http://www.eurekalert.org/pub_releases/2013-06/smri-srd061113.php

Sanford-Burnham researchers develop new drug that reverses loss of brain connections in Alzheimer's

NitroMemantine is the first drug to halt the progression of synaptic loss and to even restore these connections between nerve cells. The combination drug is now headed for clinical trials

La Jolla, Calif - The first experimental drug to boost brain synapses lost in Alzheimer's disease has been developed by researchers at Sanford-Burnham Medical Research Institute. The drug, called NitroMemantine, combines two FDA-approved medicines to stop the destructive cascade of changes in the brain that destroys the connections between neurons, leading to memory loss and cognitive decline.

The decade-long study, led by Stuart A. Lipton, M.D., Ph.D., professor and director of the Del E. Webb Center for Neuroscience, Aging, and Stem Cell Research, who is also a practicing clinical neurologist, shows that NitroMemantine can restore synapses, representing the connections between nerve cells (neurons) that have been lost during the progression of Alzheimer's in the brain. The research findings are described in a paper published June 17 by the Proceedings of the National Academy of Sciences of the United States of America (PNAS).

The focus on a downstream target to treat Alzheimer's, rather than on amyloid beta plaques and neurofibrillary tangles—approaches which have shown little success—"is very exciting because everyone is now looking for an earlier treatment of the disease," Lipton said. "These findings actually mean that you might be able to intercede not only early but also a bit later." And that means that an Alzheimer's patient may be able to have synaptic connections restored even with plaques and tangles already in his or her brain.

Targeting lost synapses

In their study, conducted in animal models as well as brain cells derived from human stem cells, Lipton and his team mapped the pathway that leads to synaptic damage in Alzheimer's. They found that amyloid beta peptides, which were once thought to injure synapses directly, actually induce the release of excessive amounts of the neurotransmitter glutamate from brain cells called astrocytes that are located adjacent to the nerve cells. Normal levels of glutamate promote memory and learning, but excessive levels are harmful. In patients suffering from Alzheimer's disease, excessive glutamate activates extrasynaptic receptors, designated eNMDA receptors (NMDA stands for N-methyl-D-aspartate), which get hyperactivated and in turn lead to synaptic loss.

How NitroMemantine works

Lipton's lab had previously discovered how a drug called memantine can be targeted to eNMDA receptors to slow the hyperactivity seen in Alzheimer's. This patented work contributed to the FDA approval of memantine in 2003 for the treatment of moderate to severe Alzheimer's disease. However, memantine's effectiveness has been limited. The reason, the researchers found, was that memantine—a positively charged molecule—is repelled by a similar charge inside diseased neurons; therefore, memantine gets repelled from its intended eNMDA receptor target on the neuronal surface.

In their study, the researchers found that a fragment of the molecule nitroglycerin—a second FDA-approved drug commonly used to treat episodes of chest pain or angina in people with coronary heart disease—could bind to another site that the Lipton group discovered on NMDA receptors. The new drug represents a novel synthesis connecting this fragment of nitroglycerin to memantine, thus representing two FDA-approved drugs connected together. Because memantine rather selectively binds to eNMDA receptors, it also functions to target nitroglycerin to the receptor. Therefore, by combining the two, Lipton's lab created a new, dual-function drug. The researchers developed 37 derivatives of the combined drug before they found one that worked, Lipton said.

By shutting down hyperactive eNMDA receptors on diseased neurons, NitroMemantine restores synapses between those neurons. "We show in this paper that memantine's ability to protect synapses is limited," Lipton said, "but NitroMemantine brings the number of synapses all the way back to normal within a few months of treatment in mouse models of Alzheimer's disease. In fact, the new drug really starts to work within hours."

To date, therapies that attack amyloid plaques and neurofibrillary tangles have failed. "It's quite disappointing because I see really sick patients with dementia. However, I'm now optimistic that NitroMemantine will be effective as we advance to human trials, bringing new hope to both early and later-stage Alzheimer's patients," Lipton said.

This research was funded by the U.S. National Institutes of Health (grants P01 AG010436, P50 AG005131, P01 DA017259, R01 AA020404, P01 HD29587, and P01 ES016738), the U.S. Department of Defense (W81XWH-10-1-0093), the National Institute of Neurological Disorders and Stroke Institutional Core (grant P30 NS076411), American Heart Association, and Ministry of Education and Science of Spain.

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http://www.eurekalert.org/pub_releases/2013-06/afot-asa061713.php

Artificial sweetener a potential treatment for Parkinson's disease

Tel Aviv University researcher says mannitol could prevent aggregation of toxic proteins in the brain

Mannitol, a sugar alcohol produced by fungi, bacteria, and algae, is a common component of sugar-free gum and candy. The sweetener is also used in the medical field — it's approved by the FDA as a diuretic to flush out excess fluids and used during surgery as a substance that opens the blood/brain barrier to ease the passage of other drugs.

Now Profs. Ehud Gazit and Daniel Segal of Tel Aviv University's Department of Molecular Microbiology and Biotechnology and the Sagol School of Neuroscience, along with their colleague Dr. Ronit Shaltiel-Karyo and PhD candidate Moran Frenkel-Pinter, have found that mannitol also prevents clumps of the protein α-synuclein from forming in the brain — a process that is characteristic of Parkinson's disease.

These results, published in the Journal of Biological Chemistry and presented at the Drosophila Conference in Washington, DC in April, suggest that this artificial sweetener could be a novel therapy for the treatment of Parkinson's and other neurodegenerative diseases. The research was funded by a grant from the Parkinson's Disease Foundation and supported in part by the Lord Alliance Family Trust.

Seeing a significant difference

After identifying the structural characteristics that facilitate the development of clumps of α-synuclein, the researchers began to hunt for a compound that could inhibit the proteins' ability to bind together. In the lab, they found that mannitol was among the most effective agents in preventing aggregation of the protein in test tubes. The benefit of this substance is that it is already approved for use in a variety of clinical interventions, Prof. Segal says.

Next, to test the capabilities of mannitol in the living brain, the researchers turned to transgenic fruit flies engineered to carry the human gene for α-synuclein. To study fly movement, they used a test called the "climbing assay," in which the ability of flies to climb the walls of a test tube indicates their locomotive capability. In the initial experimental period, 72 percent of normal flies were able to climb up the test tube, compared to only 38 percent of the genetically-altered flies.

The researchers then added mannitol to the food of the genetically-altered flies for a period of 27 days and repeated the experiment. This time, 70 percent of the mutated flies could climb up the test tube. In addition, the researchers observed a 70 percent reduction in aggregates of α-synuclein in mutated flies that had been fed mannitol, compared to those that had not.

These findings were confirmed by a second study which measured the impact of mannitol on mice engineered to produce human α-synuclein, developed by Dr. Eliezer Masliah of the University of San Diego. After four months, the researchers found that the mice injected with mannitol also showed a dramatic reduction of α-synuclein in the brain.

Delivering therapeutic compounds to the brain

The researchers now plan to re-examine the structure of the mannitol compound and introduce modifications to optimize its effectiveness. Further experiments on animal models, including behavioral testing, whose disease development mimics more closely the development of Parkinson's in humans is needed, Prof. Segal says.

For the time being, mannitol may be used in combination with other medications that have been developed to treat Parkinson's but which have proven ineffective in breaking through the blood/brain barrier, says Prof. Segal. These medications may be able to "piggy-back" on mannitol's ability to open this barrier into the brain.

Although the results look promising, it is still not advisable for Parkinson's patients to begin ingesting mannitol in large quantities, Prof. Segal cautions. More testing must be done to determine dosages that would be both effective and safe.

http://phys.org/news/2013-06-uniquely-enzyme-amazes-chemists.html

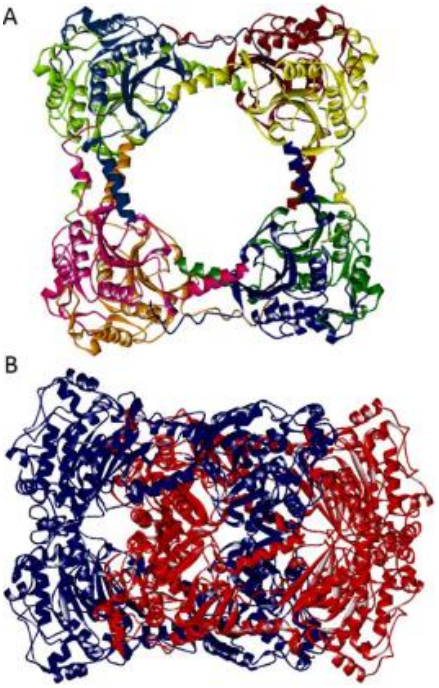
Uniquely shaped enzyme amazes chemists

Uniquely shaped enzyme that has never been seen before in biology is real: two interlocked ring structures

Chemists of Radboud University Nijmegen have found that a uniquely shaped enzyme that has never been seen before in biology is real: two interlocked ring structures, known as catenanes . The results have been published early June in Chemical Communications and were established through a cooperation by the university's chemists and microbiologists.

Microbiologist Mike Jetten is specialized in tracking down new bacteria and archea that perform remarkable chemical reactions. In 2011 he found primal archeon in the mudpots of Italian volcanic solfataras that obtain their energy by converting CS2 into H2S and CO2 with the enzyme CS2hydrolase.

Structural analysis revealed that the enzyme is composed of two forms: single ring structures and double ring structures, superposed and riveted together; also called hexadecameric catenanes.



A single ring structure (A) and a double ring structure (B), also called a hexadecameric catenane.

Mysterious rings

The interlocking rings are very special. Their locked protein structure, that is maintained via weak non-covalent interactions, has never been seen before in biology. That is why researchers first had to test whether the catenane structures were an artefact and that they were actually looking at two loose rings accidentally interlocking through each other. Jasmin Mecinovic , chemist at Radboud University Nijmegen, investigated if the 'interlockedness' of the double rings was real.

'By dissolving the enzyme, we could check the ratio of single and double rings in low concentrations. If the double rings indeed were an artefact, you would not expect them in low concentrations because the chance of accidentally superimposed rings is very small there. The ratio proved to be the same in all different solutions, showing that the interlocking rings exist. We checked this with three different chemical techniques: size exclusion chromatography, multi-angle laser light scattering and native mass spectrometric analyes.'

Evolution or coincidence

The three techniques confirmed each other's results and now Mecinovic knows for sure: the interlocking rings are real. His article already attracts a lot of attention: shortly after the online publication in Chemical Communications, the story was selected as a 'hot article' by the journal.

'We have a very special protein assembly in our hands', says Mecinovic. 'In the last decades, chemists extensively investigated artificial small molecule catenanes, but we have initiated the reseach on extremely rare biological catenanes. There are virtually no papers on this subject so there are many fundamental questions that still need to be addressed . Now I want to find out why mother nature chose this form. Maybe it's evolutionary, maybe this shape has advantages over others in catalysis or stability. But it could also be a chemical coincidence. I want to find that out by describing the molecular structure of the double rings even better.'

Explore further: Cosmic quiver: Saturn's vibrations create spirals in rings

More information: van Eldijk, M. et al. Evidence that the catenane form of CS2 hydrolase is not an artefact, Chem. Commun., 2013. pubs.rsc.org/en/content/articlelanding/2013/cc/c3cc43219j

http://phys.org/news/2013-06-jet-stream-climatically-exceptional-greenland.html

Jet stream changes cause climatically exceptional Greenland Ice Sheet melt

Unusual changes in atmospheric jet stream circulation caused the exceptional surface melt of the Greenland Ice Sheet

Phys.org - Research from the University of Sheffield has shown that unusual changes in atmospheric jet stream circulation caused the exceptional surface melt of the Greenland Ice Sheet (GrIS) in summer 2012.

An international team led by Professor Edward Hanna from the University of Sheffield's Department of Geography used a computer model simulation (called SnowModel) and satellite data to confirm a record surface melting of the GrIS for at least the last 50 years - when on 11 July 2012, more than 90 percent of the ice-sheet surface melted. This far exceeded the previous surface melt extent record of 52 percent in 2010.

The team also analysed weather station data from on top of and around the GrIS, largely collected by the Danish Meteorological Institute but also by US programmes, which showed that several new high Greenland temperature records were set in summer 2012.

