http://www.sciencedaily.com/releases/2013/10/131013163322.htm

Database of Disease Genes Shows Potential Drug Therapies

Researchers at Washington University School of Medicine in St. Louis have created a massive online database that matches thousands of genes linked to cancer and other diseases with drugs that target those genes.

Some of the drugs are approved by the U.S. Food and Drug Administration, while others are in clinical trials or just entering the drug development pipeline. The database was developed by identical twin brothers, Obi Griffith, PhD, and Malachi Griffith, PhD, whose interest in pairing drugs with genes is as much personal as it is scientific. Their mother died of breast cancer 17 years ago, just weeks before their high school graduation.

"We wanted to create a comprehensive database that is user-friendly, something along the lines of a Google search engine for disease genes," explained Malachi Griffith, a research instructor in genetics. "As we move toward personalized medicine, there's a lot of interest in knowing whether drugs can target mutated genes in particular patients or in certain diseases, like breast or lung cancer. But there hasn't been an easy way to find that information."

Details of the Drug Gene Interaction database are reported online Oct. 13 in Nature Methods. The database is weighted heavily toward cancer genes but also includes genes involved in Alzheimer's disease, heart disease, diabetes and many other illnesses. The Griffiths created the database with a team of scientists at The Genome Institute at Washington University in St. Louis.

The database is easy to search and geared toward researchers and physician-scientists who want to know whether errors in disease genes - identified through genome sequencing or other methods - potentially could be targeted with existing drug therapies. Additional genes included in the database could be the focus of future drug development efforts because they belong to classes of genes that are thought to make promising drug targets.

"Developing the database was a labor of love for the Griffiths," said senior author Richard K. Wilson, PhD, director of The Genome Institute. "There's an amazing depth to this resource, which will be invaluable to researchers working to design better treatment options for patients." Wilson and his colleagues caution that the database is intended for research purposes and that it does not recommend treatments. The primary purpose of the database is to further clinical research aimed at treating diseases more effectively.

"This database gets us one step closer to that goal," Malachi Griffith said. "It's a really rich resource, and we're excited to make it available to the scientific community."

The database, which took several years to develop, is publicly available and free to use. It includes more than 14,000 drug-gene interactions involving 2,600 genes and 6,300 drugs that target those genes. Another 6,700 genes are in the database because they potentially could be targeted with future drugs.

Before now, researchers wanting to find out whether disease genes could be targeted with drugs had to search piecemeal through scientific literature, clinical trials databases or other sources of information, some of which were not publicly available or easily searchable. Further, many of the existing databases have different ways of identifying genes and drugs, a "language" barrier that can turn a definitive search into an exhaustive exercise.

The Griffith brothers are experts in bioinformatics, a field of science that integrates biology and computing and involves analyzing large amounts of data. The brothers got the idea for the drug-gene interaction database after they repeatedly were asked whether lists of genes identified through cancer genome sequencing could be targeted with existing drugs.

"It shouldn't take a computer wizard to answer that question," said Obi Griffith, research assistant professor of medicine. "But in reality, we often had to write special software to find out. Now, researchers can quickly and easily search for themselves."

The new database brings together information from 15 publicly available databases in the United States, Canada, Europe and Asia. Users can enter the name of a single gene or lists of many genes to retrieve drugs targeting those genes. The search provides the names of drugs targeted to each gene and details whether the drug is an inhibitor, antibody, vaccine or another type. The search results also indicate the source of the information so users can dig deeper, if they choose.

The research is supported by a grant (U54 HG003079) from the National Human Genome Research Institute at the National Institutes of Health (NIH).

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http://www.eurekalert.org/pub_releases/2013-10/kp-sfe101013.php

Study finds earlier is better for measles immunization first dose

Children receiving measles-containing vaccines at 12-15 months of age have a lower increased risk of fever and seizures than those who receive them at 16-23 months of age, according to a new Kaiser Permanente study published in JAMA Pediatrics.

OAKLAND, Calif - The Centers for Disease Control and Prevention recommends a two-dose series of measles-containing vaccines, with the first dose administered at 12-15 months and the second dose at 4-6 years of age. Most children receive their first dose of a measles-containing vaccine between the ages of 12 and 23 months; approximately 85 percent of children receive it by 19 months of age. The study found that receiving the first dose by 15 months provides a benefit to children.

"We found that the magnitude of increased risk of fever and seizures following immunization with measles-containing vaccines during the second year of life depends on age," said Ali Rowhani-Rahbar, MD, MPH, PhD, lead author of the study. "While measles-containing vaccines administered at 12-15 months of age are associated with a small risk of fever and seizures following immunization, delayed administration at 16-23 months of age results in a greater risk of those adverse events."

Previous studies have shown that these vaccines administered to children 12-23 months of age are associated with an increased risk of febrile seizures one to two weeks following immunization. This is the period of time during which the vaccine virus replication is at its peak, potentially causing fever. The resulting fever may cause some children to experience a seizure.

"Kaiser Permanente's guidelines for measles-containing vaccines are in line with the CDC's recommendations," said Matthew F. Daley, MD, a pediatrician and senior investigator at Kaiser Permanente Colorado's Institute for Health Research. "This study's findings reinforce for parents that these vaccines are safer when children receive them at 12 to 15 months of age."

While febrile seizures are the most common neurologic adverse events following immunization with measles-containing vaccines, senior author and co-director of the Vaccine Study Center Nicola Klein, MD, PhD, notes that the risk is small regardless of age: "Medically attended febrile seizures following immunization with measles-containing vaccines are not common events. Concerned parents should understand that the risk for febrile seizures after any measles-containing vaccine is low - less than one febrile seizure per 1,000 injections."

Using data from the Vaccine Safety Datalink, a collaborative effort of the Centers for Disease Control and Prevention and nine managed care organizations, Kaiser Permanente researchers evaluated the potential modifying effect of age on the risk of fever and seizures following immunization with different combinations of vaccines: 1) any measles-containing vaccines; and 2) the measles, mumps, rubella and varicella vaccine (MMRV) compared with the measles, mumps and rubella vaccine (MMR) administered with or without a separate varicella vaccine (MMR+V). Researchers evaluated the records of 840,348 children 12-23 months of age who had received a measles-containing vaccine between January 2001 and December 2011.

Following immunization with any measles-containing vaccine, the incidence of fever and seizures during days 7-10 was significantly greater than any other time during the 42-day post-immunization interval in all age groups. The patterns for the incidence of fever and seizures were different during the period of observation.

The incidence of fever steadily declined from 12-13 to 19-23 months of age, while the incidence of seizures was highest among children 16-18 months of age.

The relative risk of fever and seizures during the 7- to 10-day risk interval was significantly greater among children 16-23 months of age than among children 12-15 months of age.

The risk of seizures attributable to the vaccine during the 7- to 10-day risk interval was significantly greater among children 16-23 months of age than among children 12-15 months of age.

Consistent with findings in previous studies, the incidence of fever and seizures during the 7-10 days following immunization with MMRV was significantly greater than that following immunization with MMR+V.

Kaiser Permanente operates the largest private patient-centered electronically enabled health system in the world, which allows it to deliver excellent care and conduct transformational health research. The organization's electronic health record system, Kaiser Permanente HealthConnect®, securely connects 9.1 million patients to 1,700 physicians in 611 medical offices and 37 hospitals. Kaiser Permanente's research scientists are able to conduct studies using these clinically rich, longitudinal data sources in order to shape the future of health and care delivery for Kaiser Permanente's members, the communities in which it operates, the nation, and the world.

Additional authors on the study include Bruce Fireman, MA, Edwin Lewis, MPH, and Roger Baxter, MD, of the Kaiser Permanente Vaccine Study Center, Oakland, California; James Nordin, MD, MPH, of HealthPartners Institute for Education

and Research, Minneapolis; Allison Naleway, PhD, of Kaiser Permanente Center for Health Research, Portland, Oregon; Steven J. Jacobsen, MD, PhD, of Kaiser Permanente Department of Research and Evaluation, Pasadena, California; Lisa A. Jackson, MD, MPH, of Group Health Research Institute, Seattle; Alison Tse, ScD, of Department of Population Medicine, Harvard Pilgrim Health Care Institute, Boston; Edward A. Belongia, MD, of Marshfield Clinic Research Foundation, Marshfield, Wisconsin; Simon J. Hambidge, MD, PhD, of Kaiser Permanente Institute for Health Research, Denver; and Eric Weintraub, MPH, of the Immunization Safety Office, Centers for Disease Control and Prevention, Atlanta.

http://www.eurekalert.org/pub_releases/2013-10/gumc-cdf101013.php

Compound derived from vegetables shields rodents from lethal radiation doses

Georgetown University Medical Center researchers say a compound derived from cruciferous vegetable such as cabbage, cauliflower and broccoli protected rats and mice from lethal doses of radiation.

WASHINGTON - Their study, published today in the Proceedings of the National Academy of Sciences (PNAS) suggests the compound, already shown to be safe for humans, may protect normal tissues during radiation therapy for cancer treatment and prevent or mitigate sickness caused by radiation exposure.

The compound, known as DIM (3,3'-diindolylmethane), previously has been found to have cancer preventive properties. "DIM has been studied as a cancer prevention agent for years, but this is the first indication that DIM can also act as a radiation protector," says the study's corresponding author, Eliot Rosen, MD, PhD, of Georgetown Lombardi Comprehensive Cancer Center.

For the study, the researchers irradiated rats with lethal doses of gamma ray radiation. The animals were then treated with a daily injection of DIM for two weeks, starting 10 minutes after the radiation exposure.

The result was stunning, says Rosen, a professor of oncology, biochemistry and cell & molecular biology, and radiation medicine. "All of the untreated rats died, but well over half of the DIM-treated animals remained alive 30 days after the radiation exposure." Rosen adds that DIM also provided protection whether the first injection was administered 24 hours before or up to 24 hours after radiation exposure.

"We also showed that DIM protects the survival of lethally irradiated mice," Rosen says. In addition, irradiated mice treated with DIM had less reduction in red blood cells, white blood cells and platelets - side effects often seen in patients undergoing radiation treatment for cancer.

Rosen says this study points to two potential uses of the compound. "DIM could protect normal tissues in patients receiving radiation therapy for cancer, but could also protect individuals from the lethal consequences of a nuclear disaster." Rosen and study co-authors Saijun Fan, PhD, and Milton Brown, MD, PhD, are co-inventors on a patent application that has been filed by Georgetown University related to the usage of DIM and DIM-related compounds as radioprotectors.

This work was supported by U.S. Public Health Service Grants (CA104546 and CA150646), a grant from the Center for Drug Discovery at Georgetown University, and other Georgetown funding.

http://www.sciencedaily.com/releases/2013/10/131014102357.htm

Pandoravirus: Missing Link Discovered Between Viruses and Cells

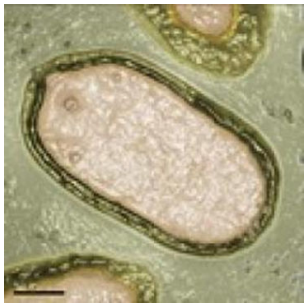
With the discovery of Mimivirus ten years ago and, more recently, Megavirus chilensis[1], researchers thought they had reached the farthest corners of the viral world in terms of size and genetic complexity.

With a diameter in the region of a micrometer and a genome incorporating more than 1,100 genes, these giant viruses, which infect amoebas of the *Acanthamoeba* genus, had already largely encroached on areas previously thought to be the exclusive domain of bacteria. For the sake of comparison, common viruses such as the influenza or AIDS viruses only contain around ten genes each.

In the article published in *Science*, the researchers announced they had discovered two new giant viruses:

***Pandoravirus salinus*, on the coast of Chile;**

***Pandoravirus dulcis*, in a freshwater pond in Melbourne, Australia.**



0.2 µm Pandoravirus salinus observed under the electron microscope. **(Credit: © IGS CNRS-AMU)**

Detailed analysis has shown that these first two Pandoraviruses have virtually nothing in common with previously characterized giant viruses. What's more, only a very small percentage (6%) of proteins encoded by *Pandoravirus salinus* are similar to those already identified in other viruses or cellular organisms. With a genome of this size, *Pandoravirus salinus* has just demonstrated that viruses can be more complex than some eukaryotic cells[2]. Another unusual feature of Pandoraviruses is that they have no gene allowing them to build a protein like the capsid protein, which is the basic building block of traditional viruses.

Despite all these novel properties, Pandoraviruses display the essential characteristics of other viruses in that they contain no ribosome, produce no energy and do not divide.

This groundbreaking research included an analysis of the *Pandoravirus salinus* proteome, which proved that the proteins making it up are consistent with those predicted by the virus' genome sequence. Pandoraviruses thus use the universal genetic code shared by all living organisms on the planet.
This shows just how much more there is to learn regarding microscopic biodiversity as soon as new environments are considered. The simultaneous discovery of two specimens of this new virus family in sediments located 15,000 km apart indicates that Pandoraviruses, which were completely unknown until now, are very likely not rare.
It definitively bridges the gap between viruses and cells - a gap that was proclaimed as dogma at the very outset of modern virology back in the 1950s.
It also suggests that cell life could have emerged with a far greater variety of pre-cellular forms than those conventionally considered, as the new giant virus has almost no equivalent among the three recognized domains of cellular life, namely eukaryota (or eukaryotes), eubacteria, and archaea.

Notes

[1] Arslan D, Legendre M, Seltzer V, Abergel C, Claverie JM (2011) "Distant Mimivirus relative with a larger genome highlights the fundamental features of Megaviridae." PNAS. 108:17486-91

[2] Parasitic microsporidia of the Encephalitozoon genus in particular.

http://www.bbc.co.uk/news/uk-scotland-edinburgh-east-fife-24525501

Seeing in 3D 'possible with one eye', St Andrews study suggests

The effect of "vivid 3D vision" can be experienced with just one eye, a study has suggested.

Researchers at St Andrews University said a method using a small circular hole could have wide implications for 3D technology. The study, published in Psychological Science, also has implications for people who have just one eye or difficulties with double-eye vision. The method was said to create 3D similar to effects used in film-making. Researchers said that current thinking was based on the need for two visual images - one from each eye - to be combined in the visual cortex, creating a sense of depth.

