signs of aging such as gradual weight gain, loss of insulin sensitivity and declines in physical activity.

The study is published Oct. 27 in the journal Cell Metabolism.

"We have shown a way to slow the physiologic decline that we see in aging mice," said Shin-ichiro Imai, MD, PhD, a professor of developmental biology and of medicine. "This means older mice have metabolism and energy levels resembling that of younger mice. Since human cells rely on this same energy production process, we are hopeful this will translate into a method to help people remain healthier as they age."

Imai is working with researchers conducting a clinical trial to test the safety of NMN in healthy people. The phase 1 trial began earlier this year at Keio University School of Medicine in Tokyo.

With age, the body loses its capacity to make a key element of energy production called NAD (***nicotinamide adenine dinucleotide***). Past work by Imai and co-senior author Jun Yoshino, MD, PhD, an assistant professor of medicine, has shown that NAD levels decrease in multiple tissues as mice age. Past research also has shown that NAD is not effective when given directly to mice so the researchers sought an indirect method to boost its levels. To do so, they only had to look one step earlier in the NAD supply chain to a compound called NMN (***nicotinamide mononucleotide***).

NMN can be given safely to mice and is found naturally in a number of foods, including broccoli, cabbage, cucumber, edamame and avocado. The new study shows that when NMN is dissolved in drinking water and given to mice, it appears in the bloodstream in less than three minutes. Importantly, the researchers also found that NMN in the blood is quickly converted to NAD in multiple tissues.

"We wanted to make sure that when we give NMN through drinking water, it actually goes into the blood circulation and into tissues," Imai said. "Our data show that NMN absorption happens very rapidly."

To determine the long-term effects of giving NMN, Imai, Yoshino and their colleagues studied three groups of healthy male mice fed regular mouse chow diets. Starting at five months of age, one group received a high dose of NMN-supplemented drinking water, another group received a low dose of the NMN drinking water, and a third group served as a control, receiving no NMN. The researchers compared multiple aspects of physiology between the groups, first at 5 months of age and then every three months, until the mice reached 17 months of age. Typical laboratory mice live about two years.

The researchers found a variety of beneficial effects of NMN supplementation, including in skeletal muscle, liver function, bone density, eye function, insulin sensitivity, immune function, body weight and physical activity levels. But these benefits were seen exclusively in older mice.

"When we give NMN to the young mice, they do not become healthier young mice," Yoshino said. "NMN supplementation has no effect in the young mice because they are still making plenty of their own NMN. We suspect that the increase in inflammation that happens with aging reduces the body's ability to make NMN and, by extension, NAD."

In skeletal muscle, the investigators -- including the study's first author, Kathryn Mills, the research supervisor in Imai's lab -- found that NMN administration helps energy metabolism by improving the function of mitochondria, which operate as cellular power plants. They also found that mice given NMN gained less weight with aging even as they consumed more food, likely because their boosted metabolism generated more energy for physical activity. The researchers also found better function of the mouse retina with NMN supplementation, as well as increased tear production, which is often lost with aging. They also found improved insulin sensitivity in the

older mice receiving NMN, and this difference remained significant even when they corrected for differences in body weight.

In a paper published earlier this year in Cell Reports, Yoshino and his colleagues revealed more details of how NAD works in influencing glucose metabolism and the body's fat tissue. In that study, the mice had a defect in the ability to manufacture NAD only in the body's fat tissue. The rest of their tissues and organs were normal.

"Even though NAD synthesis was stopped only in the fat tissue, we saw metabolic dysfunction throughout the body, including the skeletal muscle, the heart muscle, the liver and in measures of the blood lipids," Yoshino said. "When we gave NMN to these mice, these dysfunctions were reversed. That means NAD in adipose tissue is a critical regulator of whole body metabolism."

Added Imai, "This is important because Jun showed that if you mess up NAD synthesis only in fat tissue, you see insulin resistance everywhere. Adipose tissue must be doing something remarkable to control whole body insulin sensitivity."

During the long-term NMN study in healthy mice, Imai also said they monitored the animals for any potential increase in cancer development as a result of NMN administration.

"Some tumor cells are known to have a higher capability to synthesize NAD, so we were concerned that giving NMN might increase cancer incidence," Imai said. "But we have not seen any differences in cancer rates between the groups."

The phase 1 trial in Japan is using NMN manufactured by Oriental Yeast Co., which also provided the NMN used in these mouse studies. Outside of this clinical trial, high-grade NMN for human consumption is not commercially available. But there's always broccoli.