The research, published today in the International Journal of Climatology, clearly demonstrates that the record surface melting of the GrIS was mainly caused by highly unusual atmospheric circulation and jet stream changes, which were also responsible for last summer's unusually wet weather in England.
The analysis shows that ocean temperatures and Arctic sea-ice cover were relatively unimportant factors in causing the extra Greenland melt.
Professor Hanna said: "The GrIS is a highly sensitive indicator of regional and global climate change, and has been undergoing rapid warming and mass loss during the last 5-20 years. Much attention has been given to the NASA announcement of record surface melting of the GrIS in mid-July 2012. This event was unprecedented in the satellite record of observations dating back to the 1970s and probably unlikely to have occurred previously for well over a century.
"Our research found that a 'heat dome' of warm southerly winds over the ice sheet led to widespread surface melting. These jet stream changes over Greenland do not seem to be well captured in the latest Intergovernmental Panel on Climate Change (IPCC) computer model predictions of climate change, and this may indicate a deficiency in these models. According to our current understanding, the unusual atmospheric circulation and consequent warm conditions of summer 2012 do not appear to be climatically representative of future 'average' summers predicted later this century.
"Taken together, our present results strongly suggest that the main forcing of the extreme GrIS surface melt in July 2012 was atmospheric, linked with changes in the summer North Atlantic Oscillation (NAO), Greenland Blocking Index (GBI, a high pressure system centred over Greenland) and polar jet stream which favoured southerly warm air advection along the western coast.
"The next five-10 years will reveal whether or not 2012 was a rare event resulting from the natural variability of the NAO or part of an emerging pattern of new extreme high melt years. Because such atmospheric, and resulting GrIS surface climate, changes are not well projected by the current generation of global climate models, it is currently very hard to predict future changes in Greenland climate. Yet it is crucial to understand such changes much better if we are to have any hope of reliably predicting future changes in GrIS mass balance, which is likely to be a dominant contributor to global sea-level change over the next 100-1000 years."
More information: onlinelibrary.wiley.com/doi/10.1002/joc.3743/abstract

http://www.eurekalert.org/pub_releases/2013-06/uoc--amf061713.php

Aspirin may fight cancer by slowing DNA damage

Barrett's esophagus study first to probe NSAID effects on mutation rate

Aspirin is known to lower risk for some cancers, and a new study led by a UC San Francisco scientist points to a possible explanation, with the discovery that aspirin slows the accumulation of DNA mutations in abnormal cells in at least one pre-cancerous condition. "Aspirin and other non-steroidal anti-inflammatory drugs, which are commonly available and cost-effective medications, may exert cancer-preventing effects by lowering mutation rates," said Carlo Maley, PhD, a member of the UCSF Helen Diller Family Comprehensive Cancer Center, and an expert on how cancers evolve in the body over time.
In the study, published June 13 in the online journal PLOS Genetics, Maley, working with gastroenterologist and geneticist Brian Reid, MD, PhD, of the Fred Hutchinson Cancer Research Center, analyzed biopsy samples from 13 patients with a pre-cancerous condition called Barrett's esophagus who were tracked for six to 19 years. In an "observational crossover" study design, some patients started out taking daily aspirin for several years, and then stopped, while others started taking aspirin for the first time during observation. The goal was to track the rate of mutations in tissues sampled at different times.
The researchers found that biopsies taken while patients were on an aspirin had on average accumulated new mutations about 10 times more slowly than biopsies obtained during years when patients were not taking aspirin.
"This is the first study to measure genome-wide mutation rates of a pre-malignant tissue within patients for more than a decade, and the first to evaluate how aspirin affects those rates," Maley said.
Gender and ethnic distribution of study patients reflected the known demographics of esophageal cancer, which predominantly affects, white, middle-aged and elderly men, he said. Barrett's esophagus only occasionally progresses to esophageal cancer.
Cancers are known to accumulate mutations over time much more rapidly than normal tissue, and different mutations arise in different groups of cells within the same tumor. The acquisition of key mutations ultimately allows tumor cells to grow out of control, and diversity within a tumor may foster drug resistance, a phenomenon that is a major focus of Maley's research.
Maley plans to test a hypothesis that may explain the results — that aspirin's lowering of mutation rates is due to the drug's effect of reducing inflammation. Inflammation, a response of the immune system, in recent years

has been recognized as a hallmark of cancer. Maley said that less inflammation may result in less production within pre-cancerous tissue of oxidants known to damage DNA, and may dampen growth-stimulating signaling.
For the duration of the study, the rate of accumulation of mutations measured in the biopsied tissue between time points was slow, even when patients were not taking aspirin, with the exception of one patient. While mutations accumulated at a steady rate, the vast majority of mutations arose before the abnormal tissue was first detected in the clinic, the researchers concluded.
These findings are consistent with the fact that although Barrett's esophagus is a significant risk factor for esophageal cancer, the vast majority of cases do not progress to cancer, Maley said.
In the one patient who later went on to develop cancer, a population of cellular "clones" with a great number of mutations emerged shortly before he started taking aspirin.
More studies are needed to further explore the link between non-steroidal anti-inflammatory drugs, mutation rates and the development of invasive cancer, Maley said. He plans to continue studying Barrett's esophagus and esophageal cancer, and to expand his research to investigate lung cancer.
Rather than aiming to kill the most tumor cells, it may be better to try to halt or slow growth and mutation. Current drug treatments for cancer may in many cases hasten the emergence of cancer that is more difficult to eradicate, according to Maley. The capability to mutate frequently allows tumors to become resistant to drug treatment, he said. A better-adapted mutant can begin to spin off a population of genetic clones that survives and grows, while poorly adapted tumor cells die off.
Additional authors from the Fred Hutchinson Cancer Research Center include Xiaohong Li, PhD, Carissa Sanchez, PhD, Patricia Galipeau, PhD, Thomas Paulson, PhD, Patricia Blount, PhD, Thomas Vaughan, PhD, and Cassandra Sather, PhD. Amitabh Srivastava, MD, and Robert Odze, MD, from Harvard University; Rumen Kostadinov, PhD, from the University of Pennsylvania; and Mary Kuhner, PhD from the University of Washington also were members of the research team and authors of the study.
The research was funded by the American Cancer Society and the National Cancer Institute.

http://www.eurekalert.org/pub_releases/2013-06/uoe-tim061713.php

Treating infection may have sting in the tail, parasite study shows

Using drugs to treat an infection could allow other co-existing conditions to flourish, a study in wild animals has shown.

Researchers studying wild mice – which typically carry multiple parasitic infections at once – found that when these animals were treated for one type of bug, other infections they had tended to worsen.
The findings suggest that infections that co-exist in our bodies can compete with each other to alter disease. Treating one infection may have unintended consequences by enabling others to gain a stronger foothold – perhaps to the overall detriment of our health.
Scientists from the University of Edinburgh treated wild wood mice for a gut worm infection over several weeks. During treatment, researchers monitored levels not only of the worm, but also tested the animals for dozens of other common parasite infections. During treatment, levels of the gut worm fell, but levels of other parasites in the gut increased. The study is the first of its type to show that multiple infections in wild animals can compete with one another, and that treating one infection can directly impact on others that may be present.
The study, published in Proceedings of the Royal Society B, was carried out in collaboration with The University of Liverpool and supported by the Natural Environment Research Council and the Wellcome Trust.
Dr Amy Pedersen, of the University of Edinburgh's School of Biological Sciences, who led the study, said: "In nature, infections rarely occur by themselves, and this study shows for the first time that treating infections in isolation can have knock-on effects for other diseases that may be present. More work is needed to understand the effect of drug treatment for disease where individuals are prone to, or likely to be carrying a range of infections."

http://www.eurekalert.org/pub_releases/2013-06/msu-sft061413.php

Study finds the sweet spot -- and the screw-ups - that make or break environmental collective actions

Sustainability programs are a Goldilocks proposition – some groups are too big, some are too small, and the environment benefits when the size of a group of people working to save it is just right.

It has long been debated how many people working together can change the world. Whether it's joining forces to conserve gas, save a forest or stave off climate change, arguments have been made for the power of a dedicated few or the strength of numbers. It also has been a mystery what tips a group dynamic from powerful to unproductive.
Scientists at Michigan State University (MSU) have found that there is a sweet spot – a group size at which the action is most effective. More importantly, the work revealed how behaviors of group members can pull bad

policy up or drag good policy down. The work is published in this week's Proceedings of the National Academy of Sciences.
"This paper finds that group size does matter – and the answer is right in the middle," said Jianguo "Jack" Liu, who holds the Rachel Carson Chair in Sustainability at MSU and is director of the Center for Systems Integration and Sustainability (CSIS). "Collective action is of growing importance as the world becomes more interdependent. Think about big problems like climate change and conservation. One person cannot solve the problem. One country can't solve the problem. It's important to understand how collective action works if we want programs that are effective."
Wu Yang, an MSU-CSIS doctoral student, and his colleagues studied how groups in the Wolong Nature Reserve worked to participate in China's massive Natural Forest Conservation Program. That program pays all of the 1,100 rural households there to monitor the forest on which they rely to enforce logging bans intended to allow forests to recover. Since it's mostly local residents who chop down the trees for firewood or to build homes, enlisting locals has been identified as the best way to increase forest cover.
The stakes are high there. Wolong is a biodiversity hotspot that's home to endangered giant pandas.
Wolong and the conservation program became a stage on which the universal behaviors that have bogged down collective actions are played out. If groups get too big, "free riders" – individuals who dodge their duty undetected and still reap the benefits – can make the collective actions less effective.
In small groups, participants can be overburdened. In contrast, large groups need to have expensive enforcement efforts to reduce free riders and improve the effectiveness.
For both group sizes, those limiting forces drag the effectiveness down. Liu said that holds true in Wolong, as well as in other efforts, including students' class group projects.
This work for the first time tests and quantifies the non-linear relationship hypothesized by Elinor Ostrom, the first woman to win the Nobel Prize in economics for her analysis of governance, particularly how people managed "the commons" – as she referred to shared natural resources.
"We're showing that the outcomes of these actions are important," Liu said. "This can point the way to determine how to better protect the environment and utilize natural resources."
Yang thought both the big-group and small-group proponents could be right – to a point. Or more accurately, to a curve. "By looking at the big picture, we realized both could be true," Yang said. "It's important to take a holistic approach. You'll get a more objective view of the issue. "We combined both arguments, like a good diplomat."
Working in Wolong, the research team found that a group size can increase and be more effective until the free-riders weigh down the effort's momentum. Likewise, small groups can be powerful, until individuals become overwhelmed by the responsibility. Effectiveness again is weighed down. These two opposing forces directly and indirectly affect household forest monitoring and changes in forest cover. The authors indeed found the forests of Wolong recovered at an optimal rate at that sweet spot of group size. More importantly, they confirmed how other factors influence the optimal group size and outcomes of collective actions.
In addition to Jack Liu and Yang, "The nonlinear effects of group size on collective action and resource outcomes" was written by CSIS members Thomas Dietz, professor of environmental science and policy, sociology, and animal studies; Andrés Viña, assistant professor of fisheries and wildlife; and former CSIS doctoral students Wei Liu, now a postdoctoral fellow at IIASA in Laxenburg, Austria, Mao-Ning Tuanmu, now a postdoctoral researcher at the Department of Ecology and Evolutionary Biology at Yale University, and Guangming He.
The research is funded by the National Science Foundation, NASA, and Michigan State University AgBioResearch.

http://www.bbc.co.uk/news/health-22940088

'Quiet epidemic' of male cancer in UK

Action is needed to fight a "quiet epidemic" of oesophageal cancer, which is on the rise in the UK, particularly among men, cancer experts say.

By Helen Briggs BBC News

Men are almost three times more likely than women to get the cancer - one of the biggest gender divides in cancer rates, according to new figures. Early diagnosis is the key to saving lives, says a Cancer Research UK team. Scientists are working on ways to detect symptoms earlier and to decipher the genetic code of the cancer.

Poor outcomes

Oesophageal cancer - cancer of the gullet or food pipe - is the ninth most common cancer in the UK. It is one of the most difficult cancers to detect and treat, with only about one in 10 patients surviving for 10 years or more.
Latest figures show 5,600 UK men (almost 15 out of every 100,000) developed the disease in 2010, compared with 2,800 UK women (about five out of every 100,000). This equates to a lifetime risk of one in 56 for men and one in 110 for women.

There are two types of oesophageal cancer:

squamous cell carcinoma - linked to smoking, drinking and a low fruit intake

adenocarcinoma - linked to obesity, smoking and persistent acid reflux

Researchers believe a steady rise in the number of adenocarcinomas in men is behind the gender gap.

Tim Underwood, an oesophageal surgeon and researcher at the University of Southampton, said many questions remained unanswered about the cancer, but urgent action was needed.

"We need a game changer," he told a news conference.

"And we need a game changer relatively urgently. There is an epidemic of this disease and outcomes are poor."

Mr Underwood, who is running the New York Marathon to raise money for research, said diagnosing the disease earlier was key to improving the chances of survival. "Food getting stuck when you swallow and persistent heart burn are not normal," he said. "If this is happening to you, you need to see your GP. "The vast majority of people won't have anything seriously wrong with them, but it's important to get checked out.

"If left untreated acid reflux - often called heartburn - can damage cells of the oesophagus leading to a condition called Barrett's oesophagus which in turn can be a precursor of oesophageal cancer."