New hypothesis

But Dr Dhanraj Vishwanath, a psychologist at the university, believes both eyes are not necessary for this "3D experience". Dr Vishwanath said: "We have demonstrated experimentally, for the first time, that the same 'special way' in which depth is experienced in 3D movies can also be experienced by looking at a normal picture with one eye viewing through a small aperture (circular hole). "While this effect has been known for a long time, it is usually dismissed. "Now we have shown that it is in fact real, and the perceptual results are exactly like stereoscopic 3D, the kind seen in 3D movies. "Based on this finding, we have provided a new hypothesis of what the actual cause of the 3D experience might be."
The university said the 1838 invention of the stereoscope - the technology behind 3D film-making - brought with it the assumption two eyes were necessary for 3D vision.
Dr Vishwanath said: "This work has significant implications for people who don't have normal binocular vision. "First it could help them experience what it means to see in 3D. Second, it could encourage them to seek therapy to try to regain two-eye 3D vision (which produces the strongest 3D effect in everyday life) once they can see first-hand what 'seeing in 3D' is really like." Dr Vishwanath and his colleagues are now testing the method with a large group of strabismics, people with misaligned eyes. He said that nearly 15% of the population, including Hollywood actor Johnny Depp, may have some form of misalignment.
The psychologist also believes his theory suggests a 3D experience could be induced simply by increasing resolution, using ultra-high definition (4K) televisions. Seeing in 3D with just one eye: Stereopsis without binocular vision is published by Psychological Science. Further research is due to be published later this year.

http://phys.org/news/2013-10-modern-relatives-otzi-alive-austria.html

Study finds modern relatives of Otzi alive and well in Austria

A team of researchers from Innsbruck Medical University has found 19 modern humans living in Austria with the same genetic defect as the ice-man Ötzi, the APA News Agency is reporting.

Phys.org - The ice-man was found by German tourists and is believed to have lived approximately 5,300 years ago. Ötzi, named for the region in the Alps where his remains were discovered, has enjoyed worldwide fame since his discovery, owing to his well preserved remains. Over the past twenty years, the ice-man has been studied by various scientists looking for clues that might reveal the nature of the world he inhabited. In addition to his body, researchers also found artifacts that are believed to have belonged to him - the cause of his death, ranging from an arrow wound, to a blow on the head has also been the subject of much research and conjecture. In this latest effort, the researchers were looking to determine if anyone alive today can be tied genetically to the ancient ice-man.

To find out, the researchers asked males of all ages living in the Austrian state of Tyrol, to donate blood samples for DNA testing. Subsequent analysis revealed that 19 of 3,700 volunteers had the same genetic mutation as the ice-man, indicating that they were related to the same ancestors as Ötzi—no mention was made regarding whether anyone alive today could actually be one of his descendants, however. The research team has already reached out to partners in Switzerland and Italy to organize a similar study to determine if there are matches in other nearby locales. Those men identified as a match in the original study have not been told of their connection to the ice-man.

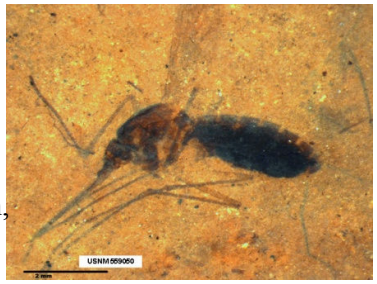
Study of the ice-man has revealed that he had Lyme disease, that he was approximately 46 years old at the time of his death, was approximately five foot two, was likely from Sardinia originally, and had a predisposition to heart disease. It's still not known what he was doing in the Alps, or why he was killed, likely from falling after being shot in the collarbone by an arrow. His stomach contents indicated he ate a diet heavy in meat and because he was carrying a bow and arrows, researchers have speculated that he was likely either a hunter or a soldier. His remains have been kept in cold storage to prevent decay since his removal from his final resting place.

http://www.livescience.com/40402-fossil-mosquito-blood-meal.html

Rare Blood-Engorged Mosquito Fossil Found

About 46 million years ago, a mosquito sunk its proboscis into some animal, perhaps a bird or a mammal, and filled up on a meal of blood.

By Douglas Main, Staff Writer | October 14, 2013 03:00pm ET



The fossil of a blood-engorged mosquito was found in northwestern Montana. **Credit: Smithsonian Institution**

Then its luck turned for the worse, as it fell into a lake and sunk to the bottom. Normally this wouldn't be newsworthy, and nobody would likely know or care about a long-dead insect in what is now northwest Montana. But somehow, the mosquito didn't immediately decompose - a fortuitous turn of events for modern-day scientists - and became fossilized over the course of many years, said Dale Greenwalt, a researcher at the National Museum of Natural History in Washington, D.C. Greenwalt discovered the mosquito fossil after it was given to the museum as a gift, and he immediately realized the specimen's rarity.

It is, in fact, the only blood-engorged mosquito fossil found, Greenwalt told LiveScience. The fossil is even stranger because it comes from shale, a type of rock formed from sediments deposited at the bottom of bodies of water, as opposed to amber, the age-old remains of dried tree sap, in which insect remnants are generally better preserved.

http://www.sciencedaily.com/releases/2013/10/131013163316.htm

Study Identifies Which Bipolar Patients Will Respond to Ketamine Therapy for Depression, Pain

Researchers have discovered how to determine which bipolar patients will benefit from Ketamine, a treatment commonly used for depression and pain relief, according to a study presented at the ANESTHESIOLOGY™ 2013 annual meeting.

Two-thirds of patients benefit from Ketamine and using a blood test, researchers can predict which patients will respond favorably.

"Doctors know that very small doses of Ketamine help relieve depression and pain," said Michael Goldberg, M.D., professor and chairman of anesthesiology, and associate dean for education at Cooper Medical School of Rowan University and chief of the Department of Anesthesiology for Cooper University Health Care, Camden, N.J. "But one in three patients do not respond to this treatment. This research will help as we seek ways to provide these patients relief."

Researchers identified the compound that Ketamine breaks down into, which they named HNK (2S, 6S hydroxynorketamine). Additionally, researchers discovered the pattern or 'fingerprint' in the fatty acids of the blood that indicates which patients will respond to HNK.

In the study, 22 patients with bipolar disorder were given intravenous doses of Ketamine. Blood was collected from each patient. Responders and non-responders were identified using a standardized depression rating scale. A positive response was defined as a 50 percent or greater improvement. Additionally, researchers examined metabolic patterns in blood samples. Researchers discovered there was a difference in how responders and nonresponders metabolized fatty acids, based on the variability in levels of 18 different metabolites.

"These are significant discoveries which should eventually help in the treatment of patients suffering from depression and chronic pain," said Irving Wainer, Ph.D., senior investigator with the Intramural Research

Program at the National Institute on Aging, Baltimore. "The next step is to look for the genetic or environmental factors that determine whether a person develops the metabolic pattern that responds to the treatment. We hope this leads to the development of customized or individualized treatment for each patient."

The above story is based on materials provided by American Society of Anesthesiologists (ASA), via Newswise.

http://phys.org/news/2013-10-evidence-lightning.html

New evidence on lightning strikes: Mountains a lot less stable than we think

New evidence on lightning strikes

Oct 15, 2013 by Kanina Foss

Phys.org - Lightning strikes causing rocks to explode have for the first time been shown to play a huge role in shaping mountain landscapes in southern Africa, debunking previous assumptions that angular rock formations were necessarily caused by cold temperatures, and proving that mountains are a lot less stable than we think.

In a world where mountains are crucial to food security and water supply, this has vast implications, especially in the context of climate change. Professors Jasper Knight and Stefan Grab from the School of Geography, Archaeology and Environmental Studies at Wits University used a compass to prove – for the first time ever – that lightning is responsible for some of the angular rock formations in the Drakensburg.

"A compass needle always points to magnetic north. But when you pass a compass over a land's surface, if the minerals in the rock have a strong enough magnetic field, the compass will read the magnetic field of the rock, which corresponds to when it was formed. In the Drakensburg, there are a lot of basalt rocks which contain a lot of magnetic minerals, so they've got a very strong magnetic signal," says Knight.

If you pass a compass over an area where a lightning strike occurred, the needle will suddenly swing through 360 degrees. "The energy of the lightning hitting the land's surface can, for a short time, partially melt the rock and when the rock cools down again, it takes on the magnetic imprint of today's magnetic field, not the magnetic field of millions of years ago when the rock was originally formed," says Knight.

Because of the movement of continents, magnetic north for the newly formed rock will be different from that of the older rock around it. "You have two superimposed geomagnetic signatures. It's a very useful indicator for identifying the precise location of where the lightning struck."

Knight and Grab mapped out the distribution of lightning strikes in the Drakensburg and discovered that lightning significantly controls the evolution of the mountain landscapes because it helps to shape the summit areas – the highest areas – with this blasting effect.

New evidence on lightning strikes

Previously, angular debris was assumed to have been created by changes typical of cold, periglacial environments, such as fracturing due to frost. Water enters cracks in rocks and when it freezes, it expands, causing the rocks to split apart.

Knight and Grab are challenging centuries old assumptions about what causes mountains to change shape. "Many people have considered mountains to be pretty passive agents, just sitting there to be affected by cold climates over these long periods of time. "This evidence suggests that that is completely wrong. African mountain landscapes sometimes evolve very quickly and very dramatically over short periods of time. These are actually very sensitive environments and we need to know more about them." It is also useful to try and quantify how much debris is moved by these blasts which can cause boulders weighing several tonnes to move tens of metres.

"We can identify where the angular, broken up material has come from, trace it back to source, and determine the direction and extent to which the debris has been blasted on either side. Of course we know from the South African Weather Service how many strikes hit the land's surface, so we can estimate how much volume is moved per square kilometre per year on average," says Knight.

The stability of the land's surface has important implications for the people living in the valleys below the mountain. "If we have lots of debris being generated it's going to flow down slope and this is associated with hazards such as landslides," said Knight.

Mountains are also inextricably linked to food security and water supply. In Lesotho, a country crucial to South Africa's water supply, food shortages are leading to overgrazing, exposing the rock surface and making mountain landscapes even more vulnerable to weathering by lightning and other processes.

Knight hopes that this new research will help to put in place monitoring and mitigation to try and counteract some of the effects. "The more we increase our understanding, the more we are able to do something about it."

A research paper to be published in the scientific journal, Geomorphology, is available here.

More information: Jasper Knight, Stefan W. Grab, Lightning as a geomorphic agent on mountain summits: Evidence from southern Africa, Geomorphology, dx.doi.org/10.1016/j.geomorph.2013.07.029, www.sciencedirect.com/science/article/pii/S0169555X13003929

http://www.eurekalert.org/pub_releases/2013-10/mc-mcs101513.php

Mayo Clinic study: Teachers more likely to have progressive speech and language disorders

The research, recently published in the American Journal of Alzheimer's Disease & Other Dementias, found that people with speech and language disorders are about 3.5 times more likely to be teachers than patients with Alzheimer's dementia.

ROCHESTER, Minn. - Speech and language disorders are typically characterized by people losing their ability to communicate - they can't find words to use in sentences, or they'll speak around a word. They may also have trouble producing the correct sounds and articulating properly. Speech and language disorders are not the same as Alzheimer's dementia, which is characterized by the loss of memory. Progressive speech and language disorders are degenerative and ultimately lead to death anywhere from 8-10 years after diagnosis.

In the study, researchers looked at a group of about 100 patients with speech and language disorders and noticed many of them were teachers. For a control, they compared them to a group of more than 400 Alzheimer's patients from the Mayo Clinic Study on Aging. Teachers were about 3.5 times more likely to develop a speech and language disorder than Alzheimer's disease. For other occupations, there was no difference between the speech and language disorders group and the Alzheimer's group.

When compared to the 2008 U.S. census, the speech and language cohort had a higher proportion of teachers, but it was consistent with the differences observed with the Alzheimer's dementia group.

This study has important implications for early detection of progressive speech and language disorders, says Mayo Clinic neurologist, Keith Josephs, M.D., who is the senior author of the study. A large cohort study focusing on teachers may improve power to identify the risk factors for these disorders.

"Teachers are in daily communication," says Dr. Josephs. "It's a demanding occupation, and teachers may be more sensitive to the development of speech and language impairments."

http://www.eurekalert.org/pub_releases/2013-10/uoc-tma101513.php

The musical ages of modern man: How our taste in music changes over a lifetime

Music stays important to us as we get older, but the music we like adapts to the particular challenge we face

The explosion in music consumption over the last century has made 'what you listen to' an important personality construct – as well as the root of many social and cultural tribes – and, for many people, their self-perception is closely associated with musical preference. We would perhaps be reluctant to admit that our taste in music alters - softens even - as we get older.

Now, a new study suggests that - while our engagement with it may decline - music stays important to us as we get older, but the music we like adapts to the particular 'life challenges' we face at different stages of our lives. It would seem that, unless you die before you get old, your taste in music will probably change to meet social and psychological needs.

One theory put forward by researchers, based on the study, is that we come to music to experiment with identity and define ourselves, and then use it as a social vehicle to establish our group and find a mate, and later as a more solitary expression of our intellect, status and greater emotional understanding.

Researchers say the study is the first to "comprehensively document" the ways people engage with music "from adolescence to middle age". The study is published in the Journal of Personality and Social Psychology.

Using data gathered from more than a quarter of a million people over a ten year period, researchers divided musical genres into five broad, "empirically derived" categories they call the MUSIC model - mellow, unpretentious, sophisticated, intense, contemporary - and plotted the patterns of preference across age-groups. These five categories incorporate multiple genres that share common musical and psychological traits - such as loudness and complexity.

"The project started with a common conception that musical taste does not evolve after young adulthood. Most academic research to date supported this claim, but - based on other areas of psychological research and our own experiences - we were not convinced this was the case," said Arielle Bonneville-Roussy from Cambridge's Department of Psychology, who led the study.

The study found that, unsurprisingly, the first great musical age is adolescence - defined by a short, sharp burst of 'intense' and the start of a steady climb of 'contemporary'. 'Intense' music - such as punk and metal - peaks in adolescence and declines in early adulthood, while 'contemporary' music - such as pop and rap - begins a rise that plateaus until early middle age. "Teenage years are often dominated by the need to establish identity, and music is a cheap, effective way to do this," said Dr Jason Rentfrow, senior researcher on the study.