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This work was supported by the National Institutes of Health (NIH), grant numbers P30 DK020579 and P30 DK56341; a Research to Prevent Blindness Physician Scientist Award; a Research to Prevent Blindness Unrestricted Grant to the Department of Ophthalmology; the Hope Center for Neurological Disorders at Washington University; the UK Research Councils; and Biotechnology and Biological Science Research Council. This work was conducted under a sponsored research agreement between Washington University and Oriental Yeast Co.

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http://bit.ly/2dZdEyq

Ten months in the air without landing

No other bird species remains in the air for as long without landing.

The common swift flies ten months on end without landing. The hypothesis on these birds' life in the air was presented by British researcher Ron Lockley back in 1970, but it is only now that researchers at Lund University in Sweden have managed to prove the extreme lifestyle of the species. No other bird species remains in the air for as long without landing.

A Common Swift is in the sky. **N. Camilleri**

Using a new type of microdata log, the researchers at the Faculty of Science in Lund have managed to prove that the common swift only lands for two months of the year, during the breeding season. The rest of the time, ten months, they spend in the air, migrating and hibernating south of the Sahara.

"This discovery significantly pushes the boundaries for what we know about animal physiology. A ten-month flight phase is the longest we know of any bird species - it's a record", says Professor Anders Hedenström at the Department of Biology in Lund.

The researchers followed 13 individual birds, some of them for two years in a row. Through a microdata log, attached to each bird, the researchers were able to determine whether the birds were in the air or not, their acceleration, and where they had been at any given time. The results show that some of the birds landed during short periods at night, sometimes during an entire night. But even these birds spent more than 99.5 per cent of their ten-month migration and hibernation period in the air. Data from other birds show that they did not land a single time in ten months.

The birds which had never landed had all moulted and gained new flight feathers (wing and tail), while the majority of those who, on some occasion, landed had not moulted their wing feathers.

"Whether they moult or not could indicate small differences in their general condition or burden of parasites, and explain the flight behaviour of individual birds within the species", says Anders Hedenström.

The new knowledge about common swifts has already generated new questions such as how they handle the high energy consumption during the ten months in the air, and how they fly and sleep at the same time? "They might do as the frigate bird and sleep while gliding. Every day, at dusk and dawn, the common swift rises up to an altitude of about two-three kilometres. Perhaps they sleep during a declining glide, but we're not sure", he says.

The method used was developed within the project Centre for Animal Movement Research (CAnMove). The results are published in an article in the scientific journal Current Biology.

http://bit.ly/2frXIKq

It's what underneath that counts

Long-standing recycling of ancient sulfur in billion-year-old rocks supplies energy to terrestrial deep subsurface biosphere and sheds insights into search for life on Mars

To the naked eye, ancient rocks may look completely inhospitable, but in reality, they can sustain an entire ecosystem of microbial communities in their fracture waters isolated from sunlight for millions, if not billions, of years. New scientific findings discovered the source of the essential energy to sustain the life kilometers below Earth's surface with implications for life not only on our planet but also on Mars.

The two essential substances used by the deep subsurface microbes are hydrogen and sulfate dissolved in the fracture water. There is a basic understanding that reactions between the water and minerals in the rock produce hydrogen, but what about sulfate?

"We are very interested in the source of sulfate and how sustainable it is in those long isolated fracture water systems" says Long Li, assistant professor in the University of Alberta's Department of Earth and Atmospheric Sciences and Canada Research Chair in Stable Isotope Geochemistry.

Li--who worked as postdoctoral fellow with Barbara Sherwood Lollar, professor in the Department of Earth Sciences at University of Toronto and Boswell Wing in the Department of Earth and Planetary Sciences at McGill University--examined the relative ratios of several types of sulfur atoms that have different neutron numbers, namely sulfur isotopes, in the dissolved sulfate in the billion-year-old water collected from 2.4 kilometers below the surface in Timmins, Ontario, Canada. They observed a unique distribution pattern called sulfur isotope mass-independent fractionation.

"To date this signature of ancient Earth sulfur has only been found in rocks and minerals," says Sherwood Lollar. "Based on the match in the isotopic signature between the dissolved sulfate and the pyrite minerals in the 2.7 billion year old host rocks, we demonstrated that the sulfate was produced by oxidation of sulfide minerals in the host rocks by oxidants generated by radiolysis of water. The same pyrite and other sulfide ores that make these rocks ideal for economic mining of metals, produce the 'fuel' for microbial metabolisms."