Lifestyle link

Dr Harpal Kumar, chief executive of Cancer Research UK, said the factors behind the rise in oesophageal cancer were unclear. "We think it may be linked to some changes that we've seen in people's lifestyles, for example increasing levels of obesity," he told BBC News. "There is a lot more that we need to do to try and understand this disease better, but at this point in time the most important thing is to increase awareness of it and get people to go and see their doctor if they have the symptoms."

Research projects are under way in the UK to understand oesophageal cancer better and develop techniques for earlier diagnosis.

A "sponge-on-a-string" device to collect cells from the gullet for diagnosis could be available on the NHS in five years, said Prof Rebecca Fitzgerald, of the Medical Research Council's Cancer Cell Unit in Cambridge.

The cytosponge test is designed to be swallowed and retrieved to detect pre-cancerous cells.

Clinical trials suggest the test shows promise as a safer and cheaper alternative to endoscopy, a procedure where the inside of the body is examined internally using a long, flexible tube.

"For the patient, this is a five-minute test - it will make your eyes water for two seconds but it is an awful lot simpler, less invasive, safer and cheaper than an endoscopy," said Prof Fitzgerald. "We're hopeful that in the future this will really transform early diagnosis by making it something much more patient-friendly and affordable."

Prof Fitzgerald said work to decode all of the genes in 500 oesophageal cancer samples, looking for genetic mistakes, was in progress, with about 100 samples completed. The long-term goal was to develop better drugs for the condition, she said.Current treatment relies on chemotherapy and radiotherapy, with surgery as an option if the cancer is detected early enough.

http://www.sciencedaily.com/releases/2013/06/130617110823.htm?

Dietary Supplement Linked to Increased Muscle Mass in the Elderly

A supplemental beverage used to treat muscle-wasting may help boost muscle mass among the elderly, according to a new study.

The supplemental beverage, called Juven®, contains three amino acids, including arginine. Amino acids are the building blocks of proteins, and are required for cell growth and repair. The amino acid arginine is especially important because it increases growth-hormone production, which causes the body to produce a critical protein called insulin-like growth factor 1, or IGF-1. This protein promotes growth and development and, as its name suggests, is similar in structure to the hormone insulin. The results were presented today at The Endocrine Society's 95th Annual Meeting in San Francisco.

Previously, studies showed that Juven® helped increase muscle mass in patients with AIDS or cancer. These earlier findings led this study's investigators to hypothesize that the increased muscle mass could result from greater blood concentrations of IGF-1. They theorized that these increased protein levels could have the same benefits among the elderly, who also experience decreased muscle mass and strength related to drops in hormone production that occur with aging. In turn, increased muscle strength could potentially improve quality of life among the elderly.

They found that participants who received Juven® had significant increases in lean body mass, while those who received placebo did not have any change. In addition, blood concentrations of IGF-1 increased among Juven® recipients, but not among the placebo group. The correlation between the improved IGF-1 concentrations and increased lean tissue, however, was not statistically significant.

"The amino acid cocktail of the dietary supplement Juven® appears to hold promise for increasing lean body in healthy older adults," said study lead author Amy C. Ellis, PhD, assistant professor at the University of Alabama at Tuscaloosa. "However, more research is needed to determine the cause-and-effect relationship and the mechanisms by which the amino acids in Juven® may favorably affect body composition of healthy, older adults."
Study participants were 29 healthy adults between the ages of 65 and 87 years. Each received either Juven® or a placebo drink twice a day, along with their regular daily diet, for six months. At the beginning of the study and again six months later, investigators used a special test to measure lean body mass. At both times, they also assessed participants' blood levels of IGF-1 after fasting.
The National Institutes of Health and the Center for Aging at the University of Alabama-Birmingham funded the study. Abbott Laboratories, the manufacturer of Juven®, provided the dietary supplement and the placebo.

http://www.eurekalert.org/pub_releases/2013-06/asfm-nvd061413.php

New virus discovered in patients with central nervous system infections

An infection from livestock?

Patients in Vietnam and other locations with central nervous system infections may well be suffering from the effects of a newly discovered virus, according to a study to be published in mBio®, the online open-access journal of the American Society for Microbiology. Researchers have detected the virus in spinal fluid from 4 percent of 642 patients with central nervous system infections of unknown cause, and in an average of 58 percent of fecal samples from pigs and poultry, suggesting animals may serve as reservoirs for transmission to humans. The virus, called CyCV-VN, belongs to the Cyclovirus genus, a group that has never before been implicated in human or animal disease.
"The detection of CyCV-VN in a usually sterile material like cerebrospinal fluid is remarkable and may point to a pathogenic role of this virus as a single or a co-infecting pathogen," says corresponding author Tan Le Van of the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam. The results in this study, Van cautions, do not provide absolute proof of disease causation, and further work is needed to see whether the virus poses a threat to human and animal health.
Acute central nervous system infections are responsible for illnesses and deaths around the world, but they are a particular problem in tropical regions. These infections can be caused by any of a number of bacterial, parasitic, fungal or viral pathogens, but the majority of cases go undiagnosed despite extensive efforts to identify a cause.
"One of our particular interests is to improve patient diagnosis," says Van. Proper diagnosis "is essential to improve clinical management and prevention of these devastating diseases, he continues.
Inspired by the high incidence of acute central nervous system infections in Vietnam, Van and his colleagues set out to identify previously uncharacterized viruses in undiagnosed patients. Using fluid samples from more than 1,700 patients with suspected central nervous system infections or suspected viral encephalitis, the researchers generated 161,000 DNA sequence reads for further analysis.
Among these thousands of sequences, the researchers identified a sequence from a member of the Cyclovirus genus that was present in two patients, one adult and one child, both with acute central nervous system infections of unknown cause. Follow-up work with a technique called inverse PCR used that short sequence to determine the entire genome sequence of the virus present in one of the samples. CyCV-VN is a unique new species of Cyclovirus, a group that includes no known pathogens.
With the full genome in hand, the researchers went back to 642 samples from patients with suspected acute central nervous system infections and were able to detect the virus in samples from 26 patients (4 percent). The virus was not detected at all in samples from patients with non-infectious conditions of the central nervous system, like multiple sclerosis, a fact that argues that the virus could well be a human pathogen.
The virus was also detected in samples from farm animals in the province where the index patient lived: between 42 percent and 100 percent of fecal samples from pigs, ducks, and chickens in that region harbored viruses that are extremely closely related to CyCV-VN. This raises the possibility - but not certainty - say the authors, that livestock could represent a source for human infection with the virus.
Van also cautions that it is too soon to point an accusing finger at CyCV-VN. "Detection of a virus in human samples alone is insufficient to provide a direct link with an ongoing infection," he says. "Addressing the question of causation requires extensive effort."
Van says they are currently trying to isolate the virus in cell culture and develop a serological assay. If they are able to identify an antibody response to the virus in patient samples, he says, they would be one step closer to linking the virus to disease. They are also working with research groups outside Vietnam to explore the geographic spread of the virus.

http://www.sciencedaily.com/releases/2013/06/130617122140.htm

BPA Linked to a Common Birth Defect in Boys

A new study links fetal exposure to a common chemical pollutant, bisphenol A (BPA), to defects of a testicular hormone in newborn boys with undescended testicles.

The results, which were presented Monday at The Endocrine Society's 95th Annual Meeting in San Francisco, suggest yet another potential harmful effect of BPA, which is widely used in many plastics, liners of food cans and dental sealants.

"Alone, our study cannot be considered as definitive evidence for an environmental cause of undescended testis," said lead author Patrick Fenichel, MD, PhD, professor and head of reproductive endocrinology at the University Hospital of Nice in France. "But it suggests, for the first time in humans, a link that could contribute to one co-factor of idiopathic [unexplained] undescended testis, the most frequent congenital malformation in male newborns."

Cryptorchidism, the medical name for undescended testicles, occurs in 2 to 5 percent of full-term male newborns, according to Fenichel. Sometimes the testicles descend on their own within six months after birth. If the condition persists and goes untreated, however, it carries an increased risk in adulthood of decreased fertility and testicular cancer, he said.

Fenichel and his colleagues studied 180 boys born after 34 weeks' gestation between 2003 and 2005. Fifty-two were born with one or two undescended testicles, 26 of whom still had the condition at 3 months of age. The other 128 newborns did not have this birth defect and were matched for pregnancy term, weight and time of birth (the control group). Using sensitive immunoassays of the infants' umbilical cord blood, the researchers measured the newborns' levels of BPA and insulin-like peptide 3, one of the two testicular hormones that regulate descent of the testicles.

Testosterone level, which also controls fetal testicular descent, did not differ between the groups and was normal in the whole population, according to Fenichel.

The infants with cryptorchidism had significantly lower levels of insulin-like peptide 3, compared with the controls, the authors reported. These infants did not have greatly increased levels of BPA or several other environmental endocrine disrupters that were measured. However, in all 180 infants, the BPA level inversely correlated with the level of insulin-like peptide 3, meaning that the higher the BPA level, the lower the level of this important testicular hormone.

Fenichel speculated that BPA, an estrogenic endocrine disruptor, might repress, as other research has shown for estrogens in rodents, expression of the gene for insulin-like peptide 3. This could be a co-factor in the development of cryptorchidism, he said. Animal research also has linked fetal BPA exposure to an increased risk of reproductive disorders and other health problems.

http://www.medscape.com/viewarticle/805280?src=rss

World's Most Widespread Zoonotic Disease Poses New Risks

Focus on Leptospirosis

CDC Division of High-Consequence Pathogens and Pathology (DHCPP)

Leptospirosis: The Most Widespread Zoonotic Disease

Emerging diseases are always a concern for clinicians. But, in addition to new diseases, existing diseases may sometime reemerge as significant public health threats. New information tells us that this may be the case with leptospirosis. Leptospirosis is a bacterial disease that affects humans and animals. Caused by bacteria of the genus Leptospira, it is considered the most widespread zoonotic disease in the world and is most commonly found in tropical or temperate climates. The disease is spread through the urine of infected wild and domestic animals, including dogs, cattle, pigs, horses, and rodents. People can get the disease when they are exposed to the urine of infected animals or soil, water, or food contaminated with the urine of infected animals.

In humans, leptospirosis can cause a wide range of symptoms, but it usually presents as an acute febrile illness that might be mistaken for other diseases. Some infected persons, however, have no symptoms at all.

Although some diseases can be prevented through vaccination, there is no human leptospirosis vaccine licensed for use in the United States. When infection occurs, however, antibiotics (such as doxycycline or penicillin) can provide effective treatment. For maximum effectiveness, antibiotics should be given early in the course of the disease. Without treatment, leptospirosis can lead to kidney damage, meningitis, liver failure, respiratory distress, and even death.

What's New in the United States: Increasing Cases and Risk Groups

Traditionally, cases of leptospirosis have been associated with occupations that require close contact with animals, such as farmers, slaughterhouse workers, veterinarians, and animal caretakers. But, according to new

data, reported cases are increasing in some states, and new groups of people may be at an increased risk for the disease.

Of note, recent trends in Hawaii represent a situation that could be happening all over the United States. From 1999 through 2008, the annual incidence in Hawaii was 1.63-2.85 per 100,000 people. This is a significant increase from the mean annual incidence of 1.29 per 100,000 people documented in Hawaii from 1974 to 1998.[1]

In addition to increasing incidence, new risk groups have been identified. Although traditional occupational groups remain at risk, infections among people who raft, kayak, and swim in fresh water (including triathletes and adventure racers) have become more common. For example, in 1998, an outbreak occurred in Illinois and Wisconsin among triathlon participants from 44 states and 7 countries. Of the participants, 90 had symptoms of leptospirosis and 30 cases were laboratory-confirmed.[2] Another outbreak occurred in 2005 among participants of an adventure race in Florida. Among participants from 32 US states and Canada, 44 suspected and 14 laboratory-confirmed cases of leptospirosis were identified.[3]

Urban children have also emerged as a risk group. A Detroit study showed that inner-city children had a significantly higher incidence of antileptospiral antibodies than did suburban children, even though none of the inner-city children had been diagnosed with leptospirosis. The findings reinforced the results of a previous study, which found that 16% of serum samples from patients at an inner-city clinic were positive for exposure to leptospires, suggesting that unrecognized leptospirosis may be common in US cities.[4]

Unrecognized urban cases are probably related to exposures to rat or dog urine. In many urban areas, social and economic conditions might lead to more persistent exposures to these reservoirs, possibly establishing an environment in which the disease could become endemic.

Identifying Suspected Cases of Leptospirosis

Even outside of particular risk groups, leptospirosis is thought to be underdiagnosed. Generally, this is the result of the protean nature of its clinical presentations, the difficulty of distinguishing leptospirosis from other undifferentiated febrile illnesses, and delayed results from clinical testing.