"Adolescents' quest for independence often takes the shape of a juxtaposed stance to the perceived 'status quo', that of parents and the establishment. 'Intense' music, seen as aggressive, tense and characterised by loud,

distorted sounds has the rebellious connotations that allow adolescents to stake a claim for the autonomy that is one of this period's key 'life challenges'."
As 'intense' gives way to the rising tide of 'contemporary' and introduction of 'mellow' – such as electronic and R & B – in early adulthood, the next musical age emerges. These two "preference dimensions" are considered "romantic, emotionally positive and danceable," write the researchers.
"Once people overcome the need for autonomy, the next 'life challenge' concerns finding love and being loved – people who appreciate this 'you' that has emerged," said Rentfrow.
"What we took away from the results is that these forms of music reinforce the desire for intimacy and complement settings where people come together with the goal of establishing close relationships – parties, bars, clubs and so on.
"Whereas the first musical age is about asserting independence, the next appears to be more about gaining acceptance from others."
As we settle down and middle age begins to creep in, the last musical age, as identified by the researchers, is dominated by 'sophisticated' – such as jazz and classical – and 'unpretentious' – such as country, folk and blues. Researchers write that both these dimensions are seen as "positive and relaxing" - with 'sophisticated' indicating the complex aesthetic of high culture that could be linked to social status and perceived intellect, while 'unpretentious' echoes sentiments of family, love and loss – emotionally direct music that speaks to the experiences most will have had by this life stage.
"As we settle into ourselves and acquire more resources to express ourselves – career, home, family, car – music remains an extension of this, and at this stage there are aspects of wanting to promote social status, intellect and wealth that play into the increased gravitation towards 'sophisticated' music," said Rentfrow, "as social standing is seen as a key 'life challenge' to be achieved by this point".
"At the same time, for many this life stage is frequently exhausted by work and family, and there is a requirement for relaxing, emotive music for those rare down times that reflects the other major 'life challenge' of this stage – that of nurturing a family and maintaining long-term relationships, perhaps the hardest of all."
Adds Bonneville-Roussy: "Due to our very large sample size, gathered from online forms and social media channels, we were able to find very robust age trends in musical taste. I find it fascinating to see how seemingly trivial behaviour such as music listening relates to so many psychological aspects, such as personality and age."

http://www.livescience.com/40440-your-liver-may-be-eating-your-brain.html

Your Liver May Be 'Eating' Your Brain

A protein called PPARalpha is needed by both the liver and the brain, a new study suggests.

By Christopher Wanjek, Columnist | October 15, 2013 02:52pm ET

Your liver could be "eating" your brain, new research suggests.
People with extra abdominal fat are three times more likely than lean individuals to develop memory loss and dementia later in life, and now scientists say they may know why. It seems that the liver and the hippocampus (the memory center in the brain), share a craving for a certain protein called PPARalpha. The liver uses PPARalpha to burn belly fat; the hippocampus uses PPARalpha to process memory.
In people with a large amount of belly fat, the liver needs to work overtime to metabolize the fat, and uses up all the PPARalpha - first depleting local stores and then raiding the rest of the body, including the brain, according to the new study. The process essentially starves the hippocampus of PPARalpha, thus hindering memory and learning, researchers at Rush University Medical Center in Chicago wrote in the study, published in the current edition of the journal Cell Reports.
Other news reports were incorrect in stating that the researchers established that obese individuals were 3.6 times more likely than lean individuals to develop dementia. That finding dates back to a 2008 study by researchers at the Kaiser Permanente Division of Research in Oakland, Calif.
In another study, described in a 2010 article in the Annals of Neurology, researchers at Boston University School of Medicine found that the greater the amount of belly fat, the greater the brain shrinkage in old age.
The surprising discovery in the new study is that the hippocampus uses PPARalpha to process memory and learning, and that this is a possible reason for the connection between belly fat and dementia and/or memory loss.
Rush University researchers, led by neurological sciences professor Kalipada Pahan, raised mice that were deficient in PPARalpha. Some mice had normal PPARalpha in the liver but depleted PPARalpha in the brain, and had poor memory and learning abilities. Others had normal PPARalpha in the brain but not the liver, and showed normal memory, as expected.
When the researchers injected PPARalpha into the hippocampus of PPARalpha-deficient mice, their learning and memory improved, Pahan said.

"Further research must be conducted to see how we could potentially maintain normal PPARalpha in the [human] brain in order to be resistant to memory loss," Pahan told LiveScience. PPARalpha thus provides a new avenue to explore in searching for a treatment or cure for Alzheimer's disease, dementia, and related memory-loss and cognition problems, Pahan said. Losing your belly fat won't hurt, either.

http://bit.ly/GWcjIh

The Nuclear Odyssey of Naoto Kan, Japan's Prime Minister during Fukushima

Having led Japan through the 2011 nuclear crisis, the elder statesman is now campaigning for a world without nuclear power

By David Biello | Wednesday, October 16, 2013 | 33

On March 10, 2011, Prime Minister Naoto Kan felt assured that nuclear power was safe and vital for Japan. By the evening of the next day, following the massive Tohoku earthquake, the ensuing tsunami and the beginnings of the crisis at the Fukushima Daiichi nuclear power plant, he had changed his thinking "180 degrees."

Kan could not help but wondering how much worse the Fukushima meltdowns might get on the dark nights spent in his office after March 11, 2011. "What was going through my mind at the time?" Kan said through a translator during a public event at the 92nd Street YMCA in New York City on October 8. "How much worse is this going to get, and how can we stop this from getting even worse?"

Kan commissioned a report for the worst-case scenario from the Japan Atomic Energy Commission, which confirmed his worst fears: a potential evacuation area reaching as far as 250 kilometers from the stricken power plant—a zone of exclusion that would have reached all the way to Tokyo and affected roughly 50 million people. The potential for disaster was so great because the Fukushima area houses a total of 10 reactors and 11 pools that store used nuclear fuel. By March 15, three of those reactors were experiencing at least partial meltdowns, and four, thanks to a spent-fuel pool that also lost water cooling of the still-hot rods, had suffered hydrogen explosions.

Gruff and dark-haired, Kan is a circumspect man, with a history of admitting mistakes and showing impatience with those who do not. In 1996, as Japan's Minister of Health, Labor and Welfare, he apologized for the government's responsibility in allowing blood bearing the human immunodeficiency virus (HIV) to spread among hospitals in years past. In 2010, as prime minister from the Democratic Party of Japan, he apologized to South Korea for Japan's annexation of that country a century earlier. Now the one-time nuclear supporter is campaigning for an end to power from fission. "There is no other disaster that would affect 50 million people—maybe a war," Kan observed. "There is only one way to eliminate such accidents, which is to get rid of all nuclear power plants."

The earthquake and tsunami killed more than 15,000 people, whereas the multiple meltdowns at Fukushima have not caused any fatalities to date and are "unlikely" to cause any detectable health effects, such as increased cancers, according to the United Nations Scientific Committee on the Effects of Atomic Radiation. But even today, more than two and a half years after the earthquake, the nuclear disaster is ongoing. Water contaminated with radioactive particles from the meltdowns continues to reach the Pacific Ocean, and radiation levels at the stricken power plant recently spiked. Typhoons, earthquakes and other natural disasters continue to threaten further disasters at the site and a total teardown may take decades. "The cause of this catastrophe is, of course, the earthquake and the tsunami but, additionally, the fact that we were not prepared," Kan said. "We did not anticipate such a huge natural disaster could happen." He also noted that the information supplied to him by the nuclear power industry in the aftermath of the meltdowns proved false.

In Japan, where Kan is currently a leader of his party's effort to promote alternative energy sources, his antinuclear campaign enjoys wide popular support, and none of the country's 50 nuclear reactors are currently operating. But the current prime minister, Shinzo Abe of the Liberal Democratic Party (LDP), supports restarting the nuclear plants, influenced in part by the tremendous cost of importing natural gas and coal to generate the electricity once produced by fission. In addition, as a result of the nuclear shutdown, Japan's emissions of greenhouse gas pollution rose nearly 6 percent in 2012, according to the International Energy Agency, after increasing 4 percent in 2011, according to Japan's own figures. "Now we are at the point where the battle will be great, and it is going to determine the future of Japan," Kan said. "The best and biggest way of achieving a different energy reliance and independence from fossil fuels is efficiency, reducing energy use."

Japan has already shown that it can cut back on energy consumption via what has been dubbed setsuden, or power savings, such as reducing air conditioning demand in summer by wearing lighter clothes rather than suits. Such setsuden efforts in summer 2011, after the Fukushima meltdowns, helped reduce peak electricity demand in the Tokyo region by nearly 20 percent. And Kan hopes that, within a decade or so, renewable power sources can replace nuclear completely. He has personally remodeled his home, installing better windows and more insulation to cut down on energy use as well as a photovoltaic system that allows him to achieve "energy self-

sufficiency." He hopes more Japanese will do the same; his last act before resigning as prime minister in August 2011 was to ensure the passage of a guaranteed higher price for electricity generated from the sun.
Kan is not the only elder statesman to join the chorus of opposition to nuclear power in Japan. Former LDP Prime Minister Junichiro Koizumi, the one-time mentor of the current prime minister, Abe, reiterated his disapproval of nuclear power in September. The Fukushima disaster helped bring about his change of mind, as did a recent visit to Finland's long-term waste storage facility, which convinced him that such a facility could never be built in Japan and that his country's unstable geology made it ill-suited for nuclear reactors. Japan already has the Monju fast-breeder reactor for recycling used nuclear fuel instead of building such permanent storage, but the facility has been plagued by fires, shutdowns and other delays.
The Fukushima disaster has already affected the course of nuclear power worldwide, slowing the growth of a technology championed as a solution to large-scale electricity generation with much less greenhouse gas pollution than the currently dominant coal-fired power plant, although other factors, such as the increasing supply of cheap natural gas, also have diminished enthusiasm. "Severe accidents can and will happen, maybe not tomorrow or in 10 years or even in 30 years, but they will happen," Gregory Jaczko, who chaired the U.S. Nuclear Regulatory Commission during the disaster and until July 2012, said at the 92nd Street Y event. "For nuclear power to be considered safe, nuclear power plants should not produce accidents like this."
Many Fukushima residents have been barred from their homes, perhaps permanently, and the disaster has hurt the entire economy of Japan. "There is nothing more challenging than to look into the eyes of a grandfather who no longer sees his children because they had to move on to find jobs," Jaczko told the audience, referring to a man he met during a visit to Japan in 2011. "That is the tragedy and human toll that the Fukushima disaster has enacted on nearly 100,000 people in Japan. You cannot put those impacts in dollar terms, but they are very real."
New designs that make reactors less susceptible to human error and hubris, or an industry shift toward smaller nuclear plants or alternative reactor technologies might allay some safety concerns. But Kan, for one, is unconvinced. "If we had a situation where by not utilizing nuclear power at all people starve to death or something, that's one thing," Kan said. But he noted that already a new energy prospect is visible off the Fukushima coast, where a floating wind turbine is being tested. It has been dubbed "Fukushima mirai," which means “Fukushima future” in Japanese. "In Japan,” Kan said, “we see that even without nuclear power plants we can actually supply energy to meet our demands."

http://www.eurekalert.org/pub_releases/2013-10/pu-wpe101613.php

Without plants, Earth would cook under billions of tons of additional carbon

Enhanced growth of Earth's leafy greens during the 20th century has significantly slowed the planet's transition to being red-hot, according to the first study to specify the extent to which plants have prevented climate change since pre-industrial times.

Researchers based at Princeton University found that land ecosystems have kept the planet cooler by absorbing billions of tons of carbon, especially during the past 60 years.
The planet's land-based carbon "sink" — or carbon-storage capacity — has kept 186 billion to 192 billion tons of carbon out of the atmosphere since the mid-20th century, the researchers report in the Proceedings of the National Academy of Sciences. From the 1860s to the 1950s, land use by humans was a substantial source of the carbon entering the atmosphere because of deforestation and logging. After the 1950s, however, humans began to use land differently, such as by restoring forests and adopting agriculture that, while larger scale, is higher yield. At the same time, industries and automobiles continued to steadily emit carbon dioxide that contributed to a botanical boom. Although a greenhouse gas and pollutant, carbon dioxide also is a plant nutrient.
Had Earth's terrestrial ecosystems remained a carbon source they would have instead generated 65 billion to 82 billion tons of carbon in addition to the carbon that it would not have absorbed, the researchers found. That means a total of 251 billion to 274 billion additional tons of carbon would currently be in the atmosphere. That much carbon would have pushed the atmosphere's current carbon dioxide concentration to 485 parts-per-million (ppm), the researchers report — well past the scientifically accepted threshold of 450 (ppm) at which the Earth's climate could drastically and irreversibly change. The current concentration is 400 ppm.
Those "carbon savings" amount to a current average global temperature that is cooler by one-third of a degree Celsius (or a half-degree Fahrenheit), which would have been a sizeable jump, the researchers report. The planet has warmed by only 0.74 degrees Celsius (1.3 degrees Fahrenheit) since the early 1900s, and the point at which scientists calculate the global temperature would be dangerously high is a mere 2 degrees Celsius (3.6 degrees Fahrenheit) more than pre-industrial levels.