The authors demonstrate that the sulfate in this ancient water is not modern sulfate from surface water flowing down, but instead, just like

the hydrogen, is actually produced in place by reaction between the water and the wall rock. What this means is that the reaction will occur naturally and can persist for as long as the water and rock are in contact, potentially billions of years.

"The wow factor is high," says Li, who explains that billion-year-old rocks, exposed or unexposed, compose more than half of Earth's continental crust. "If geological processes can naturally supply a steady energy source in these rocks, the modern terrestrial subsurface biosphere may expand significantly both in breadth and depth."

Some locations on Mars have similar mineral assemblages to the rocks in Timmins. This allows the scientists to speculate that microbial life can indeed be supported on Mars.

"Because this is a fairly common geological setting on modern Mars, we think that as long as the right minerals and liquid water are present, maybe kilometers below the Martian surface, they may interact and produce energy for life, if there is any."

Li concludes that if there is any life on Mars right now--a question that has long piqued people's curiosity--the best bet is to look below the surface.

"Sulfur mass-independent fractionation in subsurface fracture waters indicates a long-standing sulfur cycle in Precambrian rocks" appeared in the October 27 issue of Nature Communications, an open access journal part of the Nature group of publications.

http://bit.ly/2emShb7

First-Ever Dinosaur Brain Tissue Found

The fossil displays distinct similarities to the brains of modern-day crocodiles and birds.

By Kacey Deamer, Staff Writer | October 27, 2016 01:01pm ET

What was going on in dinosaurs' noggins as they dwelled in Cretaceous forests, stalking fierce prey or sitting on a nest of giant eggs? Paleontologists may never know the answer to these questions, but they just got one step closer with the first-ever discovery of brain tissue from a dinosaur.

And it's tiny.

The brainy finding looked like an unassuming brown pebble when a fossil hunter in Sussex, England, found it more than a decade ago. Discovering any soft tissue from a dinosaur is rare since that material degrades faster than other types of tissue, and dinosaurs lived more than 66 million years ago.

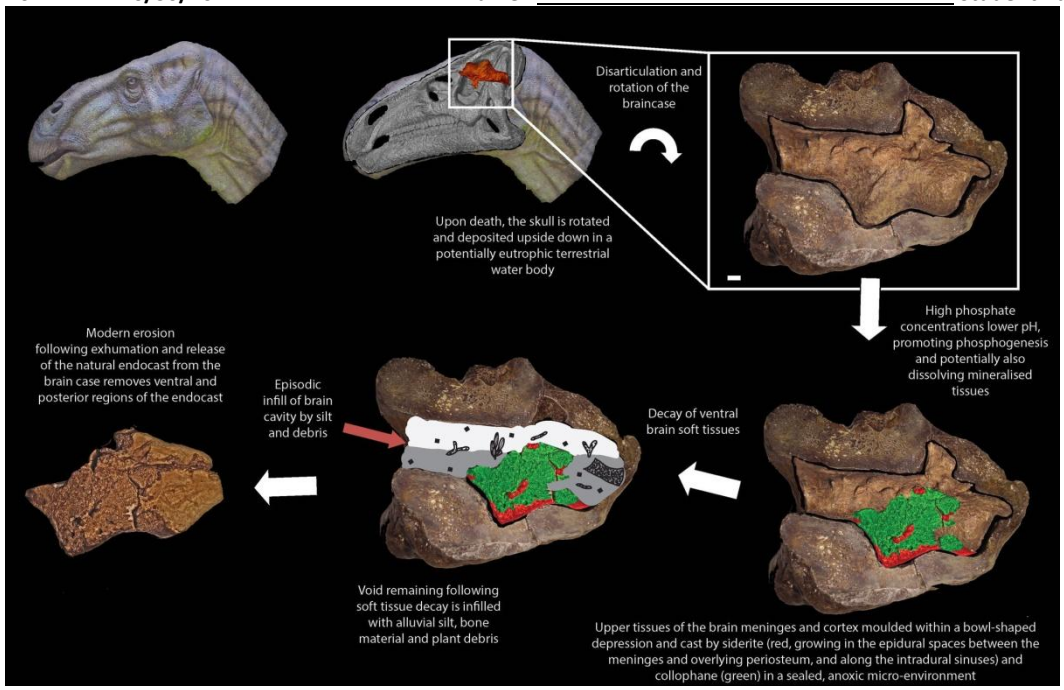
The fossil displays distinct similarities to the brains of modern-day crocodiles and birds. **Jamie Hiscocks**

This particular soft tissue was essentially pickled when the dinosaur died, according to the researchers, which is why it was so well-preserved.