Disease onset is typically 2 days to 4 weeks following exposure. About 90% of infections are subclinical or self-limited mild disease. Approximately 10% of infections, comprising the majority of recognized cases, are characterized by abrupt onset of fever, headache, muscle aches, vomiting, or diarrhea. Infected patients may experience a biphasic illness, with a short recovery period after the first week of illness followed by more severe symptoms.[5]

Approximately 10%-15% of patients with clinical disease experience severe leptospirosis, a high-mortality syndrome with multiorgan involvement, such as kidney failure, liver failure, pulmonary hemorrhage, or meningitis.[5] Because many symptoms can be mistaken for other acute febrile illnesses, use of laboratory diagnostics can help identify and treat patients with leptospirosis.

Confirmation of Leptospirosis Through Laboratory Testing

Leptospirosis is confirmed by laboratory testing of blood, urine, serum, or other clinical specimens. Many diagnostic methods are available to diagnose leptospirosis, including culture, microscopic agglutination test (MAT), immunofluorescence, darkfield microscopy, other serologic tests, and real-time polymerase chain reaction (PCR).

The MAT is considered the gold-standard serologic test to confirm leptospirosis. Because it is a difficult test to maintain, CDC is the only laboratory in the United States that offers the MAT for leptospirosis. Serum samples should be obtained at least 10-14 days apart (acute and convalescent) to identify seroconversion; a titer of at least 1:800 or a 4-fold rise in titer is confirmatory.[5]

Isolation of leptospires from a clinical specimen is confirmatory, although this lacks sensitivity and growth may be slow. Immunofluorescence is a useful diagnostic measure when performed as immunohistochemistry for antigen detection in tissues (direct); however, it is typically performed on tissues obtained at autopsy. Darkfield microscopy is timelier relative to stage of disease; however, it lacks sensitivity and specificity.

Strengthening Prevention and Response Through Collaboration

As a result of the expanded groups at risk for leptospirosis, as well as other factors that might contribute to the increasing burden of the disease, CDC encourages clinicians to work with local and state health departments to share information that can lead to better prevention and care for leptospirosis.

More than 30 states require reporting of cases of leptospirosis to the state health department. In addition, interaction between states and CDC can improve surveillance, data-sharing, prevention programs, and diagnostic methods for detection. If you suspect that a patient has leptospirosis, contact your local health department to learn about testing that can be done at the state health department or CDC, and to find out whether leptospirosis is reportable in your state.

Web Resources*CDC: Leptospirosis*
CDC: Bacterial Special Pathogens Branch -- Zoonoses and Select Agent Laboratory (guidance for shipping Leptospira isolates)
CDC: Leptospirosis Risk in Outdoor Activities
Suggested Reading*Levett PN. Leptospirosis. Clin Microbiol Rev. 2001;14:296-326.*
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http://www.eurekalert.org/pub_releases/2013-06/uoo-mho061813.php

Mars had oxygen-rich atmosphere 4,000 million years ago

Differences between Martian meteorites and rocks examined by a NASA rover can be explained if Mars had an oxygen-rich atmosphere 4000 million years ago – well before the rise of atmospheric oxygen on Earth 2500m years ago.

Scientists from Oxford University investigated the compositions of Martian meteorites found on Earth and data from NASA's 'Spirit' rover that examined surface rocks in the Gusev crater on Mars. The fact that the surface rocks are five times richer in nickel than the meteorites was puzzling and had cast doubt on whether the meteorites are typical volcanic products of the red planet.

'What we have shown is that both meteorites and surface volcanic rocks are consistent with similar origins in the deep interior of Mars but that the surface rocks come from a more oxygen-rich environment, probably caused by recycling of oxygen-rich materials into the interior,' said Professor Bernard Wood, of Oxford University's Department of Earth Sciences, who led the research reported in this week's Nature.

'This result is surprising because while the meteorites are geologically 'young', around 180 million to 1400 million years old, the Spirit rover was analysing a very old part of Mars, more than 3700 million years old.'

Whilst it is possible that the geological composition of Mars varies immensely from region to region the researchers believe that it is more likely that the differences arise through a process known as subduction – in which material is recycled into the interior. They suggest that the Martian surface was oxidised very early in the history of the planet and that, through subduction, this oxygen-rich material was drawn into the shallow interior and recycled back to the surface during eruptions 4000 million years ago. The meteorites, by contrast, are much younger volcanic rocks that emerged from deeper within the planet and so were less influenced by this process.

Professor Wood said: 'The implication is that Mars had an oxygen-rich atmosphere at a time, about 4000 million years ago, well before the rise of atmospheric oxygen on earth around 2500 million years ago. As oxidation is what gives Mars its distinctive colour it is likely that the 'red planet' was wet, warm and rusty billions of years before Earth's atmosphere became oxygen rich.'

The research was supported by the Science and Technology Facilities Council and the European Research Council.

http://phys.org/news/2013-06-african-black-slug-healthy.html

African black slug serves as healthy reminder

A new, invasive species of slug found recently in South Texas serves as a good reminder to thoroughly wash fruits and vegetables before eating them, according to an expert with the Texas A&M AgriLife Extension Service.

Several specimens found in March in a new residential area of Harlingen have since been identified as African black slugs, said Dr. Raul Villanueva, an entomologist at the Texas A&M AgriLife Research and Extension Center at Weslaco. They were identified by mollusk specialists at a laboratory of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service in Beltsville, Md., he said.

"The African black slug originated in Africa and is now endemic to Asia and several islands in the Caribbean," Villanueva said. "How it got here is anybody's guess. It could have come in on imported plants, turf, produce—who knows? It hides very well among all those products."

The African black slug is endemic to Asia and the Caribbean. Wikipedia

This is only the second find ever of the African black slug in the U. S., Villanueva said. The first find, also in the Lower Rio Grande Valley, occurred in the 1980s, but was eradicated with chemical pesticide baits called molluscicides.
"Fortunately, we have never found the nematode that can be carried by the African black slug," he said. "These nematodes, or tiny worms, pose serious health risks to humans, including meningitis. But the nematode has never been detected here. Nevertheless, it's a good idea to thoroughly wash fruits and vegetables before consuming them."
The African black slug is a slimy, black mollusk about an inch long with a distinctive white mark on its back, unlike several harmless species of black slugs native to the Lower Rio Grande Valley that are solid black.
"So far, there have been only a few of these African black slugs found in one localized urban area of Harlingen," Villanueva said. "Others have been found nearby, but they are very slow movers, so it's not likely they will spread."
Residents of the area in Harlingen where they were found have been advised to treat their lawns and not handle slugs if they find one, he said. Should anybody touch one, they are advised to wash their hands. If they must be handled, wear gloves or us forceps.
African black slugs feed on plants at night to avoid the heat of the sun, which can quickly dry them out, Villanueva said. "They require high humidity and moist areas to reproduce and thrive, so our Valley weather is not their ideal habitat. It's highly unlikely they will survive here, but as always, it's important that people wash fruits and vegetables to avoid pathogens of all kinds."

http://bit.ly/1bRKQQp

World's first baby born from 'natural' IVF

Say hello to Heath. He's the first baby in the world to be born using a new IVF technique that researchers hope will be safer for would-be mothers.

16:00 18 June 2013 by Douglas Heaven

During IVF, a woman's ovaries are stimulated to boost ovulation and harvest eggs. This is usually done by an injection of human chorionic gonadotropin (hCG), a hormone involved in progesterone secretion.
But sometimes this leads to ovarian hyperstimulation syndrome. OHSS is mild in a third of women having IVF, causing abdominal bloating, but for one woman in 20 it also causes vomiting and diarrhoea. In extreme cases it can be fatal. Women with polycystic ovary syndrome – a leading cause of infertility – are at greater risk of OHSS.
The problem with hCG is that it is too potent, says Waljit Dhillo at Imperial College London. His team hypothesised that another hormone, called kisspeptin, may be gentler. Its effects are short-lived and during pregnancy it naturally increases to 7000 times the usual level, so should have minimal side effects.
Dhillo tested the hormone in 30 women having IVF. Suzannah Kidd became the first to give birth as a result – Heath, a healthy boy, was born on 26 April. Dhillo thinks that IVF success rates will be as good with kisspeptin as they are with current methods. "We'll know in six months," he says.
Dhillo presented his results to the Endocrine Society in San Francisco this week.
Simon Fishel at CARE Fertility in Nottingham, UK, thinks the results are exciting. "It's an opportunity that needs to be studied," he says. "It could be very important if it eliminates OHSS."

http://www.eurekalert.org/pub_releases/2013-06/cu-nrb061913.php

New research backs theory that genetic 'switches' play big role in human evolution

A Cornell University study offers further proof that the divergence of humans from chimpanzees some 4 million to 6 million years ago was profoundly influenced by mutations to DNA sequences that play roles in turning genes on and off.

ITHACA, N.Y. – The study, published June 9 in Nature Genetics, provides evidence for a 40-year-old hypothesis that regulation of genes must play an important role in evolution since there is little difference between humans and chimps in the proteins produced by genes. Indeed, human and chimpanzee proteins are more than 99 percent identical.
The researchers showed that the number of evolutionary adaptations to the part of the machinery that regulates genes, called transcription factor binding sites, may be roughly equal to adaptations to the genes themselves.
"This is the most comprehensive and most direct analysis to date of the evolution of gene regulatory sequences in humans," said senior author Adam Siepel, Cornell associate professor of biological statistics and computational biology. "It's taken these 40 years to get a clear picture of what's going on in these sequences because we haven't had the data until very recently," said Leonardo Arbiza, a postdoctoral researcher in Siepel's lab and the paper's lead author.

Less than 2 percent of the human genome – the complete set of genetic material – contains genes that code for proteins. In cells, these proteins are instrumental in biological pathways that affect an organism's health, appearance and behavior.

Much less is known about the remaining 98 percent of the genome; however, in the 1960s, scientists recognized that some of the non-protein coding DNA regulates when and where genes are turned on and off, and how much protein they produce. The regulatory machinery works when proteins called transcription factors bind to specific short sequences of DNA that flank the gene, called transcription factor binding sites, and by doing so, switch genes on and off.

Among the findings, the study reports that when compared with protein coding genes, binding site DNA shows close to three times as many "weakly deleterious mutations," that is, mutations that may weaken or make an individual more susceptible to disease, but are generally not severe. Weakly deleterious mutations exist in low frequencies in a population and are eventually weeded out over time. These mutations are responsible for many inherited human diseases.

While genes generally tend to resist change, a mutation occasionally leads to a favorable trait and increases across a population; this is called positive selection. By contrast, "transcription factor binding sites show considerable amounts of positive selection," said Arbiza, with evidence for adaptation in binding sites that regulate genes controlling blood cells, brain function and immunity, among others.

"The overall picture shows more evolutionary flexibility in the binding sites than in protein coding genes," said Siepel. "This has important implications for how we think about human evolution and disease."

This is one of the first studies to combine recent data that identifies transcription factor binding sites, data on human genetic variation and genome comparisons between humans and apes. A new computational method called INSIGHT (Inference of Natural Selection from Interspersed Genomically coHerent elemenTs), designed by Ilan Gronau, a postdoctoral researcher in Siepel's lab and a co-author of the study, allowed the scientists to integrate these diverse data types and find evidence of natural selection in the regulatory DNA.

"Transcription factor binding sites are probably the regulatory elements we know the most about," said Arbiza. "If you want to understand evolution of gene expression regulation, that's a good starting point."

INSIGHT may now be used by other researchers for analyzing other short regulatory DNA sequences, such as micro-RNAs, non-coding molecules that also play a role in gene regulation.

The study was funded by the Packard Foundation, Alfred P. Sloan Foundation, National Science Foundation, National Institutes of Health, and a fellowship from the Cornell Center for Vertebrate Genomics.

http://phys.org/news/2013-06-storage-terabytes-dvd.html

More data storage? Here's how to fit 1,000 terabytes on a DVD

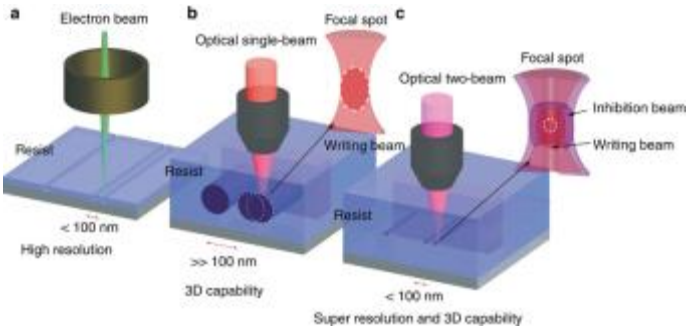
Using nanotechnology, researchers have developed a technique to increase the data storage capacity of a DVD from a measly 4.7GB to 1,000TB. Credit: Nature Communications

Jun 20, 2013 by Min Gu, Yaoyu Cao & Zongsong Gan, The Conversation

We live in a world where digital information is exploding. Some 90% of the world's data was generated in the past two years. The obvious question is: how can we store it all?