The study is the most comprehensive look at the historical role of terrestrial ecosystems in controlling atmospheric carbon, explained first author Elena Shevliakova, a senior climate modeler in Princeton's Department of Ecology and Evolutionary Biology. Previous research has focused on how plants might offset carbon in the future, but overlooked the importance of increased vegetation uptake in the past, she said.
"People always say we know carbon sinks are important for the climate," Shevliakova said. "We actually for the first time have a number and we can say what that sink means for us now in terms of carbon savings."
"Changes in carbon dioxide emissions from land-use activities need to be carefully considered. Until recently, most studies would just take fossil-fuel emissions and land-use emissions from simple models, plug them in and not consider how managed lands such as recovering forests take up carbon," she said. "It's not just climate — it's people. On land, people are major drivers of changes in land carbon. They're not just taking carbon out of the land, they're actually changing the land's capacity to take up carbon."
Scott Saleska, an associate professor of ecology and evolutionary biology at the University of Arizona who studies interactions between vegetation and climate, said that the researchers provide a potentially compelling argument for continued forest restoration and preservation by specifying the "climate impact" of vegetation. Saleska is familiar with the research but had no role in it.
"I think this does have implications for policies that try to value the carbon saved when you restore or preserve a forest," Saleska said. "This modeling approach could be used to state the complete 'climate impact' of preserving large forested areas, whereas most current approaches just account for the 'carbon impact.' Work like this could help forest-preservation programs more accurately consider the climate impacts of policy measures related to forest preservation."
Although the researchers saw a strong historical influence of carbon fertilization in carbon absorption, that exchange does have its limits, Saleska said. If carbon dioxide levels in the atmosphere continue rising, more vegetation would be needed to maintain the size of the carbon sink Shevliakova and her colleagues reported.
"There is surely some limit to how long increasing carbon dioxide can continue to promote plant growth that absorbs carbon dioxide," Saleska said. "Carbon dioxide is food for plants, and putting more food out there stimulates them to 'eat' more. However, just like humans, eventually they get full and putting more food out doesn't stimulate more eating."
The researchers used the comprehensive Earth System Model (ESM2G), a climate-carbon cycle model developed by the National Oceanic and Atmospheric Administration's Geophysical Fluid and Dynamics Laboratory (GFDL), to simulate how carbon and climate interacted with vegetation, soil and marine ecosystems between 1861 and 2005. The GFDL model predicted changes in climate and in atmospheric concentrations of carbon dioxide based on fossil fuel emissions of carbon. Uniquely, the model also predicted emissions from land-use changes — such as deforestation, wood harvesting and forest regrowth — that occurred from 1700 to 2005.
"Unless you really understand what the land-use processes are it's very hard to say what the system will do as a whole," said Shevliakova, who worked with corresponding author Stephen Pacala, Princeton's Frederick D. Petrie Professor in Ecology and Evolutionary Biology; Sergey Malyshev, a professional specialist in ecology and evolutionary biology at Princeton; GFDL physical scientists Ronald Stouffer and John Krasting; and George Hurtt, a professor of geographical sciences at the University of Maryland.
"After the 1940s and 1950s, if you look at the land-use change trajectory, it's been slowed down in the expansion of agriculture and pastures," Shevliakova said. "When you go from extensive agriculture to intensive agriculture you industrialize the production of food, so people now use fertilizers instead of chopping down more forests. A decrease in global deforestation combined with enhanced vegetation growth caused by the rapid increase in carbon dioxide changed the land from a carbon source into a carbon sink."
For scientists, the model is a significant contribution to understanding the terrestrial carbon sink, Saleska said. Scientists only uncovered the land-based carbon sink about two decades ago, while models that can combine the effects of climate change and vegetation growth have only been around for a little more than 10 years, Saleska said. There is work to be done to refine climate models and the Princeton-led research opens up new possibilities while also lending confidence to future climate projections, Saleska said.
"A unique value of this study is that it simulates the past, for which, unlike the future, we have observations," Saleska said. "Past observations about climate and carbon dioxide provide a test about how good the model simulation was. If it's right about the past, we should have more confidence in its ability to predict the future."
The paper, "Historical warming reduced due to enhanced land carbon uptake," was published Oct. 15 in the Proceedings of the National Academy of Sciences. This work was supported by the National Oceanic and Atmospheric Administration (grant NA08OAR4320752), the U.S. Department of Agriculture (grant 2011-67003-30373), and the Princeton Carbon Mitigation Initiative.

http://www.bbc.co.uk/news/magazine-24532996

Calorie burner: How much better is standing up than sitting?

Studies have claimed major health benefits for standing for much of the day as opposed to sitting. The difference is marked, explains Michael Mosley.

Guess how many hours a day you spend sitting? Fewer than eight? More than 10? A recent survey found that many of us spend up to 12 hours a day sitting on our bottoms looking at computers or watching television. If you throw in the seven hours we spend sleeping then that adds up to a remarkable 19 hours a day being sedentary.

Sitting down as much as this is clearly bad for us and some studies suggest that those who sit all day live around two years less than those who are more active. Most of us are guilty of excess sitting. We sit at work, in the car and at home, moving only to shift from one seat to another. Even if you exercise on a regular basis that may not be enough. There is mounting evidence that exercise will not undo the damage done by prolonged sitting. Our technology has made us the most sedentary humans in history.

So why is sitting so damaging? One thing it does is change the way our bodies deal with sugar. When you eat, your body breaks down the food into glucose, which is then transported in the blood to other cells.

Glucose is an essential fuel but persistently high levels increase your risk of diabetes and heart disease. Your pancreas produces the hormone insulin to help get your glucose levels back down to normal, but how efficiently your body does that is affected by how physically active you are

We wanted to see what would happen if we took a group of people who normally spend their day sitting in an office and ask them to spend a few hours a day on their feet instead.

Standing while you are working may seem rather odd, but it is a practice with a long tradition. Winston Churchill wrote while working at a special standing desk, as did Ernest Hemingway and Benjamin Franklin.

So with Dr John Buckley and a team of researchers from the University of Chester we conducted a simple experiment. We asked 10 people who work at an estate agents to stand for at least three hours a day for a week. Our lucky volunteers had mixed feelings about how they would get on.

"It'll be different, but looking forward to it, yes…"

"I think my feet might hurt - I'll have to wear sensible shoes…"

"The small of my back, it's going to hurt…"

"I'm worried that I'm not going to be able to stand up for all that time…[Laughs nervously]"

We asked all the volunteers to wear an accelerometer - a movement monitor - to record just how much moving about they were doing. They also wore heart rate monitors and had glucose monitors that measured their blood sugar levels constantly, day and night.

The evidence that standing up is good for you goes back to at least the 1950s when a study was done comparing bus conductors (who stand) with bus drivers (who don't). This study, published in the Lancet, showed that the bus conductors had around half the risk of developing heart disease of the bus drivers.

Since then prolonged sitting has not only been linked to problems with blood glucose control, but also a sharp reduction in the activity of an enzyme called lipoprotein lipase, which breaks down blood fats and makes them available as a fuel to the muscles. This reduction in enzyme activity leads to raised levels of triglycerides and fats in the blood, increasing the risk of heart disease.

We had good reason to believe that standing would make a difference to our volunteers, but we were also a little anxious as to how they would get on. This was the first time an experiment like this had been conducted in the UK. Would our volunteers stick to it?

They did. One woman with arthritis even found that standing actually improved her symptoms.

The Chester researchers took measurements on days when the volunteers stood, and when they sat around. When they looked at the data there were some striking differences. As we had hoped, blood glucose levels fell back to normal levels after a meal far more quickly on the days when the volunteers stood than when they sat. There was also evidence, from the heart rate monitors that they were wearing, that by standing they were burning more calories.

"If we look at the heart rates," John Buckley explains, "we can see they are quite a lot higher actually - on average around 10 beats per minute higher and that makes a difference of about 0.7 of a calorie per minute."

Now that doesn't sound like much, but it adds up to about 50 calories an hour. If you stand for three hours a day for five days that's around 750 calories burnt. Over the course of a year it would add up to about 30,000 extra calories, or around 8lb of fat.

"If you want to put that into activity levels," Dr Buckley says, "then that would be the equivalent of running about 10 marathons a year. Just by standing up three or four hours in your day at work."

Dr Buckley thinks that although going out and doing exercise offers many proven benefits, our bodies also need the constant, almost imperceptible increase in muscle activity that standing provides. Simple movement helps us to keep our all-important blood sugar under control.
We can't all stand up at work but the researchers believe that even small adjustments, like standing while talking on the phone, going over to talk to a colleague rather than sending an email, or simply taking the stairs, will help.
I have, of course, written this article while standing.

http://nyti.ms/17BQtjY

Breaking Through Cancer's Shield

Drugs can break cancer's protective shield so the immune system can attack

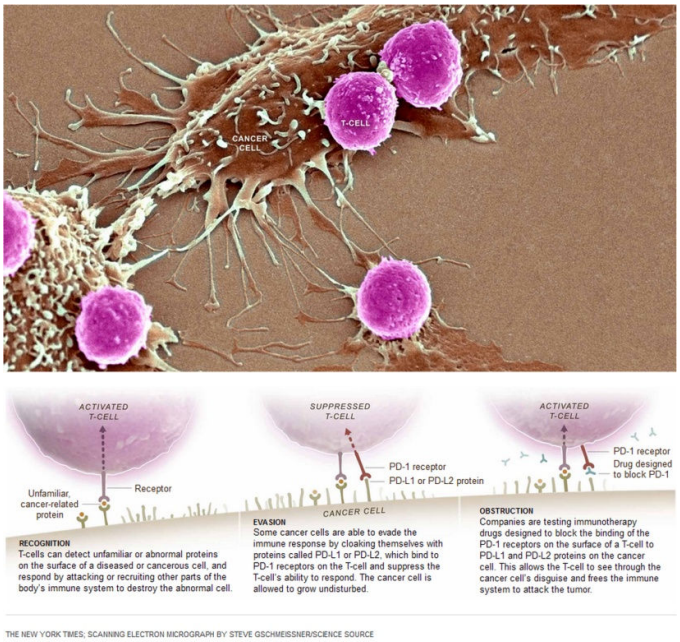
By GINA KOLATA

For more than a century, researchers were puzzled by the uncanny ability of cancer cells to evade the immune system. They knew cancer cells were grotesquely abnormal and should be killed by white blood cells. In the laboratory, in Petri dishes, white blood cells could go on the attack against cancer cells. Why, then, could cancers survive in the body?
The answer, when it finally came in recent years, arrived with a bonus: a way to thwart a cancer's strategy. Researchers discovered that cancers wrap themselves in an invisible protective shield. And they learned that they could break into that shield with the right drugs. When the immune system is free to attack, cancers can shrink and stop growing or even disappear in lucky patients with the best responses. It may not matter which type of cancer a person has. What matters is letting the immune system do its job.
So far, the drugs have been tested and found to help patients with melanoma, kidney and lung cancer. In preliminary studies, they also appear to be effective in breast cancer, ovarian cancer and cancers of the colon, stomach, head and neck, but not the prostate.
It is still early, of course, and questions remain. Why do only some patients respond to the new immunotherapies? Can these responses be predicted? Once beaten back by the immune system, how long do cancers remain at bay? Still, researchers think they are seeing the start of a new era in cancer medicine.
"Amazing," said Dr. Drew Pardoll, the immunotherapy research director at Johns Hopkins School of Medicine. This period will be viewed as an inflection point, he said, a moment in medical history when everything changed.
"A game-changer," said Dr. Renier J. Brentjens, a leukemia specialist at Memorial Sloan-Kettering Cancer Center.
"A watershed moment," said his colleague, Dr. Michel Sadelain. (Both say they have no financial interests in the new drugs; Dr. Pardoll says he holds patents involving some immunotherapy drugs, but not the ones mentioned in this article.)
Researchers and companies say they are only beginning to explore the new immunotherapies and develop others to attack cancers, like prostate, that seem to use different molecules to evade immune attacks. They are at the earliest stages of combining immunotherapies with other treatments in a bid to improve results.
"I want to be very careful that we do not overhype and raise patients' expectations so high that we can never meet them," said Dr. Alise Reicin, a vice president at Merck for research and development.
But the companies have an incentive to speed development of the drugs. They are expected to be expensive, and the demand huge. Delays of even a few months means a huge loss of potential income.
Nils Lonberg, a senior vice president at Bristol-Myers Squibb, notes that immunotherapy carries a huge advantage over drugs that attack mutated genes. The latter approach all but invites the cancer to escape, in the same way bacteria develop resistance to antibiotics.
By contrast, immunotherapy drugs are simply encouraging the immune system to do what it is meant to do; it is not going to adapt to evade the drugs. "We are hoping to set up a fair fight between the immune system and the cancer," Dr. Lonberg said.

Lowering Defenses

The story of the new cancer treatments started with the discovery of how cancers evade attacks. It turned out that they use the body's own brakes, which normally shut down the immune system after it has done its job killing virus-infected cells. One braking system, for example, uses a molecule, PD-1, on the surface of T-cells of the immune system. If a target cell has molecules known as PD-L1 or PD-L2 on its surface, the T-cell cannot attack it. So some cancer cells drape themselves in those molecules. The effect, when T-cells are near, is like turning off a light switch. The T-cells just shut down.

Cancers that do not use PD-L1 or PD-L2 are thought to use other similar systems, just starting to be explored. Body systems have a lot of redundancy to tamp down immune attacks. But for now, the PD system showed researchers how cancer cells can evade destruction.
“That is what has been realized in the past few years,” said Ira Mellman, vice president of research oncology at Genentech. “Tumor cells are making use of this brake.”
The discovery led to an idea: Perhaps a drug that covered up any of those PD molecules, on the cancer cells or on white blood cells, would allow the immune system to do its job.
(There is another immunotherapy strategy — to take white blood cells out of the body and program them with genetic engineering to attack a cancer. Studies have just begun and are promising. But researchers note that this is a very different sort of treatment that is highly labor-intensive and has been successful so far in only a few types of cancer.)



The first indication that a cancer’s protective shield might be breached came in 2010, after a trial of the drug ipilimumab in patients with otherwise untreatable melanoma. The drug unleashes the immune system, letting it overwhelm tumors even if they have a protective shield.
Patients who took the drug survived an average of 10 months, or 4 months longer than those randomly assigned to a different treatment. And about 20 percent of patients who responded have now survived up to 10 years. It was the first drug to improve survival for patients with metastatic melanoma in a randomized trial.
“It was spectacular,” said Dr.Axel Hoos, vice president for oncology research and development at GlaxoSmithKline, who helped develop the drug when he was at Bristol-Myers Squibb. “Until that tipping point, immunotherapy had a bad name. It didn’t work.”
The drug was approved for melanoma in March 2011, with a high price tag — $120,000 for a course of therapy.
It had another drawback. By unleashing the immune system, it sometimes led to attacks on normal cells. In some cases, the reaction was fatal. But the trial was a proof of concept. It showed that cancers can succumb to an attack by the immune system.
“That opened the door a crack,” said Dr. Pardoll, of Johns Hopkins. “People stood up and took notice.”