"What we think happened is that this particular dinosaur died in or near a body of water, and its head ended up partially buried in the sediment at the bottom," co-author David Norman, a scientist at the University of Cambridge, said in a statement. "Since the water had little oxygen and was very acidic, the soft tissues of the brain were likely preserved and cast before the rest of its body was buried in the sediment."

Using a scanning electron microscope (SEM) — which produces images in fine detail by moving a beam of electrons over an object — the researchers identified different structures within the pebble-size tissue. In the images, they could make out meninges (tissue that surrounds the brain), strands of collagen and blood vessels, and structures that could be from the brain's cortex (the outer layer of the brain).

Norman and his colleagues determined the brain tissue was likely from a species similar to Iguanodon, a large herbivorous dinosaur that lived during the early Cretaceous period, about 133 million years ago. The structure seen within the fossilized brain tissue showed similarities to that found in birds and crocodiles — dinosaurs' modern-day descendants.



The researchers outlined the time sequence of how the small piece of dinosaur brain tissue became the pebble-looking fossil. Despite fossilization and erosion, they were able to identify different structures within the tissue. **University of Cambridge**

"It was indeed structured rather like that seen typically in reptiles," Norman told Live Science. "It also does not show that dinosaurs were necessarily very smart — their brains did not fill their braincases in this instance."

In reptiles, and assumed for dinosaurs, the brain only takes up about half of the space within the cranial cavity. The rest of the space is a dense region of blood vessels that surrounds the brain. Based on the structures seen in the fossilized brain, the researchers said it is consistent with reptiles. Though some dinosaurs are believed to have sported quite large brains, namely those that led to modern birds, Norman said this particular fossil does not display such size.

The researchers also cautioned against drawing conclusions about the intelligence of dinosaurs from this particular fossil. However, they do posit that this dinosaur and its relatives had relatively complex behaviors.

"It is reasonable to suppose that iguanodontian dinosaurs of this type were moderately complex behaviorally (no less so than modern crocodilians, for example)," the researchers wrote.

Their findings were published today (Oct. 27) in a Special Publication of the Geological Society of London, in tribute to Martin Brasier of the University of Oxford, who died in 2014. Brasier and Norman coordinated the research into this particular fossil during the years before Brasier's death in a traffic accident.

http://bit.ly/2fiwari

Placebo sweet spot for pain relief found in brain

New study first to pinpoint unique brain region responsible for placebo response in pain

CHICAGO --- Scientists have identified for the first time the region in the brain responsible for the "placebo effect" in pain relief, when a fake treatment actually results in substantial reduction of pain, according to new research from Northwestern Medicine and the Rehabilitation Institute of Chicago (RIC).

Pinpointing the sweet spot of the pain killing placebo effect could result in the design of more personalized medicine for the 100 million Americans with chronic pain. The fMRI technology developed for the study has the potential to usher in an era of individualized pain therapy by enabling targeted pain medication based on how an individual's brain responds to a drug.

The finding also will lead to more precise and accurate clinical trials for pain medications by eliminating individuals with high placebo response before trials.

The scientists discovered a unique brain region within the mid frontal gyrus that identifies placebo pill responders in one trial and can be validated (95 percent correct) in the placebo group of a second trial.

The study will be published Oct. 27, 2016, in PLOS Biology.

"Given the enormous societal toll of chronic pain, being able to predict placebo responders in a chronic pain population could both help the design of personalized medicine and enhance the success of clinical trials," said Marwan Baliki, research scientist at RIC and an assistant professor of physical medicine and rehabilitation at Northwestern University Feinberg School of Medicine. Baliki and Vania Apkarian, professor of physiology at Feinberg in whose lab the research was conducted, are both corresponding authors on the paper.

Using drugs to treat patients' pain has been trial and error, with physicians changing dosage or trying another type of drug if one doesn't work.

"The new technology will allow physicians to see what part of the brain is activated during an individual's pain and choose the specific drug to target this spot," Apkarian said. "It also will provide more evidence-based measurements. Physicians will be able to measure how the patient's pain region is affected by the drug."

Currently, placebo response is primarily studied in healthy subjects within controlled experimental settings. While such experiments aid understanding of the biological and behavioral underpinning of placebo response in experimental (applied) pain, they translate poorly to the clinic, where pain is mainly chronic in nature, Baliki said.