In Nature Communications today, we, along with Richard Evans from CSIRO, show how we developed a new technique to enable the data capacity of a single DVD to increase from 4.7 gigabytes up to one petabyte (1,000 terabytes). This is equivalent of 10.6 years of compressed high-definition video or 50,000 full high-definition movies.

So how did we manage to achieve such a huge boost in data storage? First, we need to understand how data is stored on optical discs such as CDs and DVDs.



(a) EBL can achieve high resolution of ~10–20 nm; however, EBL is incapable of 3D fabrication. (b) Single-beam OBL can fabricate 3D arbitrary geometry; however, the diffraction nature of light limits fabrication resolution. (c) Two-beam OBL has the advantage of fabricating 3D arbitrary geometry with nanometer feature size and resolution comparable to EBL by the photoinhibition strategy. The image in the inset shows the focal spot of the writing beam and the inhibition beam.

The basics of digital storage

Although optical discs are used to carry software, films, games, and private data, and have great advantages over other recording media in terms of cost, longevity and reliability, their low data storage capacity is their major limiting factor.

The operation of optical data storage is rather simple. When you burn a CD, for example, the information is transformed to strings of binary digits (0s and 1s, also called bits). Each bit is then laser "burned" into the disc, using a single beam of light, in the form of dots.
The storage capacity of optical discs is mainly limited by the physical dimensions of the dots. But as there's a limit to the size of the disc as well as the size of the dots, many current methods of data storage, such as DVDs and Blu-ray discs, continue to have low level storage density.
To get around this, we had to look at light's fundamental laws.

Circumnavigating Abbe's limit

In 1873, German physicist Ernst Abbe published a law that limits the width of light beams.
On the basis of this law, the diameter of a spot of light, obtained by focusing a light beam through a lens, cannot be smaller than half its wavelength – around 500 nanometres (500 billionths of a metre) for visible light. And while this law plays a huge role in modern optical microscopy, it also sets up a barrier for any efforts from researchers to produce extremely small dots – in the nanometre region – to use as binary bits.
In our study, we showed how to break this fundamental limit by using a two-light-beam method, with different colours, for recording onto discs instead of the conventional single-light-beam method.
Both beams must abide by Abbe's law, so they cannot produce smaller dots individually. But we gave the two beams different functions:

The first beam (red, in the figure right) has a round shape, and is used to activate the recording. We called it the writing beam

The second beam – the purple donut-shape – plays an anti-recording function, inhibiting the function of the writing beam

The two beams were then overlapped. As the second beam cancelled out the first in its donut ring, the recording process was tightly confined to the centre of the writing beam. This new technique produces an effective focal spot of nine nanometres – or one ten thousandth the diameter of a human hair.

The technique, in practical terms

Our work will greatly impact the development of super-compact devices as well as nanoscience and nanotechnology research.
The exceptional penetration feature of light beams allow for 3D recording or fabrication, which can dramatically increase the data storage – the number of dots – on a single optical device.
The technique is also cost-effective and portable, as only conventional optical and laser elements are used, and allows for the development of optical data storage with long life and low energy consumption, which could be an ideal platform for a Big Data centre.
As the rate of information generated worldwide continues to accelerate, the aim of more storage capacity in compact devices will continue. Our breakthrough has put that target within our reach.
More information: www.nature.com/ncomms/2013/130619/ncomms3061/full/ncomms3061.html

http://www.eurekalert.org/pub_releases/2013-06/uoc--sdp061913.php

Scientists date prehistoric bacterial invasion still present in today's cells

Cyanobacteria became symbiotic with one-celled plants 900 million years ago, more recently than thought

Long before plants and animals inhabited the earth, when life consisted of single-celled organisms afloat in a planet-wide sea, bacteria invaded these organisms and took up permanent residence. One bacterium eventually became the mitochondria that today power all plant and animal cells; another became the chloroplast that turns sunlight into energy in green plants.
A new analysis by two University of California, Berkeley, graduate students more precisely pinpoints when these life-changing invasions occurred, placing the origin of photosynthesis in plants hundreds of millions of years earlier than once thought.
"When you are talking about these really ancient events, scientists have estimated numbers that are all over the board," said coauthor Patrick Shih. Estimates of the age of eukaryotes – cells with a nucleus that evolved into all of today's plants and animals – range from 800 million years ago to 3 billion years ago.
"We came up with a novel way of decreasing the uncertainty and increasing our confidence in dating these events," he said. The two researchers believe that their approach can help answer similar questions about the origins of ancient microscopic fossils.
Shih and colleague Nicholas Matzke, who will earn their Ph.D.s this summer in plant and microbial biology and integrative biology, respectively, employed fossil and genetic evidence to estimate the dates when bacteria set up shop as symbiotic organisms in the earliest one-celled eukaryotes. They concluded that a proteobacterium invaded eurkaryotes about 1.2 billion years ago, in line with earlier estimates.

They found that a cyanobacterium – which had already developed photosynthesis – invaded eukaryotes 900 million years ago, much later than some estimates, which are as high as 2 billion years ago.
Previous estimates used hard-to-identify microbial fossils or ambiguous chemical markers in fossils to estimate the time when bacteria entered ancestral eurkaryotic cells, probably first as parasites and then as symbionts.
Shih and Matzke realized that they could get better precision by studying today's mitochondria and chloroplasts, which still retain genes from their free-living days that are evolutionarily related to genes currently present in plant and animal DNA.
"These genes, such as ATP synthase – a gene critical to the synthesis of the energy molecule ATP – were present in our single-celled ancestors and present now, and are really, really conserved," Matzke said. "These go back to the last common ancestor of all living things, so it helps us constrain the tree of life."
Since mitochrondrial, chloroplast and nuclear genes do not evolve at exactly the same rate, the researchers used Bayesian statistics to estimate the rate variation as well as how long ago the bacteria joined forces with eukaryotes. They improved their precision by focusing on plant and animal fossils that have more certain dates and identities than microbial fossils.
The paper appeared online on June 17 in advance of publication in the Proceedings of the National Academy of Sciences. Matzke also is a member of UC Berkeley's Center for Theoretical Evolutionary Genomics.

http://scitechdaily.com/nitromemantine-restores-brain-connections-in-models-of-alzheimers/

NitroMemantine Restores Brain Connections in Models of Alzheimer's

A newly published decade-long study reveals that NitroMemantine can restore connections between nerve cells that have been lost during the progression of Alzheimer's in the brain.

June 18, 2013 by Staff

The first experimental drug to boost brain synapses lost in Alzheimer's disease has been developed by researchers at Sanford-Burnham Medical Research Institute. The drug, called NitroMemantine, combines two FDA-approved medicines to stop the destructive cascade of changes in the brain that destroys the connections between neurons, leading to memory loss and cognitive decline.
The decade-long study, led by Stuart A. Lipton, M.D., Ph.D., professor and director of the Del E. Webb Center for Neuroscience, Aging, and Stem Cell Research, who is also a practicing clinical neurologist, shows that NitroMemantine can restore synapses, representing the connections between nerve cells (neurons) that have been lost during the progression of Alzheimer's in the brain. The research findings are described in a paper published June 17 by the Proceedings of the National Academy of Sciences of the United States of America (PNAS).
The focus on a downstream target to treat Alzheimer's, rather than on amyloid beta plaques and neurofibrillary tangles—approaches which have shown little success—"is very exciting because everyone is now looking for an earlier treatment of the disease," Lipton said. "These findings actually mean that you might be able to intercede not only early but also a bit later." And that means that an Alzheimer's patient may be able to have synaptic connections restored even with plaques and tangles already in his or her brain.

Targeting lost synapses

In their study, conducted in animal models as well as brain cells derived from human stem cells, Lipton and his team mapped the pathway that leads to synaptic damage in Alzheimer's. They found that amyloid beta peptides, which were once thought to injure synapses directly, actually induce the release of excessive amounts of the neurotransmitter glutamate from brain cells called astrocytes that are located adjacent to the nerve cells.
Normal levels of glutamate promote memory and learning, but excessive levels are harmful. In patients suffering from Alzheimer's disease, excessive glutamate activates extrasynaptic receptors, designated eNMDA receptors (NMDA stands for N-methyl-D-aspartate), which get hyperactivated and in turn lead to synaptic loss.

How NitroMemantine works

Lipton's lab had previously discovered how a drug called memantine can be targeted to eNMDA receptors to slow the hyperactivity seen in Alzheimer's. This patented work contributed to the FDA approval of memantine in 2003 for the treatment of moderate to severe Alzheimer's disease. However, memantine's effectiveness has been limited. The reason, the researchers found, was that memantine—a positively charged molecule—is repelled by a similar charge inside diseased neurons; therefore, memantine gets repelled from its intended eNMDA receptor target on the neuronal surface.
In their study, the researchers found that a fragment of the molecule nitroglycerin—a second FDA-approved drug commonly used to treat episodes of chest pain or angina in people with coronary heart disease—could bind to another site that the Lipton group discovered on NMDA receptors. The new drug represents a novel synthesis connecting this fragment of nitroglycerin to memantine, thus representing two FDA-approved drugs connected together. Because memantine rather selectively binds to eNMDA receptors, it also functions to target

nitroglycerin to the receptor. Therefore, by combining the two, Lipton's lab created a new, dual-function drug. The researchers developed 37 derivatives of the combined drug before they found one that worked, Lipton said.
By shutting down hyperactive eNMDA receptors on diseased neurons, NitroMemantine restores synapses between those neurons. "We show in this paper that memantine's ability to protect synapses is limited," Lipton said, "but NitroMemantine brings the number of synapses all the way back to normal within a few months of treatment in mouse models of Alzheimer's disease. In fact, the new drug really starts to work within hours."
To date, therapies that attack amyloid plaques and neurofibrillary tangles have failed. "It's quite disappointing because I see really sick patients with dementia. However, I'm now optimistic that NitroMemantine will be effective as we advance to human trials, bringing new hope to both early and later-stage Alzheimer's patients," Lipton said.
This research was funded by the U.S. National Institutes of Health (grants P01 AG010436, P50 AG005131, P01 DA017259, R01 AA020404, P01 HD29587, and P01 ES016738), the U.S. Department of Defense (W81XWH-10-1-0093), the National Institute of Neurological Disorders and Stroke Institutional Core (grant P30 NS076411), the American Heart Association, and the Ministry of Education and Science of Spain.
Publication: Maria Talantova, et al., "Aβ induces astrocytic glutamate release, extrasynaptic NMDA receptor activation, and synaptic loss," PNAS June 17, 2013; doi: 10.1073/pnas.1306832110
Source: Sanford-Burnham Medical Research Institute

http://www.eurekalert.org/pub_releases/2013-06/aaft-bau061413.php

BigBrain: An ultra-high resolution 3-D roadmap of the human brain

Freely available reference brain shows virtual human brain anatomy in fine detail