A Signal Emerges

Dr. Suzanne Topalian, a professor of surgery and oncology at Johns Hopkins, was one of the first to test the new drugs in patients. The trial began in 2006, with 39 patients who got a PD-1 blocker, made by Medarex, since bought by Bristol-Myers Squibb. The study included patients with a variety of advanced cancers, who had failed all traditional treatments; most had tried at least three, without any luck.
The study looked at safety, not effectiveness. But Dr. Topalian noticed something intriguing. One patient with lung cancer treated at a collaborating medical center had a partial regression of her tumor. “It was very temporary; it was not enough to call it a response,” Dr. Topalian said. “But it was a signal; it was there.”
That was surprising because researchers had assumed the cancers most vulnerable to an immune system attack were melanoma and kidney cancer. Lung cancer was supposed to be out of the question.
“Julie and I got on the phone with Medarex and said, ‘You have to include lung cancer in your next clinical trial,’ ” Dr. Topalian said, referring to her colleague Dr. Julie Brahmer.
That led to studies of two Bristol-Myers drugs: one that blocks PD-1 and another that blocks PD-L1. The studies included a 503 patients with a variety of advanced cancers who had exhausted other options.
The findings, presented in October last year at a meeting of the American Society of Clinical Oncology, were striking. A significant proportion of patients responded, including 18 percent of 76 lung cancer patients who got the PD-1 drug and 10 percent of 49 who got PD-L1 drug. Dr. Pardoll, who is married to Dr. Topalian, said that when she and her colleagues presented the data, “it was almost like a hush fell over the room: ‘Can this really be?’ ”

Emblems of Hope

As researchers continue to study the new drugs and ask if they can improve their results by combining them with other therapies, they are heartened by some of the rare patients whose cancers were halted by the drugs.

They caution that these patients are unusual; critical studies to reveal the drugs' effects on populations of cancer patients are still under way. "What you really want to know," said Dr. Roger M. Perlmutter, the president of Merck Research Laboratories, "is, are people living longer?" For that, "you just have to wait," he continued, adding, "What I don't want to do is give people false hope."

But some patients, like two treated at Hopkins, have become emblems of hope. In 2007, M. Dennis Sisolak, who is 72 and a retired engineer from Bel Air, Md., learned he had kidney cancer. The tumor was huge, and the cancer had spread. After he tried two new drugs to no avail, his doctor, Dr. Charles G. Drake, a kidney cancer specialist at Johns Hopkins, enrolled him in an early phase clinical trial of a PD-1 inhibitor. His cancer disappeared on scans and has not returned, even though he has had no treatment for a year.

"I have a lot of people praying for me," Mr. Sisolak said.

Dr. Drake said three of his patients had similar responses, including one who was treated five years ago in the first study. All, with advanced disease, would have been dead by now, he said, adding, "I have never seen anything like this, personally."

David Gobin, 63, a retired Baltimore police officer, has a similar story. He learned he had lung cancer in 2008. He had surgery to remove the two lower lobes of his right lung, then radiation and chemotherapy.

The treatment was grueling: he lost 70 pounds. Two years later, the cancer was back, and it had spread to the wall of his chest. He had more surgery, more chemotherapy, more radiation.

In 2010, Mr. Gobin entered a clinical trial of an experimental drug that interferes with cell growth, but had no success. Then his doctor at Johns Hopkins suggested a Phase 1 trial of an anti-PD-1 drug.

"Sure, I'll do it," Mr. Gobin recalled saying. "What do I have to lose?"

His tumors shrank significantly and have not grown, even though he stopped taking the drug eight months ago.

"Every day I have my feet on the grass is a good day," Mr. Gobin said. "I was in the right place at the right time. I will always have cancer, but you know what, I can live with it.

"The Lord wanted me to be alive, and I am alive."

http://bit.ly/1a3uPsZ

Back from the dead: Reversing walking corpse syndrome

ONE moment you are alive. The next you are dead. A few hours later and you are alive again. Pharmacologists have discovered a mechanism that triggers Cotard's syndrome – the mysterious condition that leaves people feeling like they, or parts of their body, no longer exist.

16 October 2013 by Helen Thomson

With the ability to switch the so-called walking corpse syndrome on and off comes the prospect of new insights into how conscious experiences are constructed.

Acyclovir – also known by the brand name Zovirax – is a common drug used to treat cold sores and other herpes infections. It usually has no harmful side effects. However, about 1 per cent of people who take the drug orally or intravenously experience some psychiatric side effects, including Cotard's. These occur mainly in people who have renal failure.

To investigate the potential link between acyclovir and Cotard's, Anders Helldén at Karolinska University Hospital in Stockholm and Thomas Lindén at the Sahlgrenska Academy in Gothenburg pooled data from Swedish drug databases along with hospital admissions. They identified eight people with acyclovir-induced Cotard's.

One woman with renal failure began using acyclovir to treat shingles. She ran into a hospital screaming, says Helldén. After an hour of dialysis, she started to talk: she said the reason she was so anxious was that she had a strong feeling she was dead. After a few more hours of dialysis she said, "I'm not quite sure whether I'm dead any more but I'm still feeling very strange." Four hours later: "I'm pretty sure I'm not dead any more but my left arm is definitely not mine." Within 24 hours, the symptoms had disappeared.

Blood analysis suggests an explanation. When someone takes acyclovir, it is broken down in the body before being removed via the kidneys. One of these breakdown products, CMMG, is usually found at very low levels. But those who had symptoms of Cotard's had much higher levels. All but one of these eight people had renal failure. Helldén and Lindén found that lowering the dose or removing the drug via dialysis appears to stop the symptoms (Journal of the Neurological Sciences, doi.org/nz7).

"Several of the patients developed very high blood pressure," says Helldén, "so we have a feeling that CMMG is causing some kind of constriction of the arteries in the brain." He is now investigating what happens in people who experience other acyclovir-induced psychiatric effects. He says there may be a genetic link between how people metabolise acyclovir and the symptoms they get. What's fascinating, he says, is that there is now, in theory, a way to turn Cotard's on and off. "That's a very interesting model to investigate how you develop disorders of consciousness," says Helldén.

In July, Steven Laureys at Liège University Hospital in Belgium performed the first brain scan of a person with Cotard's. "I wasn't aware of the acyclovir link, it's terribly interesting," he says. "It would be good to do functional imaging in these patients, especially since it seems to be reversible, so you can make a strong claim of cause and effect."
It would be unethical to recreate Cotard's in humans, says Helldén, but animal models might provide some insight about the system in the brain that generates a sense of self. "That to me is very, very interesting," he says.

Delusions of existence

In 1880, French neurologist Jules Cotard first described the mysterious symptoms of a 43-year-old woman who believed that she had no brain. "Mademoiselle X" requested that her body be burned since she was already dead. Cotard said she had "délire des negations" – the delirious belief in her non-existence.
As well as appearing as a rare side effect to certain drugs (see main story), Cotard's has occurred in other contexts – often preceded by episodes of depression or bipolar disorder. In 2009, a 46-year-old woman with bipolar disorder became convinced her brain had vanished and her body was translucent. She refused to wash, afraid that she was soluble and would disappear down the drain (Current Psychiatry Reports, doi.org/ccrvbn).
The cause of Cotard's remains a mystery: several anatomical, psychological and metabolic abnormalities have been suggested. The first PET scan of a person with Cotard's revealed that metabolic activity in the frontal and parietal regions of the brain was so low as to resemble that of someone in a vegetative state (Cortex, doi.org/mmt). Antipsychotics, mood stabilisers and electroconvulsive therapy can help, although the disorder has also been known to disappear spontaneously.

http://www.sciencedaily.com/releases/2013/10/131016213215.htm

Elusive Secret of HIV Long-Term Immunity

Scientists have discovered a critical new clue about why some people are able to control the HIV virus long term without taking antiviral drugs. The finding may be useful in shortening drug treatment for everyone else with HIV.

These rare individuals who do not require medicine have an extra helping of a certain type of immune protein that blocks HIV from spreading within the body by turning it into an impotent wimp, Northwestern Medicine® scientists report. The new finding comes from analyzing cells from these rare individuals and HIV in the lab.
Scientists have been trying to solve the mystery of why 1 percent of people with HIV -- called "controllers" -- have enduring control of the virus without medications, in some cases for life. The controllers' early defense against HIV is quickly extinguished by the virus, so how do they have long-term immunity? The Northwestern discovery represents what scientists have long sought: a second line of defense deep in the immune system backing up the short-lived early defense.
This discovery suggests a novel approach involving much earlier treatment that could potentially make every HIV-infected person into a controller for the long term by protecting the reserves of this defensive immune protein. The goal would be for them to eventually be free from anti-retroviral drugs.
Currently most HIV patients need to take powerful anti-retroviral drugs every single day for life. If the medicines are stopped, the virus quickly reactivates to harmful levels even after years of treatment.
"Preserving and even increasing this defense in cells may make more HIV-infected persons into controllers and prevent HIV from rebounding to high and damaging levels when anti-HIV medications are stopped," said Richard D'Aquila, M.D., the director of the Northwestern HIV Translational Research Center. He is the senior author of the study, which will be published Oct. 16 in the journal PLOS ONE.
D'Aquila also is the Howard Taylor Ricketts Professor of Medicine at Northwestern University Feinberg School of Medicine and a physician at Northwestern Memorial Hospital.
D'Aquila and colleagues now are working to develop a medicine that would boost this defensive immune protein called APOBEC3G, or A3 for short.

The Missing Second Defensive Line

Much is known about how the immune system of controllers initially fights the virus. But HIV quickly escapes from that first line of defense by mutating and evading the adaptive immune system. How these individuals control HIV long term without medications to keep from developing AIDS has been under study by many researchers. It seemed there must be a second defensive line in the immune system.

Turning HIV Into a Wimp

In the new study, D'Aquila and his team have found that controllers, long after they have acquired HIV, have a more abundant supply of the critical immune protein A3 in specific white blood cells called resting memory T cells. This is where the virus lies silently in an inactive form and roars back when anti-retroviral drugs are

stopped. In controllers, though, their bounty of A3 means that any new HIV made from those cells inherits a helping of A3, which turns the new viruses into harmless wimps that can't infect other cells.

You Can't Fool A3

The feisty A3 is a critical part of the newly characterized intrinsic immune system, and it resides in many cells of the immune system including resting T cells. Unlike the adaptive immune system, which fails to recognize the virus once it mutates its pieces, the intrinsic immune system can't be fooled.

"The intrinsic immune system recognizes the basic guts of the virus -- the nucleic acids -- that HIV can't change and then damages those nucleic acids," D'Aquila said.

D'Aquila theorizes that the controllers' first line of defense slows down the ability of HIV to destroy all the A3. "Perhaps starting anti-HIV drugs very soon after HIV is caught, rather than the current practice of waiting until later to start, would work like the controllers' first line of defense," D'Aquila suggested. "If we preserve A3, it could minimize HIV's spread through the body as this protein seems to do in controllers." Otherwise, D'Aquila theorizes, all reserves of the protein are wiped out if HIV replicates unchecked for several months.

Babies and Other Controllers

D'Aquila pointed to several recent examples of early treatment sometimes resulting in lasting control of HIV in humans that are consistent with this theory.

In January 2013, a baby was born to an HIV-positive woman in Memphis who didn't take preventive medicines that are routinely given to these women. The baby got infected, and doctors began anti-HIV drug treatment within 36 hours of birth. After some treatment, the baby is now off anti-HIV medicines and appears to be cured of HIV.

Two studies published earlier this year show the protective effect of starting the medicines within three to four months after infection for a relatively short course, resulting in a lower level of HIV in the blood and better control of the virus for some who stopped the anti-retroviral medication.

A group of patients in a European study were started on anti-HIV drugs very early after infection. Their medications were stopped after three years but some continued to have a suppressed virus at such low levels it did not cause any damage.

Earlier Detection Just Got Easier

"Early-as-possible detection -- much easier with our new technology -- and early drug treatment will be the future of HIV therapy," D'Aquila said. He added that the Affordable Care Act mandates that insurance companies pay for routine HIV testing, which they did not always cover in the past.

D'Aquila Helped Developed Personalized Approach to HIV Medicine

D'Aquila is a leading HIV scientist who began investigating AIDS in 1982, the first year it was identified. He was a senior resident in Philadelphia when the early cases appeared at the hospital where he was working. D'Aquila began investigating, calling other area hospitals to see if they had seen similar cases. He discovered there were lots of them. The same month, Morbidity and Mortality Weekly Report sounded the first alarm that a new disease had erupted.

Over the last 30 years, D'Aquila has helped develop anti-HIV medicines and resistance testing for HIV -- the latter is the first widely used clinical application of DNA sequencing in personalized medicine. Since the 1990s, HIV patients have their virus sequenced to determine which medicines are going to work best for them at that time -- a result of research done by D'Aquila and others.

MariaPia De Pasquale, Yordanka Kourteva, Tara Allos, Richard T. D'Aquila. Lower HIV Provirus Levels Are Associated with More APOBEC3G Protein in Blood Resting Memory CD4 T Lymphocytes of Controllers In Vivo. PLoS ONE, 2013; 8 (10): e76002 DOI: 10.1371/journal.pone.0076002

http://www.eurekalert.org/pub_releases/2013-10/aaft-csf101113.php

Complete skull from early Homo evokes a single, evolving lineage

The skull of an ancient human ancestor implies that all Homo species were one

What if the earliest members of our Homo genus—those classified as Homo habilis, Homo rudolfensis, Homo erectus and so forth—actually belonged to the same species and simply looked different from one another? That's precisely the implication of a new report, which describes the analysis of a complete, approximately 1.8-million-year-old skull that was unearthed in Dmanisi, Georgia.

Unlike other Homo fossils, this skull, known as Skull 5, combines a small braincase with a long face and large teeth. It was discovered alongside the remains of four other early human ancestors, a variety of animal fossils and some stone tools—all of them associated with the same location and time period—which makes the find truly unique. The site has only been partially excavated so far, but it's already providing the first opportunity for researchers to compare and contrast the physical traits of multiple human ancestors that apparently coincided in the same time and geological space.

David Lordkipanidze from the Georgian National Museum in Tbilisi, Georgia, along with colleagues from Switzerland, Israel and the United States, say that the differences between these Dmanisi fossils are no more pronounced than those between five modern humans or five chimpanzees.

This is the Dmanisi D4500 early Homo cranium in situ. **Photo courtesy of Georgian National Museum**

Traditionally, researchers have used variation among Homo fossils to define different species. But in light of these new findings, Lordkipanidze and his colleagues suggest that early, diverse Homo fossils, with their origins in Africa, actually represent variation among members of a single, evolving lineage—most appropriately, Homo erectus.

Their report is published in the 18 October issue of Science.