In this new study and for the first time, scientists used functional magnetic resonance imaging (fMRI) combined with a standard clinical trial design to derive an unbiased brain-based neurological marker to predict analgesia associated with placebo treatment in patients with chronic knee osteoarthritis pain. Scientists showed placebo pill ingestion is associated with a strong analgesia effect, with more than half of the patients reporting significant pain relief.

If future similar studies can further expand and eventually provide a brain-based predictive best-therapy option for individual patients, it would dramatically decrease unnecessary exposure of patients to ineffective therapies and decrease the duration and magnitude of pain suffering and opioid use, Baliki and Apkarian said.

Other Northwestern authors include Pascal Te ?treault, Ali Mansour, Etienne Vachon-Presseau and Thomas J. Schnitzer.

The study was supported by grant NS035115 from the National Institute of Neurological Disorders and Stroke and grant AT007987 from the National Center for Complementary and Integrative Health, both of the National Institutes of Health. The Canadian Institutes of Health Research and Eli Lilly Pharmaceuticals also supported the research.

http://bit.ly/2fis82u

How lack of oxygen makes bacteria cause acne and how to stop it

It's like Jekyll and Hyde. One moment bacteria on the skin are harmless, the next they are causing a full-on spotty break out.

By Andy Coghlan

Now researchers have discovered exactly why this happens – a breakthrough that could yield new acne treatments, possibly in two years. Richard Gallo of the University of California, San Diego, and his colleagues have discovered that a harmless bacterium that lives on the surface of the skin can turn nasty, triggering inflammation and zits, when it finds itself trapped in airless, oily conditions like those found in hair follicles.

Cascade of chemicals

The airless environment causes the bacterium, Propionibacterium acnes, to turn sebum – an oily matter found in the skin – into fatty acids that activate inflammation in nearby skin cells. By analysing mixtures of the bacteria alongside human skin and hair cells, Gallo's team found that the fatty acids deactivate enzymes called histone deacetylases that normally act as a brake on inflammation. Once that brake is off, cascades of chemicals are produced by skin cells, aggravating the type of inflammation that causes acne.

"For the first time, it shows how fatty acids derived from P. acnes act on skin cells to induce inflammation," says Holger Brüggemann of Aarhus University in Denmark, who in 2004 unravelled the entire genome of the skin bacterium.

Unfortunately, scrubbing your face isn't the answer, because the bacteria clump together to form structures called biofilms, which help

anchor them to the skin. Potential therapies are further complicated by the fact that certain strains of P. acnes are actually beneficial to skin health. Nevertheless, Gallo is confident that his team's breakthrough could lead to new treatments. "We can either inhibit these fatty acids, or block their impact on the skin," says Gallo. "We're working on how to do this."

Hormone surge

Gallo says the discovery could also help to explain why some people seem more prone than others to developing acne. It could be that some people's hair follicles are especially suffocating. Alternatively, some people might inherit genes that make their skin cells more vulnerable to inflammation from the fatty acids produced by P. acnes, or they may have strains of the bacteria on their skin that make excessive amounts of the fatty acids. "I think all of these aspects probably play a role," he says.

Brüggemann says that teenagers are most vulnerable to outbreaks because surges in sex hormones during puberty drive the production of extra sebum in the skin. This extra sebum enables any P. acnes in the hair follicles to produce more of the fatty acids that aggravate inflammation, leading to more spots.

Gallo wants to do further work on skin samples to corroborate the findings. "If we get lucky, it could lead to new medications in two to five years," he says.

Journal reference: Science Immunology, DOI: 10.1126/sciimmunol.aah4609

http://bit.ly/2eZLy8J

Physics tweak solves five of the biggest problems in one go

It's not a bad day at work. Five of the biggest fundamental problems in physics seem sorted in one go.

By Shannon Hall

The model that can do this, formulated by Guillermo Ballesteros at the University of Paris-Saclay in France and his colleagues, may explain dark matter, neutrino oscillations, baryogenesis, inflation and the strong CP problem.

Dubbed SMASH, the model is based on the standard model of particle physics, but has a few bits tacked on. The standard model is a collection of particles and forces that describes the building blocks of the universe. Although it has passed every test thrown at it, it can't explain some phenomena.

For example, we don't understand dark matter, the mysterious substance that makes up 84 per cent of the universe's mass. Nor why there is more matter than antimatter. Nor why the universe grew so rapidly in its youth during a period known as inflation. The list continues.

So something is still missing from the standard model. "Presumably we need some new particles," says Mikhail Shaposhnikov at the Swiss Federal Institute of Technology in Lausanne. "The question is, how many new particles do we need?"