A landmark three-dimensional (3-D) digital reconstruction of a complete human brain, called the BigBrain, now for the first time shows the brain anatomy in microscopic detail—at a spatial resolution of 20 microns, smaller than the size of one fine strand of hair—exceeding that of existing reference brains presently in the public domain. The new tool is made freely available to the broader scientific community to advance the field of neuroscience.
Researchers from Germany and Canada, who collaborated on the ultra-high resolution brain model, present their work in the 21 June issue of the journal Science, which is published by AAAS, the international non-profit science society.
"The authors pushed the limits of current technology," said Science's senior editor Peter Stern about the international scientific effort. "Such spatial resolution exceeds that of presently available reference brains by a factor of 50 in each of the three spatial dimensions."
The sophisticated modern image processing methods reveal an unprecedented look at the very fine details of the human brain's microstructure, or cellular level. The anatomical tool will allow for three-dimensional cytoarchitectonic mapping of the human brain and serve as an atlas for small cellular circuit data, or single layers or sublayers of the cerebral cortex, explained the researchers.
Until recently, reference brains did not probe further than the macroscopic, or visible, components of the brain. Now, the BigBrain provides a resolution much finer than the typical 1 mm resolution from MRI studies.
The project "has been a tour-de-force to assemble images of over 7,400 individual histological sections, each with its own distortions, rips and tears, into a coherent 3-D volume," said senior author Dr. Alan Evans, a professor at the Montreal Neurological Institute at McGill University in Montreal, Canada. "This dataset allows for the first time a 3-D exploration of human cytoarchitectural anatomy."
Thin sections of a 65-year-old human female brain, which was embedded in paraffin wax, were cut with a special large-scale tool called a microtome. Then, the 20-micrometer thick histological sections were mounted on slides, stained to detect cell structures and finally digitized with a high-resolution flatbed scanner so researchers could reconstruct the high-resolution 3-D brain model. It took approximately 1,000 hours to collect the data. The resulting images reveal differences in the laminar pattern between brain areas.
The new reference brain, which is part of the European Human Brain Project, serves as a powerful tool to facilitate neuroscience research and "redefines traditional maps from the beginning of the 20th century," explained lead author Dr. Katrin Amunts from the Research Centre Jülich and director of the Cecile and Oskar Vogt Institute for Brain Research at the Heinrich Heine University Düsseldorf in Germany. "The famous cytoarchitectural atlases of the early 1900's were simplified drawings of a brain and were based on pure visual analysis of cellular organization patterns," added Dr. Amunts.
Because of the sheer volume of this dataset, the researchers say that there will be a push by those who want to use it to develop new and valuable tools for visualization, data management and analysis.
"We plan to repeat this process in a sample of brains so that we can quantify cytoarchitectural variability," said Dr. Evans. "We will also integrate this dataset with high-resolution maps of white matter connectivity in post-

mortem brains. This will allow us to explore the relationship between cortical microanatomy and fiber connectivity," said Dr. Amunts.
"We are planning to integrate our receptor data of the human brain in the reference frame provided by the BigBrain," continued senior co-author Dr. Karl Zilles, who is senior professor of the Jülich Aachen Research Alliance and former director of the Cecile and Oskar Vogt Institute for Brain Research at the Heinrich Heine University Düsseldorf in Germany. "We will also transfer high-resolution maps of quantitative data on the regional and laminar distribution of native receptor complexes to the BigBrain. This will allow us to explore the relationship between cortical microanatomy and key molecules of neurotransmission."
The fine-grained anatomical resolution will allow scientists to gain insights into the neurobiological basis of cognition, language, emotions and other processes, according to the study. The researchers also stated that they plan to extract measurements of cortical thickness to gain insights into understanding aging and neurodegenerative disorders; create cortical thickness maps to compare data from in vivo imaging; integrate gene expression data from the Allen Institute; and generate a brain model with a resolution of 1 micron to capture details of single cell morphology.
Public access of the BigBrain dataset will be provided through the CBRAIN Portal with free registration, stated the researchers.
The report by Amunts et al. was supported by CANARIE for the software development of the CBRAIN portal and the Portfolio project "Supercomputing and Modeling the Human Brain," which is funded by the Helmholtz Association Germany.
Katrin Amunts et al, BigBrain: An Ultrahigh-Resolution 3D Human Brain Model, Science, 21. Juni 2013, Vol. 340, p. 1472-1475 DOI: 10.1126/science.1235381
Institute of Neuroscience and Medicine, Structural and Functional Organization of the Brain (INM-1): http://www.fz-juelich.de/inm/inm-1/EN/Home/home_node.html
Link to the BigBrain software tool: https://bigbrain.loris.ca/main.php
Link to the Human Brain Project: http://www.humanbrainproject.eu/

http://www.sciencedaily.com/releases/2013/06/130619195133.htm

Flu Shot Likely Prevented 13 Million Illnesses, 110,000 Hospitalizations from 2005-2011

Flu Shot Likely Prevented 13 Million Illnesses, 110,000 Hospitalizations from 2005-2011

Approximately 13 million illnesses and over 110,00 hospitalizations may have been averted by the flu vaccine over the last 6 years in the U.S, according to calculations published June 19 in the open access journal PLOS ONE by Deliana Kostova and colleagues from the U.S Centers for Disease Control and Prevention.
The researchers calculated the healthcare burden of flu cases that would have occurred in the absence of vaccination based on factors such as illness and hospitalization rates during the flu season, vaccination coverage and vaccine effectiveness. Based on these data, Kostova and colleagues estimate that flu vaccines averted several million instances of illness and over 110,000 flu-related hospitalizations in the flu seasons of 2006 to 2011. The largest number of averted cases occurred during the most recent period studied, 2010-2011, when 5 million flu cases, 2.1 million medical visits and 40,400 hospitalizations were prevented by vaccination.
The U.S is the only country with universal influenza vaccine recommendations that suggest everyone aged 6 months and older should receive an annual dose of the vaccine. However, previous studies have not provided ways to reliably assess the number of flu cases or hospitalizations that are prevented by vaccination each year.
Senior author on the study Joseph Bresee adds, ""These results confirm the value of influenza vaccination, but highlight the need for more people to get vaccinated and the imperative for vaccines with greater efficacy, especially in the elderly."
Deliana Kostova, Carrie Reed, Lyn Finelli, Po-Yung Cheng, Paul M. Gargiullo, David K. Shay, James A. Singleton, Martin I. Meltzer, Peng-jun Lu, Joseph S. Bresee. Influenza Illness and Hospitalizations Averted by Influenza Vaccination in the United States, 2005–2011. PLoS ONE, 2013; 8 (6): e66312 DOI: 10.1371/journal.pone.0066312

http://news.sciencemag.org/sciencenow/2013/06/trying-to-learn-a-foreign-langua.html?ref=hp

Trying to Learn a Foreign Language? Avoid Reminders of Home

Reminders of one's homeland can hinder the ability to speak a new language

by Emily Underwood on 17 June 2013, 3:50 PM |

Something odd happened when Shu Zhang was giving a presentation to her classmates at the Columbia Business School in New York City. Zhang, a Chinese native, spoke fluent English, yet in the middle of her talk, she glanced over at her Chinese professor and suddenly blurted out a word in Mandarin. "I meant to say a transition word like 'however,' but used the Chinese version instead," she says. "It really shocked me."
Shortly afterward, Zhang teamed up with Columbia social psychologist Michael Morris and colleagues to figure out what had happened. In a new study, they show that reminders of one's homeland can hinder the ability to speak a new language. The findings could help explain why cultural immersion is the most effective

way to learn a foreign tongue and why immigrants who settle within an ethnic enclave acculturate more slowly than those who surround themselves with friends from their new country.
Previous studies have shown that cultural icons such as landmarks and celebrities act like "magnets of meaning," instantly activating a web of cultural associations in the mind and influencing our judgments and behavior, Morris says. In an earlier study, for example, he asked Chinese Americans to explain what was happening in a photograph of several fish, in which one fish swam slightly ahead of the others. Subjects first shown Chinese symbols, such as the Great Wall or a dragon, interpreted the fish as being chased. But individuals primed with American images of Marilyn Monroe or Superman, in contrast, tended to interpret the outlying fish as leading the others. This internally driven motivation is more typical of individualistic American values, some social psychologists say, whereas the more externally driven explanation of being pursued is more typical of Chinese culture.
To determine whether these cultural icons can also interfere with speaking a second language, Zhang, Morris, and their colleagues recruited male and female Chinese students who had lived in the United States for a less than a year and had them sit opposite a computer monitor that displayed the face of either a Chinese or Caucasian male called "Michael Lee." As microphones recorded their speech, the volunteers conversed with Lee, who spoke to them in English with an American accent about campus life.
Next, the team compared the fluency of the volunteers' speech when they were talking to a Chinese versus a Caucasian face. Although participants reported a more positive experience chatting with the Chinese version of "Michael Lee," they were significantly less fluent, producing 11% fewer words per minute on average, the authors report online today in the Proceedings of the National Academy of Sciences. "It's ironic" that the more comfortable volunteers were with their conversational partner, the less fluent they became, Zhang says. "That's something we did not expect."

Tongue twister. Bilingual immigrants are more likely to slip back into their first languages when reminded of home.
Credit: Michael Morris and Shu Zhang; Image of pistachio nut © Dmitry Rukhlenko/iStockphoto.com

To rule out the possibility that the volunteers were speaking more fluently to the Caucasian face on purpose, thus explaining the performance gap, Zhang and colleagues asked the participants to invent a story, such as a boy swimming in the ocean, while simultaneously being exposed to Chinese and American icons rather than faces. Seeing Chinese icons such as the Great Wall also interfered with the volunteers' English fluency, causing a 16% drop in words produced per minute. The icons also made the volunteers 85% more likely to use a literal translation of the Chinese word for an object rather than the English term, Zhang says. Rather than saying "pistachio," for example, volunteers used the Chinese version, "happy nuts."
Understanding how these subtle cultural cues affect language fluency could help employers design better job interviews, Morris says. For example, taking a Japanese job candidate out for sushi, although a well-meaning gesture, might not be the best way to help them shine.
"It's quite striking that these effects were so robust," says Mary Helen Immordino-Yang, a developmental psychologist at the University of Southern California in Los Angeles. They show that "we're exquisitely attuned to cultural context," she says, and that "even subtle cues like the ethnicity of the person we're talking to" can affect language processing. The take-home message? "If one wants to acculturate rapidly, don't move to an ethnic enclave neighborhood where you'll be surrounded by people like yourself," Morris says. Sometimes, a familiar face is the last thing you need to see.
**Correction, 10:50 a.m., 18 June: Volunteers conversed with Michael Lee, not Michael Yee, as previously reported. The name has been corrected.*

http://phys.org/news/2013-06-astronomers-pulsations-crystalized-dying-star.html

Astronomers discover pulsations in crystalized, dying star

Pulsations discovered from the crystalized remnant of a burnt-out star

Phys.org - Astronomers from The University of Texas at Austin and colleagues have used the 2.1-meter Otto Struve Telescope at the university's McDonald Observatory to discover pulsations from the crystalized remnant of a burnt-out star. The finding will allow astronomers to see below the star's atmosphere and into its interior, much like earthquakes allow geologists to study compositions below Earth's surface. The findings appear in the current issue of The Astrophysical Journal Letters.

The Texas astronomers made their discovery in collaboration with astronomers from Brazil's Universidade Federal do Rio Grande do Sul, the University of Oklahoma, and the Smithsonian Astrophysical Observatory.
The star, GD 518, is roughly 170 light years from Earth in the constellation Draco, but far too faint to be seen without a telescope. It is a white dwarf, a star at the end of its life cycle that is essentially just a burnt-out core, the ashy byproduct of previous epochs of nuclear fusion.
The star is unique in that much of it is likely suspended in a state more akin to a solid than a liquid or gas. The interiors of dying stars can become crystalized similar to the way in which frigid water freezes into ice, like the slow formation of glaciers in cooling ocean water.
"GD 518 is special because it is a very massive white dwarf: It has about 1.2 times the mass of the Sun, packed into a volume smaller than Earth," said lead author J.J. Hermes, a graduate student at The University of Texas at Austin. "Few white dwarfs are endowed with so much mass, and this is by far the most massive white dwarf discovered to pulsate."
The star also likely has an interior composed of heavier elements than those found in typical burnt-out stars. Our Sun will only get hot enough in its center for nuclear fusion to burn hydrogen into helium, and in turn the helium to carbon and oxygen. The Sun will end its life in more than five billion years as a white dwarf with its central regions composed mostly of the nuclei of carbon and oxygen atoms.
But unlike the Sun, the star that died to become the white dwarf GD 518 was so massive —probably more than seven times the Sun's mass—that it burned elements heavier than carbon and oxygen, and is now likely a white dwarf composed of oxygen and neon nuclei.
The discovery of pulsations —periodic brightness changes on the surface of a star that, in this case, keep a regular tune every 400-600 seconds—will allow astronomers an unprecedented opportunity to understand what makes up this highly evolved star's interior.
Team member Barbara Castanheira is a postdoctoral researcher with McDonald Observatory. "Like a child at a museum, astronomers are only allowed to look, not touch, when they perform experiments," Castanheira said. "This means we usually can only understand the surface of a star. Pulsations, like the sound of a bell, tell us more of the story, since they can unravel secrets about the much deeper interior of a star."
White dwarf stars no longer fuse elements in their interior to generate energy; they simply cool, like coal embers removed from a fire. But at a certain point the atomic nuclei in the star's interior get cool enough to begin to settle into a lattice structure and crystalize, just like water freezing into ice. This happens sooner in the interiors of more massive white dwarfs, and in the case of GD 518, it has likely started before the star had the right conditions to excite pulsations. The transition to a solid-like star should also affect the way the white dwarf vibrates from these pulsations.
Astronomers now face the difficult task of matching the pulsation periods observed in the star with those predicted by different models of the structure of its interior. The discovery observations show promise in this direction, Hermes said.
"We see evidence that the strength of pulsations in this star are very inconsistent; some nights the star is as still as a whisper," he said. "This could be because the white dwarf is highly crystalized, and the pulsations are only allowed to propagate in a tiny bit of the outermost parts of the star. They thus have little inertia, and are more susceptible to changes than the pulsations in a typical pulsating white dwarf."
University of Texas astronomers will continue watching GD 518 from McDonald Observatory, listening closely for any new notes that can unravel the song being sung by light from this ultramassive dying star.
More information: dx.doi.org/10.1088/2041-8205/771/1/L2

http://phys.org/news/2013-06-grocery-cabbage-alive.html

Does your salad know what time it is?