"Had the braincase and the face of Skull 5 been found as separate fossils at different sites in Africa, they might have been attributed to different species," said Christoph Zollikofer from the Anthropological Institute and Museum in Zurich, Switzerland—a co-author of the Science report. That's because Skull 5 unites some key features, like the tiny braincase and large face, which had not been observed together in an early Homo fossil until now.

Given their diverse physical traits, the fossils associated with Skull 5 at Dmanisi can be compared to various Homo fossils, including those found in Africa, dating back to about 2.4 million years ago, as well as others unearthed in Asia and Europe, which are dated between 1.8 and 1.2 million years ago.

"[The Dmanisi finds] look quite different from one another, so it's tempting to publish them as different species," explained Zollikofer. "Yet we know that these individuals came from the same location and the same geological time, so they could, in principle, represent a single population of a single species."

The hominid fossils from Dmanisi represent ancient human ancestors from the early Pleistocene epoch, soon after early Homo diverged from Australopithecus and dispersed from Africa. The jaw associated with Skull 5 was found five years before the cranium was discovered but when the two pieces were put together, they formed the most massively built skull ever found at the Dmanisi site. For this reason, the researchers suggest that the individual to whom Skull 5 belonged was male.

The braincase of Skull 5 is only about 33.3 cubic inches (546 cubic centimeters), however, which suggests that this early Homo had a small brain despite his modern human-like limb proportions and body size.

"Thanks to the relatively large Dmanisi sample, we see a lot of variation," continued Zollikofer. "But the amount of variation does not exceed that found in modern populations of our own species, nor in chimps and bonobos."

"Furthermore, since we see a similar pattern and range of variation in the African fossil record… it is sensible to assume that there was a single Homo species at that time in Africa," he concluded. "And since the Dmanisi hominids are so similar to the African ones, we further assume that they both represent the same species."

Skull 5 seemingly indicates that, rather than several ecologically specialized Homo species, a single Homo species—able to cope with a variety of ecosystems—emerged from the African continent. And accordingly, our classification system for these early human ancestors may never be the same.

The report by Lordkipanidze et al. was supported by the Rustaveli Georgian National Science Foundation, the Swiss National Science Foundation, the U.S. National Science Foundation, the National Geographic Society, the L.S.B. Leakey Foundation, the American Philosophical Society, the American School for Prehistoric Research, a Rolex Award for Enterprise, BP Georgia, the Fundación Duques de Soria, the A.H. Schultz Foundation, and the Foundation for Scientific Research at the University of Zurich.

http://www.eurekalert.org/pub_releases/2013-10/yu-rra101413.php

Researchers rewrite an entire genome -- and add a healthy twist

Scientists from Yale and Harvard have recoded the entire genome of an organism and improved a bacterium's ability to resist viruses, a dramatic demonstration of the potential of rewriting an organism's genetic code.

"This is the first time the genetic code has been fundamentally changed," said Farren Isaacs, assistant professor of molecular, cellular, and developmental biology at Yale and co-senior author of the research published Oct. 18 in the journal Science. "Creating an organism with a new genetic code has allowed us to expand the scope of biological function in a number of powerful ways." The creation of a genomically recoded organism raises the possibility that researchers might be able to retool nature and create potent new forms of proteins to accomplish a myriad purposes — from combating disease to generating new classes of materials.

The research — headed by Isaacs and co-author George Church of Harvard Medical School — is a product of years of studies in the emerging field of synthetic biology, which seeks to re-design natural biological systems for useful purposes. In this case, the researchers changed fundamental rules of biology.
Proteins, which are encoded by DNA's instructional manual and are made up of 20 amino acids, carry out many important functional roles in the cell. Amino acids are encoded by the full set of 64 triplet combinations of the four nucleic acids that comprise the backbone of DNA. These triplets (sets of three nucleotides) are called codons and are the genetic alphabet of life.
Isaacs, Jesse Rinehart of Yale,,and the Harvard researchers explored whether they could expand upon nature's handywork by substituting different codons or letters throughout the genome and then reintroducing entirely new letters to create amino acids not found in nature. This work marks the first time that the genetic code has been completely changed across an organism's genome.
In the new study, the researchers working with E. coli swapped a codon and eliminated its natural stop sign that terminates protein production. The new genome enabled the bacteria to resist viral infection by limiting production of natural proteins used by viruses to infect cells. Isaacs — working with Marc Lajoie of Harvard, Alexis Rovner of Yale, and colleagues — then converted the "stop" codon into one that encodes new amino acids and inserted it into the genome in a plug-and-play fashion.
The work now sets the stage to convert the recoded bacterium into a living foundry, capable of biomanufacturing new classes of "exotic" proteins and polymers. These new molecules could lay the foundation for a new generation of materials, nanostructures, therapeutics, and drug delivery vehicles, Isaacs said.
"Since the genetic code is universal, it raises the prospect of recoding genomes of other organisms," Isaacs said. "This has tremendous implications in the biotechnology industry and could open entirely new avenues of research and applications."
Other participating researchers from Yale University are Hans Aerni and Adrian Haimovich.

http://www.eurekalert.org/pub_releases/2013-10/nerc-art101713.php

Archaeologists rediscover the lost home of the last Neanderthals

A record of Neanderthal archaeology, thought to be long lost, has been re-discovered by NERC-funded scientists working in the Channel island of Jersey.

The study, published yesterday in the Journal of Quaternary Science, reveals that a key archaeological site has preserved geological deposits which were thought to have been lost through excavation 100 years ago.
The discovery was made when the team undertook fieldwork to stabilise and investigate a portion of the La Cotte de St Brelade cave, on Jersey's south eastern coastline.
A large portion of the site contains sediments dating to the last Ice Age, preserving 250,000 years of climate change and archaeological evidence.
The site, which has produced more Neanderthal stone tools than the rest of the British Isles put together, contains the only known late Neanderthal remains from North West Europe. These offer archaeologists one of the most important records of Neanderthal behaviour available.
"In terms of the volume of sediment, archaeological richness and depth of time, there is nothing else like it known in the British Isles. Given that we thought these deposits had been removed entirely by previous researchers, finding that so much still remains is as exciting as discovering a new site," says Dr Matt Pope of the Institute of Archaeology at University College London, who helped lead the research.
The team dated sediments at the site using a technique called Optically Stimulated Luminesce, which measures the last time sand grains were exposed to sunlight. This was carried out at the Luminescence Dating Research Laboratory for Archaeology and the History of Art at Oxford University.
The results showed that part of the sequence of sediments dates between 100,000 and 47,000 years old, indicating that Neanderthal teeth which were discovered at the site in 1910 were younger than previously thought, and probably belonged to one of the last Neanderthals to live in the region.
"The discovery that these deposits still exist and can be related to previously excavated deposits opens up a range of exciting possibilities," says Dr Martin Bates, University of Trinity St Davids, who is leading current fieldwork at the site.
The findings bring the large collections of stone tools, animal bone and the Neanderthal remains from the area under renewed study. "Excavation in the future will provide us with the opportunity to subject the site to the wide range of approaches we use today in Palaeolithic archaeology and Quaternary science.
For example we are hoping to be able to link our site with the broader Neanderthal landscapes through study of similarly aged deposits around the island and, through bathymetric survey, on the seabed," says Bates.
"We were sure from the outset that the deposits held some archaeological potential, but these dates indicate we have uncovered something exceptional," explains Pope. "We have a sequence of deposits which span the last

120,000 years still preserved at the site. Crucially, this covers the period in which Neanderthal populations apparently went 'extinct'."
It was during this period that Neanderthals appear to have been replaced by our own species – Homo sapiens.
The NERC-funded work represented the first formal programme of scientific research to be focused on the site since the early 1980s. The site has since then been managed and preserved by the Société Jerisaise, the Jersey-based academic society involved in early investigation of the site and which continues to manage and protect the site through to the present day.
"For over a hundred years the Societe has tried to maintain the interest of the wider academic world in La Cotte, having realised its international importance from the beginning. We are delighted, therefore, that such a prestigious team is now studying the site, and, in addition, the wider Palaeolithic landscape of Jersey," says Neil Molyneux, president of the Société Jersiaise.
The wider project, supported also by the Arts and Humanities Research Council and the Jersey Government will now continue to investigate the site and material excavated from it over the past 110 years.
"Working with our partners to bring these rediscovered sediments under new analysis will allow us to bring the lives of the last Neanderthal groups to live in North West Europe into clearer focus," says Pope.
"We may be able to use this evidence to better understand when Neanderthal populations disappeared form the region and whether they ever shared the landscape with the species which ultimately replaced them, us," he concludes.

http://www.eurekalert.org/pub_releases/2013-10/uoa-mah101513.php

Mysterious ancient human crossed Wallace's Line

Scientists have proposed that the most recently discovered ancient human relatives -- the Denisovans -- somehow managed to cross one of the world's most prominent marine barriers in Indonesia, and later interbred with modern humans moving through the area on the way to Australia and New Guinea.

Three years ago the genetic analysis of a little finger bone from Denisova cave in the Altai Mountains in northern Asia led to a complete genome sequence of a new line of the human family tree -- the Denisovans. Since then, genetic evidence pointing to their hybridisation with modern human populations has been detected, but only in Indigenous populations in Australia, New Guinea and surrounding areas. In contrast, Denisovan DNA appears to be absent or at very low levels in current populations on mainland Asia, even though this is where the fossil was found.
Published today in a Science opinion article, scientists Professor Alan Cooper of the University of Adelaide in Australia and Professor Chris Stringer of the Natural History Museum in the UK say that this pattern can be explained if the Denisovans had succeeded in crossing the famous Wallace's Line, one of the world's biggest biogeographic barriers which is formed by a powerful marine current along the east coast of Borneo. Wallace's Line marks the division between European and Asian mammals to the west from marsupial-dominated Australasia to the east.
"In mainland Asia, neither ancient human specimens, nor geographically isolated modern Indigenous populations have Denisovan DNA of any note, indicating that there has never been a genetic signal of Denisovan interbreeding in the area," says Professor Cooper, Director of the University of Adelaide's Australian Centre for Ancient DNA. "The only place where such a genetic signal exists appears to be in areas east of Wallace's Line and that is where we think interbreeding took place -- even though it means that the Denisovans must have somehow made that marine crossing."
"The recent discovery of another enigmatic ancient human species Homo floresiensis, the so-called Hobbits, in Flores, Indonesia, confirms that the diversity of archaic human relatives in this area was much higher than we'd thought," says Professor Stringer, Research Leader in Human Origins, Natural History Museum, in London.
"The morphology of the Hobbits shows they are different from the Denisovans, meaning we now have at least two, and potentially more, unexpected groups in the area.
"The conclusions we've drawn are very important for our knowledge of early human evolution and culture. Knowing that the Denisovans spread beyond this significant sea barrier opens up all sorts of questions about the behaviours and capabilities of this group, and how far they could have spread."
"The key questions now are where and when the ancestors of current humans, who were on their way to colonise New Guinea and Australia around 50,000 years ago, met and interacted with the Denisovans," says Professor Cooper.
"Intriguingly, the genetic data suggest that male Denisovans interbred with modern human females, indicating the potential nature of the interactions as small numbers of modern humans first crossed Wallace's Line and entered Denisovan territory."

http://phys.org/news/2013-10-mythical-yeti-descended-ancient-polar.html

DNA links mysterious Yeti to ancient polar bear (Update 3)

A British scientist says he may have solved the mystery of the Abominable Snowman—the elusive ape-like creature of the Himalayas. He thinks it's a bear.

Purported Yeti scalp at Khumjung monastery. **Credit: Nuno Nogueira / Wikipedia.**

DNA analysis conducted by Oxford University genetics professor Bryan Sykes suggests the creature, also known as the Yeti, is the descendant of an ancient polar bear. Sykes compared DNA from hair samples taken from two Himalayan animals—identified by local people as Yetis—to a database of animal genomes. He found they shared a genetic fingerprint with a polar bear jawbone found in the Norwegian Arctic that is at least 40,000 years old.

Sykes said Thursday that the tests showed the creatures were not related to modern Himalayan bears but were direct descendants of the prehistoric animal. He said, "it may be a new species, it may be a hybrid" between polar bears and brown bears. "The next thing is go there and find one."

Sykes put out a call last year for museums, scientists and Yeti aficionados to share hair samples thought to be from the creature. One of the samples he analyzed came from an alleged Yeti mummy in the Indian region of Ladakh, at the Western edge of the Himalayas, and was taken by a French mountaineer who was shown the corpse 40 years ago. The other was a single hair found a decade ago in Bhutan, 800 miles (1,300 kilometers) to the east.

Sykes said the fact the hair samples were found so far apart, and so recently, suggests the members of the species are still alive. "I can't imagine we managed to get samples from the only two 'snow bears' in the Himalayas," he said.

Finding a living creature could explain whether differences in appearance and behavior to other bears account for descriptions of the Yeti as a hairy hominid. "The polar bear ingredient in their genomes may have changed their behavior so they act different, look different, maybe walk on two feet more often," he said.

Sykes' research has not been published, but he says he has submitted it for peer review. His findings will be broadcast Sunday in a television program on Britain's Channel 4.

Tom Gilbert, professor of paleogenomics at the Natural History Museum of Denmark, said Sykes' research provided a "reasonable explanation" for Yeti sightings. "It's a lot easier to believe that than if he had found something else," said Gilbert, who was not involved in the study. "If he had said it's some kind of new primate, I'd want to see all the data."

Sykes' findings are unlikely to lay the myth of the Yeti to rest.

The Yeti or Abominmable Snowman is one of a number of legendary ape-like beasts—along with Sasquatch and Bigfoot—reputed to live in heavily forested or snowy mountains. Scientists are skeptical, but decades of eyewitness reports, blurry photos and stories have kept the legend alive.

"I do not think the study gives any comfort to Yeti-believers," David Frayer, a professor of biological anthropology at the University of Kansas, said in an email. But "no amount of scientific data will ever shake their belief." "If (Sykes') motivation for doing the analyses is to refute the Yeti nonsense, then good luck," he said.

Sykes said he was simply trying "to inject some science into a rather murky field." "The Yeti, the Bigfoot, is surrounded in myth and hoaxes," he said. "But you can't invent a DNA sequence from a hair."

http://phys.org/news/2013-10-neanderthals-meal-animal-stomachs.html

Neanderthals may have made a meal of animal stomachs

Evidence from Neanderthal teeth sheds light on a more complex diet.