Smashing theories together

Some models, like supersymmetry, add hundreds of particles – none of which have been spotted at colliders like the LHC. But SMASH adds only six: three neutrinos, a fermion and a field that includes two particles.

That's a reasonable approach, Shaposhnikov says. "I would start by assuming that the number of new particles is very small," he says. "And then add new particles only if you really need them."

SMASH is several theories smashed together, says co-author Andreas Ringwald at the German Electron Synchrotron, DESY, in Hamburg. It builds on Shaposhnikov's model from 2005, which added three neutrinos to the three already known in order to solve four fundamental problems in physics: dark matter, inflation, some questions about the nature of neutrinos, and the origins of matter.

SMASH adds a new field to explain some of those problems a little differently. This field includes two particles: the axion, a dark horse candidate for dark matter, and the inflaton, the particle behind inflation.

As a final flourish, SMASH uses the field to introduce the solution to a fifth puzzle: the strong CP problem, which helps explain why there is more matter than antimatter in the universe.

Testable predictions

"The best thing about the theory is that it can be tested or checked within the next 10 years or so," Ringwald says. "You can always invent new theories, but if they can only be tested in 100 years, or never, then this is not real science but meta-science."

SMASH predicts that the axion should be about ten billion times lighter than the electron. Particles this small could be probed by the CULTASK experiment running in South Korea, or the proposed ORPHEUS experiment in the US and the planned MADMAX experiment in Germany.

This doesn't mean it's game over. It's more like game on. Physicists will continue to compete to find experimental evidence or a better model. "The battle is open," Ringwald says.

Journal reference: https://arxiv.org/pdf/1608.05414v1.pdf

http://nyti.ms/2f4ipb5

Pushing That Crosswalk Button May Make You Feel Better, but …

It is a reflex born of years of habit: You see a button, press it and then something happens.

By CHRISTOPHER MELEOCT. 27, 2016

The world is filled with them, such as doorbells, vending machines, calculators and telephones.

But some buttons we regularly rely on to get results are mere artifices — placebos that promote an illusion of control but that in reality do not work.

No matter how long or how hard you press, it will not change the outcome. Be prepared to be surprised — and disappointed — by some of these examples.

Door-close buttons on elevators

Pressing the door-close button on an elevator might make you feel better, but it will do nothing to hasten your trip.

Karen W. Penafiel, executive director of National Elevator Industry Inc., a trade group, said the close-door feature faded into obsolescence a few years after the enactment of the Americans With Disabilities Act in 1990.

The legislation required that elevator doors remain open long enough for anyone who uses crutches, a cane or wheelchair to get on board, Ms. Penafiel said in an interview on Tuesday. "The riding public would not be able to make those doors close any faster," she said.

The buttons can be operated by firefighters and maintenance workers who have the proper keys or codes.

No figures were available for the number of elevators still in operation with functioning door-close buttons. Given that the estimated useful life of an elevator is 25 years, it is likely that most elevators in service today have been modernized or refurbished, rendering the door-close buttons a thing of the past for riders, Ms. Penafiel said.

Take heart, though: The door-open buttons do work when you press them.

Crosswalk signals

New Yorkers (those who don't jaywalk, that is) have for years dutifully followed the instructions on the metal signs affixed to crosswalk poles:

To Cross Street
Push Button
Wait for Walk Signal

But as The New York Times reported in 2004, the city deactivated most of the pedestrian buttons long ago with the emergence of computer-controlled traffic signals. More than 2,500 of the 3,250 walk buttons that were in place at the time existed as mechanical placebos. Today there are 120 working signals, the city said.

About 500 were removed during major construction projects. But it was estimated that it would cost $1 million to dismantle the nonfunctioning mechanisms, so city officials decided to keep them in place.

Most of the buttons were scattered throughout the city, mainly outside of Manhattan. They were relics of the 1970s, before computers began choreographing traffic signal patterns on major arteries.

ABC News reported in 2010 that it found only one functioning crosswalk button in a survey of signals in Austin, Tex.; Gainesville, Fla.; and Syracuse.

Office thermostats

The same problem that confronts couples at home — one person's perception that a room is too cold is another's that it is too warm — faces office workers as well.

Depending on where you work, you might find the thermostat in a plastic case under lock and key, but if you're lucky you might have control over one.

Well, you might think you have control.

The Air Conditioning, Heating and Refrigeration News reported in 2003 that it asked readers in an informal online survey whether they had ever installed "dummy thermostats." Of 70 who responded, 51 said they had.