Managing vegetables' 'internal clocks' postharvest could have health benefits

Does your salad know what time it is? It may be healthier for you if it does, according to new research from Rice University and the University of California at Davis.
"Vegetables and fruits don't die the moment they are harvested," said Rice biologist Janet Braam, the lead researcher on a new study this week in Current Biology. "They respond to their environment for days, and we found we could use light to coax them to make more cancer-fighting antioxidants at certain times of day."
Braam is professor and chair of Rice's Department of Biochemistry and Cell Biology.
Braam's team simulated day-night cycles of light and dark to control the internal clocks of fruits and vegetables, including cabbage, carrots, squash and blueberries. The research is a follow-up to her team's award-winning 2012 study of the ways that plants use their internal circadian clocks to defend themselves from hungry insects. That study found that Arabidopsis thaliana—a widely used model organism for plant studies—begins ramping up production of insect-fighting chemicals a few hours before sunrise, the time that hungry insects begin to feed.

Braam said the idea for the new research came from a conversation with her teenage son.
"I was telling him about the earlier work on Arabidopsis and insect resistance, and he said, 'Well, I know what time of day I'll eat my vegetables!' Braam said. "That was my 'aha!' moment. He was thinking to avoid eating the vegetables when they would be accumulating the anti-insect chemicals, but I knew that some of those chemicals were known to be valuable metabolites for human health, so I decided to try and find out whether vegetables cycle those compounds based on circadian rhythms."
Arabidopsis and cabbage are related, so Braam's team began their research by attempting to "entrain" the clocks of cabbage in the same way they had Arabidopsis. Entrainment is akin to the process that international travelers go through as they recover from jet lag. After flying to the other side of the globe, travelers often have trouble sleeping until their internal circadian clock resets itself to the day-night cycle in their new locale.
Using controlled lighting in a sealed chamber, Rice graduate student and study lead author Danielle Goodspeed found she could entrain the circadian clocks of postharvest cabbage just as she had those of Arabidopsis in the 2012 study. Following the success with cabbage, Goodspeed and co-authors John Liu and Zhengji Sheng studied spinach, lettuce, zucchini, carrots, sweet potatoes and blueberries.
"We were able to entrain each of them, even the root vegetables," Goodspeed said. She and Braam said the findings suggest that storing fruits and vegetables in dark trucks, boxes and refrigerators may reduce their ability to keep daily rhythms.
"We cannot yet say whether all-dark or all-light conditions shorten the shelf life of fruits and vegetables," Braam said. "What we have shown is that keeping the internal clock ticking is advantageous with respect to insect resistance and could also yield health benefits."
In the cabbage experiments, Braam, Goodspeed and Rice co-authors John Liu, Zhengji "Jim" Sheng and Wassim Chehab found they could manipulate cabbage leaves to increase their production of anti-insect metabolites at certain times of day. One of these, an antioxidant called glucoraphanin, or 4-MSO, is a known anti-cancer compound that has been previously studied in broccoli and other vegetables.
A time-lapse comparison of caterpillars eating postharvest lettuce
Braam's team has already begun follow-up research, which is supported by the Bill and Melinda Gates Foundation, into whether light and other stimuli, like touch, may be used to enhance pest resistance of food crops in developing countries.
"It's exciting to think that we may be able to boost the health benefits of our produce simply by changing the way we store it," Goodspeed said.
More information: Current Biology, Goodspeed et al.: "Postharvest Circadian Entrainment Enhances Crop Pest Resistance and Phytochemical Cycling." dx.doi.org/10.1016/j.cub.2013.05.034

http://bit.ly/15nedXb

Silver Makes Antibiotics Thousands of Times More Effective

The antimicrobial treatment could help to solve modern bacterial resistance

By Brian Owens and Nature magazine | Thursday, June 20, 2013 | 11

Like werewolves and vampires, bacteria have a weakness: silver. The precious metal has been used to fight infection for thousands of years — Hippocrates first described its antimicrobial properties in 400 bc — but how it works has been a mystery. Now, a team led by James Collins, a biomedical engineer at Boston University in Massachusetts, has described how silver can disrupt bacteria, and shown that the ancient treatment could help to deal with the thoroughly modern scourge of antibiotic resistance. The work is published today in Science Translational Medicine.
“Resistance is growing, while the number of new antibiotics in development is dropping,” says Collins. “We wanted to find a way to make what we have work better.”
Collins and his team found that silver — in the form of dissolved ions — attacks bacterial cells in two main ways: it makes the cell membrane more permeable, and it interferes with the cell’s metabolism, leading to the overproduction of reactive, and often toxic, oxygen compounds. Both mechanisms could potentially be harnessed to make today’s antibiotics more effective against resistant bacteria, Collins says.

Resistance is futile

Many antibiotics are thought to kill their targets by producing reactive oxygen compounds, and Collins and his team showed that when boosted with a small amount of silver these drugs could kill between 10 and 1,000 times as many bacteria. The increased membrane permeability also allows more antibiotics to enter the bacterial cells, which may overwhelm the resistance mechanisms that rely on shuttling the drug back out.
That disruption to the cell membrane also increased the effectiveness of vancomycin, a large-molecule antibiotic, on Gram-negative bacteria — which have a protective outer coating. Gram-negative bacterial cells can often be impenetrable to antibiotics made of larger molecules.

"It's not so much a silver bullet; more a silver spoon to help the Gram-negative bacteria take their medicine," says Collins.

Toxic assets

Vance Fowler, an infectious-disease physician at Duke University in Durham, North Carolina, says the work is "really cool" but sounds a note of caution about the potential toxicity of silver. "It has had a checkered past," he says.

In the 1990s, for example, a heart valve made by St. Jude Medical, based in St. Paul, Minnesota, included parts covered with a silver coating called Silzone to fight infection. "It did a fine job of preventing infection," says Fowler. "The problem was that the silver was also toxic to heart tissue." As a result the valves often leaked.

Before adding silver to antibiotics, "we'll have to address the toxicity very carefully", says Fowler. Ingesting too much silver can also cause argyria, a condition in which the skin turns a blue-grey color — and the effect is permanent.

Collins says that he and his colleagues saw good results in mice using non-toxic amounts of silver. But, he adds, there are ways to reduce the risk even further. "We're also encouraging people to look at what features of silver caused the helpful effects, so they can look for non-toxic versions," he says.

http://phys.org/news/2013-06-green-algae-air-cell-haemoglobin.html

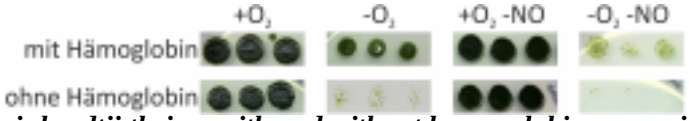
When green algae run out of air: Single cell organisms need haemoglobin to survive in an oxygen-free environment

When green algae run out of air: Single cell organisms need haemoglobin to survive in an oxygen-free environment

When green algae "can't breathe", they get rid of excess energy through the production of hydrogen. Biologists at the Ruhr-Universität Bochum have found out how the cells notice the absence of oxygen. For this, they need the messenger molecule nitric oxide and the protein haemoglobin, which is commonly known from red blood cells of humans. With colleagues at the UC Los Angeles, the Bochum team reported in the journal PNAS.

In the human body, haemoglobin transports oxygen from the lungs to the organs and brings carbon dioxide, which is produced there, back to the lungs. "However, scientists have known for years that there is not just the one haemoglobin", says Prof. Thomas Happe from the Work Group Photobiotechnology. Nature has produced a large number of related proteins which fulfil different functions. The green alga Chlamydomonas reinhardtii has what is known as a "truncated" haemoglobin, the function of which was previously unknown. Happe's team has deciphered its role in surviving in an oxygen-free environment.

When Chlamydomonas has no oxygen available, the algae transfer excess electrons to protons, creating hydrogen (H2). "For this to work, the green alga activates a certain gene programme and creates many new proteins", Happe explains. "But how exactly the cells even notice that oxygen is missing is something we did not know." The research team looked for genes that are particularly active when green algae have to live without oxygen – and found a gene that forms the blueprint for a haemoglobin. In an oxygen-rich environment, however, this gene was completely idle.



In an oxygen-rich environment (+ O2), Chlamydomonas reinhardtii thrives with and without haemoglobin – even if the cell has no nitric oxide (NO) available. However, if there is a lack of oxygen (-O2), the single-cell organism only grows if it possesses haemoglobin. Without haemoglobin and without nitric oxide (-NO) growth is basically impossible.
Credit: © AG Photobiotechnologie, RUB

The scientists studied the haemoglobin protein and its genetic blueprint in more detail using molecular biological and biochemical analyses. "One thing became clear very quickly", says Dr. Anja Hemschemeier from the Work Group Photobiotechnology. "Algae in which we switched this gene off could hardly grow without oxygen." From previous studies it is known that in many organisms, haemoglobin detoxifies nitric oxide, because an overdose of this gas poisons the cells. The biologists therefore tested whether green algae which are no longer able to form haemoglobin after genetic manipulation die of nitric oxide poisoning. Their expectations: the green algae should fare better if the gas is removed using a chemical scavenger. "Surprisingly, then the algae were not able to grow at all", says Hemschemeier. The researchers concluded that, under oxygen-free conditions, haemoglobin and nitric oxide are in cahoots.

Nitric oxide acts in many living organisms as a signalling molecule – apparently also in green algae. Experiments in vitro have shown that the green algal haemoglobin interacts with nitric oxide. When the researchers artificially introduced the gas to the single cell organisms, certain genes became active that are otherwise only "turned on" in the absence of oxygen. "From all this data we can conclude that Chlamydomonas uses nitric oxide to pass on the 'no oxygen!' signal within the cell, and that our haemoglobin is involved in this process", Happe sums up. His team wants to go on exploring the role of this protein in green algae, as the

biologists have discovered another eleven haemoglobin genes in the organism. "Now things are really getting going", says the Bochum scientist. "The map of haemoglobin research has many blank spots that we want to fill with content. The fact that a single cell requires twelve haemoglobin proteins indicates that these fulfil finely tuned functions in the cell."

More information: A. Hemschemeier, M. Düner, D. Casero, S.S. Merchant, M. Winkler, T. Happe (2013): Hypoxic survival requires a 2-on-2 hemoglobin in a process involving nitric oxide, Proceedings of the National Academy of Sciences, doi: 10.1073/pnas.1302592110

http://www.sciencedaily.com/releases/2013/06/130621141806.htm

How Cancer Cells Avoid Cell Death

Study provides insight into how cancer cells can avoid cell death and may suggest an approach to prevent spread of cancers

A new study by a team of researchers from the University of Notre Dame provides an important new insight into how cancer cells are able to avoid the cell death process. The findings may suggest a chemotherapeutic approach to prevent the spread of cancers.

Metastasis, the spread of cancer from one organ to other parts of the body, relies on cancer cells ability to evade a cell death process called anoikis, according to Zachary T. Schafer, Coleman Assistant Professor of Cancer Biology at Notre Dame. Metalizing cancer cells are able to survive anoikis, which normally results from detachment from the extracellular matrix. However, Schafer notes that the molecular mechanisms cancer cells detached from the extracellular matrix use to survive has not been well understood.

"This paper reveals that cancer cells that are detached from their normal environment, as they would be during metastasis, relay on the activity of antioxidant enzymes to facilitate their survival," Schafer said. "This class of enzymes is critical for neutralizing oxidative stress and function much like the compounds that are present in a variety of foods."

The paper describes a prominent role for antioxidant enzymes in facilitating the survival of breast cancer cells after detachment from the extracellular matrix. Conversely, the researchers report, silencing antioxidant enzyme expression reduced tumor formation. "The results in this paper suggest that targeting antioxidant enzymes with novel therapeutics may selectively kill off metastasizing cancer cells," Schafer said.

The paper appears in the journal Cancer Research, which is the most frequently cited cancer journal in the world. The researchers collaborated with Matthew Leevy in Notre Dame's in vivo imaging facility.

Other authors of the paper include doctoral student Calli Davison, rising junior Sienna Durbin, 2011 alum Matthew Thau, graduate student Victoria Zellmer, and Sarah Chapman, Justin Diner and Connor Wathen from the Notre Dame Integrated Imaging Facility.

C. A. Davison, S. M. Durbin, M. R. Thau, V. R. Zellmer, S. E. Chapman, J. Diener, C. Wathen, W. M. Leevy, Z. T. Schafer. Antioxidant Enzymes Mediate Survival of Breast Cancer Cells Deprived of Extracellular Matrix. Cancer Research, 2013; 73 (12): 3704 DOI: 10.1158/0008-5472.CAN-12-2482

http://www.bbc.co.uk/news/health-22991838

Plants 'do maths' to control overnight food supplies

Plants have a built-in capacity to do maths, which helps them regulate food reserves at night, research suggests.