Phys.org - Plant material found on Neanderthal teeth suggests they had a better understanding of their food than previously thought. In a new article published in the journal Quaternary Science Reviews, Museum anthropologists Laura Buck and Prof Chris Stringer propose that evidence of bitter root plants found on Neanderthal teeth may point to a practice of eating the stomach contents of their prey.

Previous research has suggested that the presence of bitter and nutritionally-poor camomile and yarrow residue on the plaque of 50,000-year-old Neanderthal teeth hints at plants being consumed for medicinal purposes. Buck and Stringer have put forward a different theory. They suggest instead that the plant compounds could be from the part-digested stomach contents (chyme) of hunted animals.

Nutritious meal

This is a practice still carried out by many cultures, including Australian Aborigines, who eat the chyme of kangaroo, and Greenland Inuit who consume the stomachs of reindeer as a delicacy.

Arctic explorer Fridtjof Nansen in 1893 described reindeer as 'gourmets', living off 'the finest moss and grasses'. In harsh conditions, such as desert or tundra, eating animal stomach contents allows people to gain nutrients from plants they could not easily obtain otherwise.

Nansen described how reindeer stomach was a prized delicacy for the Inuit: 'The last thing an Eskimo lady enjoins upon her lover, when he sets off reindeer-hunting, is that he must reserve for her the stomach of his prey.' Drawing parallels with these cultures, Buck and Stringer looked back at the original plaque research and determined that the plant material could well have come from eating animal stomachs.

Sophisticated eating

Neanderthals have long been thought of as pure big game hunters, largely ignoring vegetables and small game, a factor which, it is argued, could have led to their extinction. But new evidence from tooth plaque and other dietary analyses shows they did eat vegetation, including some types that required complex preparation.

Buck said that consuming yarrow and camomile could have been both for medicine and nutrition, in different times and places, but that either reason suggests Neanderthals had a more diverse diet and better understanding of food in their environment. 'It shows a level of dietary complexity not always appreciated before,' she said.

While some modern cultures consume animal chyme for ritual purposes, and the possibility of ritual behaviour has been suggested for other Neanderthal finds, Stringer said this is not indicated in their research and that nutrition is a simpler explanation. 'Having gone to the time and trouble of securing the carcass of a large herbivore, why would our ancestors have wasted such a source of nutrition?' said Stringer.

Visitors can learn more about Prof Chris Stringer's human origins research and see rare specimens, including Neanderthal skulls, in our new exhibition, Britain: One Million Years of the Human Story, opening February 2014.

http://phys.org/news/2013-10-mega-giga-year-storage-medium.html

A mega to giga year storage medium can outlive the human race

Researcher demonstrates that it is possible to store data for extremely long periods.

Mankind has been storing information for thousands of years. From carvings on marble to today's magnetic data storage. Although the amount of data that can be stored has increased immensely during the past few decades, it is still difficult to actually store data for a long period. The key to successful information storage is to ensure that the information does not get lost. If we want to store information that will exist longer than mankind itself, then different requirements apply than those for a medium for daily information storage. Researcher Jeroen de Vries from the University of Twente MESA+ Institute for Nanotechnology demonstrates that it is possible to store data for extremely long periods. He will be awarded his doctorate on 17 October.

Current hard disk drives have the ability to store vast amounts of data but last roughly ten years at room temperature, because their magnetic energy barrier is low so that the information is lost after a period of time. CDs, DVDs, paper, tape, clay and tablets and stone also have a limited life. Alternatives will have to be sought if information is to be retained longer.

Archival storage for up to one billion years

It is possible to conceive of a number of scenarios why we wish to store information for a long time. "One scenario is that a disaster has devastated the earth and society must rebuild the world. Another scenario could be that we create a kind of legacy for future intelligent life that evolves on Earth or comes from other worlds. You must then think about archival storage of between one million and one billion years," according to researcher De Vries.

Optical information carrier

De Vries has developed an optical information carrier that can store information for extremely long periods of time, with each bit being written using etching techniques. The chosen information carrier is a wafer consisting of tungsten encapsulated by silicon nitride. Tungsten was chosen because it can withstand extreme temperatures. A QR code is etched into the tungsten (see picture) and is protected by the nitride. Each pixel of the large QR code contains a smaller QR code that in turn stores different information. "In principle, we can store everything on the disc that we believe is worthwhile saving: for example, a digital image of the Mona Lisa. In this study we tested a digital copy of the chapter about this medium from my thesis", says De Vries.

Ageing test at high temperatures

In order to ensure the stability of the data, an energy barrier that separates the information from the non-information is required. In order to prove that the data is still legible after millions of years, an ageing test is

required to see if the energy barriers are high enough to prevent data loss. De Vries: "According to the Arrhenius model, the medium should keep working for at least 1 million years if it is heated to a temperature of 473 Kelvin (200 degrees Celsius) and kept in the oven for an hour." After the test there was no visible degradation of the tungsten, and it was still easy to read the information. Things become complicated at higher temperatures. When heated to 713 Kelvin (440 degrees Celsius) it becomes a lot more difficult to decypher the QR codes even if the tungsten is not affected. De Vries: "A follow-up study would be to investigate whether the data carrier also can withstand higher temperatures, for example during a house fire. But if we can find a place that is very stable, such as a nuclear storage facility, then the disc itself and the data that is on it should be able to endure millions of years." The thesis is titled 'Energy barriers in patterned media.'

http://bit.ly/1a3FmV8

Universal law of urination found in mammals

You'll never look at Dumbo in the same way again. Elephants, cows, goats and dogs all take roughly 21 seconds to empty their bladders. A "law of urination" now explains the physics behind what happens when you just gotta go.

18:17 17 October 2013 by Jacob Aron

Patricia Yang and colleagues at the Georgia Institute of Technology in Atlanta use high-speed video to study how fluids and animals interact; they have previously investigated how dogs shake themselves dry.

While filming at a local zoo, they noticed that animals of various sizes, both male and female, took a similar time to empty their bladders.

The team filmed rats, dogs, goats, cows and elephants urinating and gathered footage from YouTube of others relieving themselves. Combining this with data on mass, bladder pressure and urethra size, they were able to create a mathematical model of urinary systems to show why mammals take the same time to empty their bladder, despite the difference in bladder size. Previous models have only considered the effects of bladder pressure, but the length of the urethra turns out to be important as well.

Elephant pee

"Most of the research is on humans or animals smaller than humans," says Yang. In these species, the effect of gravity can be ignored. That's not true of elephants, whose urethral dimensions are comparable to a household pipe: a diameter of around 10 centimetres and a length of about 1 metre.

In this case size matters, as it means urine has time to reach higher speeds. This means that as it travels down the pipe, the urine accelerates and its flow rate rises, resulting in an elephant's large bladder being emptied in a similar time to those of smaller animals.

Medium-sized animals like dogs and goats have shorter urethras, so get less of a gravitational boost: their flow is slower. In addition, they have smaller bladders. The result of both effects is that they empty their bladders in roughly the same time as elephants.

According to the team's model, an animal's size does make a difference to urination time – but only very slightly. Their law of urination says that the time a mammal takes to empty a full bladder is proportional to the animal's mass raised to the power of a sixth, meaning even very large changes in mass have little effect on the time.

There are limits to this scaling. Gravity only plays a small role in the urination of very small mammals like rats and bats, which urinate in under a second. Instead, viscosity and surface tension dominate, which explains why their urine is released as a stream of individual drops rather than the continuous jet seen in larger mammals.

The team will present the results at the American Physical Society Division of Fluid Dynamics meeting in Pittsburgh, Pennsylvania, next month. Yang hopes the law of urination might help diagnose urinary problems in elephants and other large mammals. It might even inspire new designs for water towers, which also pump water using the force of gravity, she says.

Journal reference: arxiv.org/abs/1310.3737

http://www.livescience.com/40505-earliest-humans-one-species.html

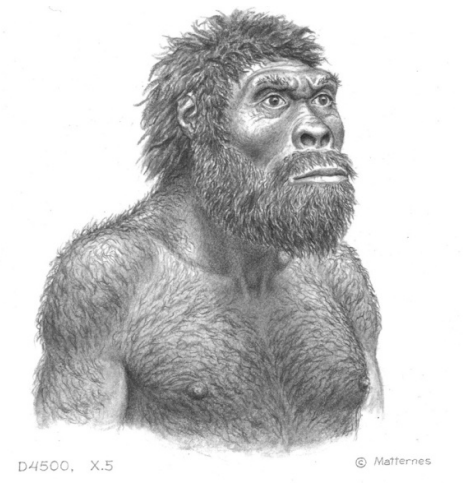
Were Earliest Humans All 1 Species? Oddball Skull Sparks Debate

The earliest, now-extinct human lineages, once thought to be multiple species, may actually have been one species, researchers now controversially suggest.

By Charles Q. Choi, LiveScience Contributor | October 17, 2013 02:01pm ET

Modern humans, Homo sapiens, are the only living member of the human lineage, Homo, which is thought to have arisen in Africa about 2 million years ago at the beginning of the ice age, also referred to as the Pleistocene Epoch. Many extinct human species were thought to once roam the Earth, such as Homo habilis, suspected to be among the first stone-tool makers; the relatively larger-brained Homo rudolfensis; the relatively slender Homo ergaster; and Homo erectus, the first to regularly keep tools it made.

To learn more about the roots of the human family tree, scientists investigated a completely intact, approximately 1.8-million-year-old skull excavated from the medieval hilltop town of Dmanisi in the Republic of Georgia. Archaeological excavations there about 30 years ago unexpectedly revealed that Dmanisi is one of the oldest-known sites for ancient human species out of Africa and the most complete collection of Homo erectus skulls and jaws found so far. The world's largest, extinct cheetah species once lived in the area, and scientists cannot rule out whether it fed on these early humans.



This fossil, the most massively built skull ever found at Dmanisi, is the best-preserved fossil of an early human species discovered yet. It probably belonged to a male, and its right cheekbone has signs that it healed from a fracture.

"We can only guess how the fracture was inflicted on the individual — it could be that it had an argument with another member of the group it lived in, or it could be that it fell down," study co-author Christoph Zollikofer, a neurobiologist at the Anthropological Institute and Museum in Zurich, Switzerland, told LiveScience.

An artist's conception revealing what "Skull 5" may have looked like some 1.8 million years ago when he (the scientists suspect the remains come from a male) lived.
Credit: Art courtesy of J.H. Matternes

Unique skull

This new skull, called Skull 5, was discovered alongside the remains of four other skulls of ancient humans, all of them associated with the same location and period of time, which back 1.8 million years ago was a relatively temperate mix of forest and steppe near a river. The fossil is unlike any other Homo remains on record — it combines a long face, massive jaw and large teeth with a small braincase, just about a third the size of that found in modern humans and no larger than those of much more primitive African fossils and even modern gorillas. Scientists hadn't observed such a combination of features in an early Homo fossil until now. [In Photos: Fossils Reveal Our Closest Human Ancestor]

"Had the braincase and the face of Skull 5 been found as separate fossils at different sites in Africa, they might have been attributed to different species," Zollikofer said in a statement.

The level of variation seen in Homo fossils is typically used to define separate species. However, the scientists found the level of diversity now seen between the five sets of fossils at Dmanisi — Skull 5 and the four other specimens — is no greater than any seen between five modern humans or five chimpanzees.

"If you take the biggest skull there and compare it to the smallest, the smallest one is 75 percent the size of the bigger one, and that's absolutely standard in what you would see in modern humans," Zollikofer said.

This discovery is supported by recent findings from these researchers showing that differences seen in Dmanisi jawbones that might seem to suggest they came from different species actually are mostly due to differences in how teeth get worn down.

"The Dmanisi individuals all belong to a population of a single early Homo species," Zollikofer said. At the same time, "the five Dmanisi individuals are conspicuously different from each other, but not more different than any five modern human individuals, or five chimpanzee individuals from a given population."

The scientists also investigated the level of variation seen among ancient African Homo fossils. They found their level of diversity was similar to that seen in Dmanisi. As such, the researchers suggest that early, diverse Homo fossils may not represent several human species each specialized for their habitat, but rather variants of a single lineage that emerged from Africa capable of coping with a variety of habitats.

In other words, instead of Africa once being home to multiple human species such as Homo erectus, Homo habilis, Homo ergaster andHomo rudolfensis, "we think it is sensible to attribute all specimens to Homo erectus," Zollikofer told LiveScience. "We now have one global human species," Zollikofer said. "What we can infer from our study at Dmanisi is that at 1.8 million years ago, there was another single global human species."

Controversial human find

The researchers caution they do not propose all fossil human specimens, including Neanderthals and modern humans, are lumped into Homo erectus. "We only refer to the time between 2 million and 1.8 million years ago," Zollikofer said. "We are not compulsive lumpers."

The researchers expect their interpretation of their findings to prove controversial among some other scientists. In rebuttal to any who suggest early Homo fossils all belong to multiple species and not one, Zollikofer asks "opponents to present us the magic-wand methods that they use to recognize species from single specimens."

Although paleoanthropologist Ian Tattersall, who did not participate in this research, told LiveScience from Laos in Southeast Asia that "this is a most amazing and important specimen," he added, "I believe it is a mistake to force it into Homo erectus in the interests of maintaining a linear picture of human evolution. It is actually very distinctive morphologically, and it dramatically underscores that human evolution involved vigorous diversification and experimentation with the hominid potential."

"I think they will be proved right that some of those early African fossils can reasonably join a variable Homo erectus species," paleoanthropologist Chris Stringer at the Natural History Museum in London, who did not take part in this study, told LiveScience. "But Africa is a huge continent with a deep record of the earliest stages of human evolution, and there certainly seems to have been species-level diversity there prior to 2 million years ago, so I still doubt that all of the 'early Homo' fossils can reasonably be lumped into an evolving Homo erectus lineage. We need similarly complete African fossils from 2 million to 2.5 million years ago to test that idea properly." The scientists detailed their findings in the Oct. 18 issue of the journal Science.

http://www.livescience.com/40510-sleep-cleans-brain-harmful-toxins.html

A Night's Sleep Cleans Brain of Harmful Toxins

A good night's sleep conveys many benefits to a person, including boosts to memory, concentration and learning. Now, another benefit of sleep has been discovered — it flushes out harmful toxins that build up in the brain during the day, researchers say.