One respondent, David Trimble of Fort Collins, Colo., wrote The News that people "felt better" that they could control the temperature in their work space after a nonfunctioning thermostat was installed. "This cut down the number of service calls by over 75 percent," he wrote.

Sense of control

Though these buttons may not function, they do serve a function for our mental health, Ellen J. Langer, a psychology professor at Harvard University who has studied the illusion of control, said in an email.

"Perceived control is very important," she said. "It diminishes stress and promotes well being."

John Kounios, a psychology professor at Drexel University in Philadelphia, said in an email there was no harm in the "white lie" that these buttons present. Referring to the door-close button on an elevator, he said, "A perceived lack of control is associated with depression, so perhaps this is mildly therapeutic."

Knowing that pushing these buttons is futile does not mean it will stop people from trying, he added. The reward of the elevator door closing always occurs eventually, he said.

"If the door never closed, we would stop pressing the button," he continued. "But in that case, of course, we would stop using the elevator altogether. So, that habit is here to stay. Similarly, even though I have grave doubts about the traffic light buttons, I always press them. After all, I've got nothing else to do while waiting. So why not press the button on the off chance that *this one* will work?"

http://bit.ly/2eZJGNn

Always-deadly measles complication more common than believed

Herd-immunity by vaccination protects infants too young to be immunized

NEW ORLEANS - A complication of measles that kills children years after they have the infection is more common than thought, according to a study being presented at IDWeek 2016™. The research underscores the vital importance of herd immunity by vaccination: All who are eligible should be vaccinated to protect those who can't be immunized, including infants.

Subacute sclerosing panencephalitis (SSPE) is a neurological disorder that is 100 percent fatal. Infants younger than 12 months, who are too young to receive measles, mumps and rubella (MMR) vaccine, can get infected with measles and later develop SSPE, which may lay dormant for years. While it was once thought the risk of post-measles SSPE was one in 100,000, recent research identified a rate as low as 1 in 1,700 in Germany among children infected with measles before they

were 5 years old, and the new study found it is about one in 600 for those who get measles as infants before being vaccinated.

There is no cure for SSPE and the only way to prevent it is to vaccinate everyone against measles.

"This is really alarming and shows that vaccination truly is life saving," said James D. Cherry, MD, MSc, an author of the study, and a distinguished research professor of pediatrics and infectious diseases at the David Geffen School of Medicine at the University of California Los Angeles. "Measles is a disease that could be eliminated worldwide, but that means vaccinating at least 95 percent of all who are eligible with two doses of measles vaccine in order to protect everyone, including those who aren't old enough to get the vaccine."

Researchers identified 17 cases of SSPE in California between 1998 and 2016, all of whom had measles prior to being vaccinated. Although all got measles as children, SSPE did not develop right away: The average age at diagnosis was 12, but the range was from 3 to 35 years old. In a subanalysis of California children who got measles while living in the United States, 1 in 1,387 who got it younger than 5 years and 1 in 609 who got it younger than 12 months developed SSPE. Many of these patients had ongoing cognitive or movement problems before they were definitively diagnosed. A majority of the children (67 percent) were living in the United States when they got measles.

Measles infection causes fever, runny nose, cough, red eyes, sore throat and rash. The virus spreads throughout the body and is cleared within 14 days. In rare cases the virus spreads to the brain, but then becomes dormant. Eventually it can lead to SSPE, resulting in deterioration and death. Researchers don't know what causes the virus to reactivate.

Vaccinating a very high portion of the population ensures herd immunity, meaning even those who can't be vaccinated are protected because the disease is less likely to spread. The MMR vaccine isn't recommended until infants are 12 months old because they retain some of their mother's antibodies until that age, making the vaccine less effective, but leaving them vulnerable to measles. Others who can't get vaccinated include those with immune system disorders.

The first dose of MMR is given between 12 and 15 months old. Because there is a 5 percent vaccination failure rate, a second dose is given to children before they begin school. Measles is so contagious that 95 percent of people need to be vaccinated with two doses to protect those who aren't, said Dr. Cherry. Therefore, all who are eligible - including adults who had not previously been vaccinated - should receive two doses of the vaccine. Nearly 92 percent of U.S. children 19-35 months old have received the MMR vaccine, according to the CDC.

"Parents of infants who have not yet been vaccinated should avoid putting their children at risk," said Dr. Cherry. "For example, they should postpone trips overseas - including to Europe - where measles is endemic and epidemic until after their baby has been vaccinated with two doses. It's just not worth the risk."