By Helen Briggs BBC News

UK scientists say they were "amazed" to find an example of such a sophisticated arithmetic calculation in biology. Mathematical models show that the amount of starch consumed overnight is calculated by division in a process involving leaf chemicals, a John Innes Centre team reports in e-Life journal. Birds may use similar methods to preserve fat levels during migration. The scientists studied the plant Arabidopsis, which is regarded as a model plant for experiments.

'Astonished'

Overnight, when the plant cannot use energy from sunlight to convert carbon dioxide into sugars and starch, it must regulate its starch reserves to ensure they last until dawn.

Experiments by scientists at the John Innes Centre, Norwich, show that to adjust its starch consumption so precisely, the plant must be performing a mathematical calculation - arithmetic division.

"They're actually doing maths in a simple, chemical way - that's amazing, it astonished us as scientists to see that," study leader Prof Alison Smith told BBC News. "This is pre-GCSE maths they're doing, but they're doing maths."

The scientists used mathematical modelling to investigate how a division calculation can be carried out inside a plant. During the night, mechanisms inside the leaf measure the size of the starch store. Information about time comes from an internal clock, similar to the human body clock.

'Sophisticated'

The researchers proposed that the process is mediated by the concentrations of two kinds of molecules called "S" for starch and "T" for time.

If the S molecules stimulate starch breakdown, while the T molecules prevent this from happening, then the rate of starch consumption is set by the ratio of S molecules to T molecules. In other words, S divided by T.

"This is the first concrete example in biology of such a sophisticated arithmetic calculation," said mathematical modeller Prof Martin Howard, of the John Innes Centre.

The scientists think similar mechanisms may operate in animals such as birds to control fat reserves during migration over long distances, or when they are deprived of food when incubating eggs.

Commenting on the research, Dr Richard Buggs of Queen Mary, University of London, said: "This is not evidence for plant intelligence. It simply suggests that plants have a mechanism designed to automatically regulate how fast they burn carbohydrates at night. Plants don't do maths voluntarily and with a purpose in mind like we do."

http://www.sciencedaily.com/releases/2013/06/130622154450.htm

Findings Emphasize Importance of Vitamin D in Pregnancy

Pregnant women pass low levels of vitamin D on to their babies at almost three times the extent previously thought, according to new research carried out at London's Kingston University.

While current studies suggest that around a fifth (19 per cent) of a newborn baby's supply or deficiency of vitamin D comes directly from its mother, experts from Kingston's School of Life Sciences have discovered that the figure is, in fact, almost three times as high at 56 per cent. The results have been revealed using a new measuring technique, developed in the laboratories at Kingston, which is able to examine eight different forms of vitamin D in greater detail for the first time.

The study, just published in Nutrition Journal, focused on 120 samples taken from 60 Greek mothers and their babies. The research was conducted with the Department of Obstetrics and Gynaecology at Aristotle University of Thessaloniki in Greece. Although the Mediterranean nation enjoys more hours of sunshine than the United Kingdom, the research revealed that many of the mothers had low levels of vitamin D, suggesting that what they ate was an equally important source.

Professor Declan Naughton, who headed the Kingston University research team, said the findings made it more important than ever that mothers-to-be received the key nutrient not only through sunlight but also through foods such as oily fish. "The impact that mothers deficient in vitamin D have on their babies' levels is a much bigger problem than we thought," Professor Naughton said. "Maintaining good supplies during pregnancy is clearly of vital importance for both mothers' and babies' long term health."

Lack of the vitamin in pregnant women has been linked to diabetes and increased rates of caesarean section births, while babies can be smaller than average. In children, the deficiency can cause rickets -- a soft bone disease.

Vitamin D plays an important role in maintaining good levels of calcium and phosphate which help form healthy bones and teeth. The two main forms are vitamin D3, which primarily comes from sunlight, and D2 which is found in a small number of foods including egg yolk, mushrooms, farmed salmon, mackerel, sardines and fortified bread and cereals. Processes in the body convert the vitamin into what is known as the circulating form -- the type commonly measured in routine blood tests -- followed by the active form -- the type that promotes calcium absorption, cell growth and immunity.

Professor Naughton and his team found that the type of vitamin D commonly measured in blood tests was not as reliable an indicator of vitamin D activity as other strands. They went on to discover that two epimer forms, previously thought to be unimportant, influenced levels in babies. "This shows the need for more accurate measurement to assess levels of vitamin D as well as the need to look more closely at its different forms," Professor Naughton said.

Further clinical studies would be required to examine the effectiveness of vitamin D supplements in pregnant women to see whether particular factors made it difficult for them to absorb the nutrient, Professor Naughton added.

The research forms part of wider investigations being conducted by Professor Naughton and his team into vitamin D's role in conditions including Alzheimer's disease, diabetes and multiple sclerosis.

Spyridon N Karras, Iltaf Shah, Andrea Petroczi, Dimitrios G Goulis, Helen Bili, Fotini Papadopoulou, Vikentia Harizopoulou, Basil C Tarlatzis, Declan P Naughton. An observational study reveals that neonatal vitamin D is primarily determined by maternal contributions: implications of a new assay on the roles of vitamin D forms. Nutrition Journal, 2013; 12 (1): 77 DOI: 10.1186/1475-2891-12-77

http://www.sciencedaily.com/releases/2013/06/130623145100.htm

Unexpected Discovery of the Ways Cells Move Could Boost Understanding of Complex Diseases

A new discovery about how cells move inside the body may provide scientists with crucial information about disease mechanisms such as the spread of cancer or the constriction of airways caused by asthma.

Led by researchers at Harvard School of Public Health (HSPH) and the Institute for Bioengineering of Catalonia (IBEC), investigators found that epithelial cells -- the type that form a barrier between the inside and the outside of the body, such as skin cells -- move in a group, propelled by forces both from within and from nearby cells -- to fill any unfilled spaces they encounter.

The study appears June 23, 2013 in an advance online edition of Nature Materials.

"We were trying to understand the basic relationship between collective cellular motions and collective cellular forces, as might occur during cancer cell invasion, for example. But in doing so we stumbled onto a phenomenon that was totally unexpected," said senior author Jeffrey Fredberg, professor of bioengineering and physiology in the HSPH Department of Environmental Health and co-senior investigator of HSPH's Molecular and Integrative Cellular Dynamics lab.

Biologists, engineers, and physicists from HSPH and IBEC worked together to shed light on collective cellular motion because it plays a key role in functions such as wound healing, organ development, and tumor growth. Using a technique called monolayer stress microscopy -- which they invented themselves -- they measured the forces affecting a single layer of moving epithelial cells. They examined the cells' velocity and direction as well as traction -- how some cells either pull or push themselves and thus force collective movement.

As they expected, the researchers found that when an obstacle was placed in the path of an advancing cell layer -- in this case, a gel that provided no traction -- the cells moved around it, tightly hugging the sides of the gel as they passed. However, the researchers also found something surprising -- that the cells, in addition to moving forward, continued to pull themselves collectively back toward the gel, as if yearning to fill the unfilled space. The researchers dubbed this movement "kenotaxis," from the Greek words "keno" (vacuum) and "taxis" (arrangement), because it seemed the cells were attempting to fill a vacuum.

This new finding could help researchers better understand cell behavior -- and evaluate potential drugs to influence that behavior -- in a variety of complex diseases, such as cancer, asthma, cardiovascular disease, developmental abnormalities, and glaucoma. The finding could also help with tissue engineering and regenerative medicine, both of which rely on cell migration.

In carcinomas, for instance -- which represent 90% of all cancers and involve epithelial cells -- the new information on cell movement could improve understanding of how cancer cells migrate through the body. Asthma research could also get a boost, because scientists think migration of damaged epithelial cells in the lungs are involved in the airway narrowing caused by the disease.

"Kenotaxis is a property of the cellular collective, not the individual cell," said Jae Hun Kim, the study's first author. "It was amazing to us that the cellular collective can organize to pull itself systematically in one direction while moving systematically in an altogether different direction."

Jae Hun Kim, Xavier Serra-Picamal, Dhananjay T. Tambe, Enhua H. Zhou, Chan Young Park, Monirosadat Sadati, Jin-Ah Park, Ramaswamy Krishnan, Bomi Gweon, Emil Millet, James P. Butler, Xavier Trepat, Jeffrey J. Fredberg. Propulsion and navigation within the advancing monolayer sheet. Nature Materials, 2013; DOI: 10.1038/nmat3689

http://phys.org/news/2013-06-discovery-deadly-cat-virus.html

Discovery offers hope against deadly cat virus

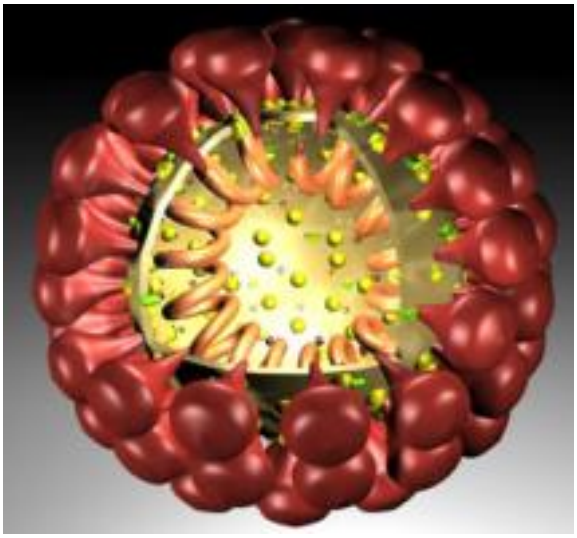
What makes a harmless virus turn lethal? For the deadliest infectious disease in cats, Cornell scientists now know.

After gathering the world's largest sample collection for feline infectious peritonitis (FIP), they uncovered the holy grail of a 30-year quest for the mutation that turns it fatal. Scheduled to be published in Emerging Infectious Disease in July 2013, their study provides a long-sought breakthrough, opening the door to development of the first working diagnostics, vaccines and treatments for FIP.

Dramatic and usually fatal, FIP develops when feline enteric coronavirus (FECV), a common benign intestinal virus, mutates into the malignant FIPV virus. Discovered by a Cornell veterinarian in 1963, this mutant moves from intestinal cells to white blood cells called macrophages. Traveling through the body, it kills most cats within weeks. Kittens are particularly vulnerable, especially in shelters and catteries. Current tests cannot distinguish between the common FECV and the killer FIPV. There are no effective vaccines or therapies.

"FIP is a tragic disease for families falling in love with new kittens and for veterinarians who can do nothing to stop it," said Gary Whittaker, virology professor at Cornell's College of Veterinary Medicine. "Comparing viral

genetics, our lab found exactly what changes when FECV mutates into FIPV. This knowledge will prove pivotal in developing tests, vaccines and treatments to protect cats from this devastating disease."
Scientists have searched for this mutation for the last three decades. Part of the challenge, Whittaker said, might have been the scale at which they searched. Like flu viruses, coronaviruses code genes with RNA. RNA-based viruses make many mistakes when replicating, allowing them to quickly mutate, dodge vaccines and therapeutics, and move to new territory.
"These viruses are so rife with mutations that even samples of the same virus from the same tissue in the same cat rarely match to the letter," said Whittaker. "Sifting through for something that distinguishes FIPV was like looking for a needle in a haystack."
So Whittaker deviated from taking the traditional birds-eye view, focusing instead on a specific functional part of the virus. Coronavirus particles brim with crowns of spikey proteins that activate the virus when chopped by the right proteases – ax-like enzymes in the host cell. FECV prefers proteases from its main ride, intestinal cells. When FIPV hijacks macrophages instead, Whittaker suspected its spike proteins have changed shape to respond to macrophage proteases.
Using novel biochemical analysis and traditional comparative genomic analysis, Whittaker focused on the area where proteases cut spike proteins. He amassed an unprecedented collection of feline coronavirus, gathering hundreds of samples donated from pet owners, veterinarians and – with help from pathology professor Gerald Duhamel – Cornell's pathology vault.



A model of coronavirus structure. The particle's main body is crowned with spike proteins (red), which activate the virus when cleaved by the right protease.

Comparing the spot in quiet FECV to the same spot in killer FIPV, he found a distinct set of differences in the spike proteins and the genes that code them. This set of mutations matched FIPV's behavioral change and appeared across samples with consistency unparalleled in the quest for the mutation.
"Using a unique interdisciplinary approach, we've found the first known molecular basis for FIP," said Whittaker. "This could have implications for similar coronaviruses, such as FIPV's deadly cousin in ferrets and another human-infecting cousin emerging in the Middle East. For now, it finally unlocks the door to developing the world's first effective diagnostics, preventions and therapies for FIP in cats."
Provided by Cornell University