The lead author of the study is Kristen Wendorf, MD, MS. The co-authors are Kathleen Winter, MPH, PhD, Kathleen Harriman, PhD, MPH, RN, Jennifer Zipprich, MS, PhD, Robert Schecter, MD, Jill Hacker, PhD, MPH, Chris Preas, BA, Carol Glaser, DVM, MPVM, MD, and Dr. Cherry.

http://bit.ly/2e9PZ1D

How Frankenstein saved humankind from probable extinction, Dartmouth-UC Merced study

How Mary Shelley's novel, 'Frankenstein,' is rooted in biology

Frankenstein as we know him, the grotesque monster that was created through a weird science experiment, is actually a nameless Creature created by scientist Victor Frankenstein in Mary Shelley's 1818 novel, "Frankenstein." Widely considered the first work of science fiction for exploring the destructive consequences of scientific and moral transgressions, a new study published in "BioScience" argues that the horror of Mary Shelley's gothic novel is rooted in a fundamental principle of biology. (A pdf of the study is available upon request).

The co-authors point to a pivotal scene when the Creature encounters Victor Frankenstein and requests a female companion to mitigate his loneliness. The Creature distinguishes his dietary needs from those of humans and expresses a willingness to inhabit the "wilds of South America," suggesting distinct ecological requirements. Frankenstein concedes to this reasoning given that humans would have few competitive interactions with a pair of isolated creatures, but he then reverses his decision after considering the creatures' reproductive potential and the probability of human extinction, a concept termed competitive exclusion. In essence, Frankenstein was saving humankind.

"The principle of competitive exclusion was not formally defined until the 1930s," said Nathaniel J. Dominy, a professor of anthropology and biological sciences at Dartmouth. "Given Shelley's early command of this foundational concept, we used computational tools developed by ecologists to explore if, and how quickly, an expanding population of creatures would drive humans to extinction."

The authors developed a mathematical model based on human population densities in 1816, finding that the competitive advantages of creatures varied under different circumstances. The worst-case scenario for humans was a growing population of creatures in South America, as it was a region with fewer humans and therefore less competition for resources. "We calculated that a founding population of two creatures could drive us to extinction in as little as 4,000 years," said Dominy. Although the study is merely a thought experiment, it casts new light on the underlying horror of the novel: our own extinction. It also has real-world implications for how we understand the biology of invasive species.

"To date, most scholars have focused on Mary Shelley's knowledge of then-prevailing views on alchemy, physiology and resurrection; however, the genius of Mary Shelley lies in how she combined and repackaged existing scientific debates to invent the genre of science fiction," said Justin D. Yeakel, an Omidyar fellow at the Santa Fe Institute and an assistant professor in the School of Natural Sciences at the University of California, Merced. "Our study adds to Mary Shelley's legacy, by showing that her science fiction accurately anticipated fundamental concepts in ecology and evolution by many decades."

http://bit.ly/2dRWYxv

Scientists discover way to make milk chocolate have dark chocolate health benefits

Peanut skin extracts to make milk chocolate that has even more nutritional benefits of dark chocolate

CHICAGO -- Dark chocolate can be a source of antioxidants in the diet, but many consumers dislike the bitter flavor. The taste of milk chocolate is more appealing to a greater number of consumers, but it doesn't have the same antioxidants properties as dark chocolate. In a recent Journal of Food Science study, researchers found a way to use peanut skin extracts to make milk chocolate that has even more nutritional benefits of dark chocolate without affecting the taste.

Researchers from the Department of Food, Bioprocessing, and Nutrition Sciences at North Carolina State University extracted phenolic compounds from peanut skins, a waste product of peanut production, and encapsulated them into maltodextrin powder which is an edible carbohydrate with a slightly sweet flavor that comes from starchy foods such as potatoes, rice or wheat. The maltodextrin powder was incorporated into the milk chocolate.

Consumer testing of 80 subjects who compared samples of both milk chocolates with peanut extracts and without showed that the fortified chocolates were liked as well as the untreated milk chocolate. These tests also showed that the threshold for detecting the presence of the peanut skin extract was higher than that needed to fortify the milk chocolate to antioxidant levels comparable to dark chocolate.

Because peanut skins are a waste product of the blanching process of the peanut industry, the authors say that including these extracts would allow for a value-added use of the discarded skins.

"If applied to commercial products, peanut skin extracts would allow consumers to enjoy mild tasting products and have exposure to compounds that have proven health benefits," lead author Lisa L. Dean explained.

The researchers noted that peanut allergenicity was not investigated, but that work is now ongoing.

Read the Journal of Food Science abstract here.