By Charles Choi, Contributing writer | October 17, 2013 02:06pm ET

The point of sleep remains one of the greatest unsolved mysteries in science. Although people spend about one-third of life asleep, researchers still do not know why.

We do know that when people are sleep-deprived, they have problems making decisions and trouble learning, and no human can go without sleep for more than a handful of days. Research has also revealed sleep helps memories form, and it gives the body time to repair itself.

Now, scientists find changes in the brain that are unique to bedtime.

"We show that the brain cleans itself during sleep," study author Dr. Maiken Nedergaard, co-director of the University of Rochester Medical Center's Center for Translational Neuromedicine in Rochester, N.Y., told LiveScience.

The researchers investigated the flow of fluids in the brains of sleeping and awake mice. They focused on the flow within the glymphatic system, the spaces between brain cells. The glymphatic system acts much like a sewer, helping to clear out the waste products that brain cells generate during regular tasks.

Experiments revealed these interstitial spaces in the brains of sleeping or anesthetized mice were 60 percent larger than those of the brains of mice that are awake. Interstitial space takes up 14 percent of the volume of the brain of awake mice, while it makes up 23 percent of the brain of sleeping or anesthetized mice.

These changes make the brains of sleeping mice much better equipped to remove its trash. The scientists detailed their findings in the Friday (Oct. 18) issue of the journal Science.

"The brain only has limited energy at its disposal, and it appears that it must [choose] between two different functional states — awake and aware, or asleep and cleaning up," Nedergaard said in a statement. "You can think of it like having a house party. You can either entertain the guests, or clean up the house, but you can't really do both at the same time."

For instance, the protein beta-amyloid, which is linked with Alzheimer's disease, flowed out of the brains of sleeping mice twice as fast as it flowed out of the brains of awake mice. Overall, the flow of waste out of the brain while awake was only 5 percent of what it was when mice slept.

Also, the researchers surprisingly found that cells in the brain shrink by 60 percent during sleep. This creates more space between the cells, helping waste to wash out the brain's plumbing more effectively.

The scientists noted that a hormone called noradrenaline is less active in sleep. This chemical is released in bursts when the brain needs to become alert, often in response to threats. The research team speculated noradrenaline might help control how brain cells expand and contract during sleeping and waking.

"These findings have significant implications for treating 'dirty brain' disease like Alzheimer's," Nedergaard said. "Understanding precisely how and when the brain activates the glymphatic system and clears waste is a critical first step in efforts to potentially modulate this system and make it work more efficiently."

This discovery might also help explain why larger animal species typically sleep less than smaller ones, neuroscientist Suzana Herculano-Houzel, of the Federal University of Rio de Janeiro in Brazil, who did not take part in the new study, wrote in a review on this work.

For instance, bats sleep as many as 20 hours a day, while giraffes and elephants sleep as little as three to four hours daily. It could be that larger brains have more interstitial space to accumulate toxins, and so could withstand much longer periods of waking before the need for sleep, Herculano-Houzel said.

http://www.sciencedaily.com/releases/2013/10/131017144700.htm

Men-Only Hepatitis B Mutation Explains Higher Cancer Rates

A team of researchers has identified a novel mutation in the hepatitis B virus (HBV) in Korea that appears only in men and could help explain why HBV-infected men are roughly five times more likely than HBV-infected women to develop liver cancer

Although some women do progress to cirrhosis and liver cancer, the mutation is absent in HBV in women. The research is published ahead of print in the Journal of Clinical Microbiology.

"This is the first mutation found that can explain the gender disparity in incidence of hepatocellular carcinoma," says Bum-Joon Kim of Seoul National University, Korea, an author on the study.

In the study, the researchers randomly collected and analyzed serum samples from 292 patients with chronic HBV infection who visited one of 3 hospitals in Korea from 2003-2005. Previous studies had suggested that a gene mutation known as W4P/R was associated with higher incidence of liver cancer and cirrhosis. They developed an assay to specifically identify HBV with the W4P/R mutation. When compared to patient outcomes, the W4P/R mutation was significantly associated with severe liver disease and was found exclusively in male patients.

The investigators believe the assay they developed to discover the mutation may hold promise as a diagnostic for predicting male progression to cirrhosis and liver cancer. They caution that first larger studies are necessary to confirm their findings, as only 67 of the 292 samples came from women.

HBV infection is a global health problem, with 350 million chronic carriers of the virus, a number that is roughly equivalent to the combined populations of the US and Canada. The prevalence of infection ranges from less than half a percent in the United States to around 10 percent in Asia, to as high as 15 percent in parts of Africa. Major means of transmission include injection drug abuse, unprotected sex, and transmission via childbirth. Worldwide mortality is about 600,000 annually, according to the World Health Organization. In the US, despite the availability of a vaccine, an estimated 3,000 die annually from hepatocellular cancer or chronic liver disease caused by hepatitis B.

http://www.bbc.co.uk/news/magazine-24551945

The drugs derived from deadly poisons

These days we have access to a huge array of medicines to protect us from pain, disease and death. But, as Michael Mosley has been discovering, the source of many of our more remarkable medicines have been deadly poisons.

Take a look at this picture.

It is the most poisonous substance known to man. A couple of teaspoons would be enough to kill everyone in the UK. A couple of kilos would kill every human on earth. It is so dangerous that it is manufactured in military installations and at around £100 trillion per kilo it is also the most expensive substance ever made. Yet despite being so toxic and so costly it is in huge demand. Many people pay large amounts of money to have it injected into their foreheads.

It is botulinum toxin - better known as Botox - a toxin produced by bacteria first discovered in poorly prepared sausages during the 18th Century. It was named after the Latin for sausage - botulus.

On the LD50 toxicity scale, which measures how much of a substance you would need to kill half the people it is given to, Botox measures just 0.000001 mg/kg. In other words you need would need around 0.00007mg to kill a 70kg man like me. Or to put it another way, a lethal dose for me would weigh less than one cubic millimetre of air.

Botulinum toxin kills its victims by causing respiratory failure. It is a neurotoxin - it enters nerves and destroys vital proteins. This stops communication between nerves and muscles. Only the growth of new nerve endings can restore muscle function, and that can take months.

Its main claim to fame is that it will iron out wrinkles in ageing faces and does so by destroying the nerves that cause frowning. The quantities used are tiny - a few billionths of a gram, dissolved in saline. In the name of science I tried Botox a few years ago. It certainly smoothed away the wrinkles but it also gave me a weird expression, until the new nerve endings grew.

But botulinum toxin is far more than simply a vanity product. It is extremely useful for treating a number of medical conditions, ranging from eye squints to migraines, excess sweating to leaky bladders. In fact there are currently more than 20 different medical conditions that botulinum toxin is being used to treat. More are being discovered all the time.

Botulinum toxin is just one example of extraordinarily dangerous poisons that have useful medical applications. Captopril, a $1bn antihypertensive drug, was developed from studies made on snake venoms. Exenatide, marketed as Byetta, is an effective and extremely lucrative drug used to treat type-2 diabetics. It comes from studies of the saliva of the Gila monster, a large venomous lizard that lives in the south-western US and Mexico
But the impact of poisons on modern medicine go deeper than simply providing new forms of treatment. One poison in particular helped shape the entire modern pharmaceutical industry.
In Victorian Britain, life insurance was a booming industry. This easy money led to a surge in murders, many of them by poison.
One of the most high profile cases was a woman called Mary Ann Cotton who, in 1873, was tried for multiple murders. She had been married four times and three of her husbands, all heavily insured, died. The one who survived seems to have done so because he refused to take out insurance. So she left him.
In all, 10 of her children died of what seemed to be gastric-related illnesses. Each must have been a tragic loss, but fortunately for Cotton most were insured.
Her mother, her sister-in-law, and her lover all died. And in each case, she benefited. By 1872, the unfortunate woman had lost an astonishing 16 close friends or family members. But there was one left - her seven-year-old stepson, Charles. She tried to give him away to the local workhouse but they wouldn't have him. So young Charles soon died.
The manager of the workhouse, however, got suspicious and contacted the police. They soon decided Cotton must have poisoned the boy and thought they knew how she'd done it - with arsenic.
Arsenic oxides are minerals and as a poison are almost unrivalled. They are tasteless, dissolve in hot water and take less than a hundredth of an ounce to kill. Yet in the 19th Century, marketed as a rat poison, arsenic oxide was cheap and easily available. Children would blithely collect it from the shops along with the tea, sugar and dried fruits.
The trial of Mary Ann Cotton would hinge on whether they could find traces of arsenic in the body of her stepson. Forensic science was still in its infancy but they did have a good test for arsenic. This was because there was an awful lot of arsenic poisoning around.
A sample from the boy's stomach and intestines was heated with acid and copper. If arsenic was present, the copper would turn dark grey and, when placed on paper soaked in mercury bromide, produce a tell-tale yellowy-brown stain.
When they tested the body of poor little Charles they discovered that he had indeed died of a lethal dose of arsenic. Cotton was convicted of his murder and hanged in Durham Jail. She was never taken to trial for the mysterious deaths of her mother, three husbands, two friends and 10 other children.
It was a rash of murders and poisonings like this one that led first to the Arsenic Act and then to the Pharmacy Act 1868. This act ruled that the only people who could sell poisons and dangerous drugs were qualified pharmacists and druggists.
So it was from poisonings, accidents and murders that the modern legitimate business of pharmacy finally emerged. And one compound - arsenic trioxide - has also found a legitimate medical use, as an anti-cancer agent.
Pus, Pain and Poison is on BBC Four, Thursday 17 October at 21:00 BST and you can catch up on iPlayer.
http://bit.ly/179L5tW

For instant climate change, just add one large comet

A COMET may have sent temperatures soaring 55 million years ago.

18 October 2013 by Colin Barras

Two geologists claim they have evidence that carbon dioxide levels in Earth's atmosphere more than doubled in a single year at the end of the Palaeocene. The increase helped trigger the most extreme change in surface temperatures since dinosaurs ruled the land. The speed of the change makes an extraterrestrial impact the likely cause, they say.
Global temperatures rose by about 5 °C at the end of the Palaeocene – an event known as the Palaeocene-Eocene Thermal Maximum (PETM). Because more CO2 in the atmosphere makes the oceans more acidic, the event can be tracked by looking at the amount of calcium carbonate deposited on the ocean floor by marine organisms. In more acidic waters, less is deposited. Sediment analysis has suggested the increase in CO2 that caused the PETM took between 750 and 30,000 years.
But James Wright and Morgan Schaller at Rutgers University in Piscataway, New Jersey, think it happened much more rapidly. They analysed sediments from a shallow Atlantic Ocean shelf where sediment accumulates faster than it does in the deep sea, making it easier to see seasonal fluctuations in the amount deposited. The pair say that within just one annual cycle about 55 million years ago, the amount of calcium carbonate laid

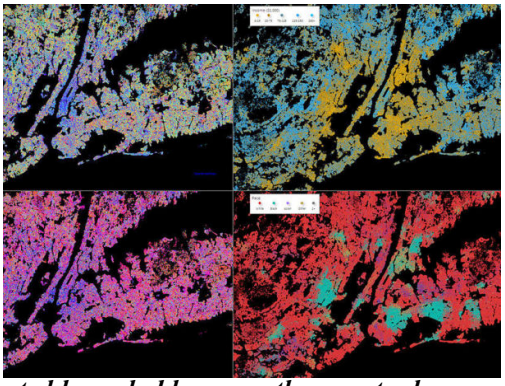
down dropped by 5 per cent. This suggests a very sudden addition – within a year – of atmospheric CO2 (PNAS, doi.org/n8t).
So what could have caused so rapid a release of such a vast amount of CO2? "A large comet impact meets the criteria," says Wright. If the change to the carbon cycle really was instantaneous, a comet is a good candidate, agrees Dallas Abbott at Columbia University in Palisades, New York – although it would have to have been large to have such a dramatic effect.

http://www.sciencedaily.com/releases/2013/10/131017144418.htm

Web-Based Map Allows Users to See Intricate Patterns in U.S. Population

A new web-based mapping site allows users to see stark racial boundaries, subtle shifts in income, and intricate patterns of race, age, household size and income for any location in the United States.

The map, known as the ***synthetic population viewer*** and developed by researchers at RTI International, allows users to look at how the U.S. population organizes itself across the landscape and how age, income, race and household size vary within cities.



"This new era of complex, synthetic household data enables fine-scale, multidimensional demographic patterns and microcommunities to emerge from simple-to-use, web-based maps," said Bill Wheaton, director of RTI's Geospatial Science and Technology program.
The interactive map contains a representation of more than 112 million households and more than 280 million individuals in all 50 U.S. states and Washington, D.C. The information is based on the 2005-2009 American Community Survey.

Synthetic population viewer allows users to look at realistic, computer-generated households across the country by age, income, race and household size **(Credit: RTI International)**

Unlike typical census maps by county or census tract, these synthetic microdata are a representation of individual households. "The data represent the reality of the U.S. household population very well. By representing each and every household as a point on the map, a wealth of complex patterns becomes apparent," Wheaton said. "In order to protect privacy, the interactive map doesn't show actual households in their exact locations like Google Earth. Nonetheless, the data represent real households in reasonably accurate detail, enabling the map to show complex population distributions."
"It's a rich tool for anyone interested in exploring the amazing diversity of human household populations in the U.S.," Wheaton said.
Available online, the map and underlying data are free for use by everyone, from GIS professionals to college students working on projects to the general public simply interested in looking at population patterns.
"The underlying data can be used in computer simulations to track the spread of infectious disease or to understand how transportation networks are used, how people make choices about where to live, how a given intervention might affect obesity, how best to optimize supply chain operations, and many other uses," Wheaton said. "But, aside from these complex research simulations, simply mapping the data as we've done with this viewer tells a story that everyone can understand."
The project was funded as part of the Models of Infectious Disease Agent Study (MIDAS) grant from the National Institute of General Medical Sciences. MIDAS is a multimillion dollar bioterrorism defense initiative to help infectious disease researchers understand the dynamics of disease and test various mitigation options to reduce the effects of epidemics.

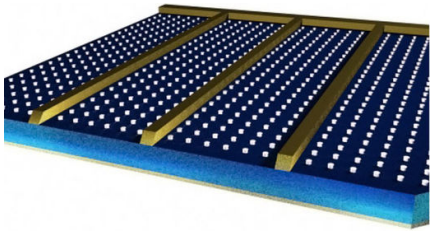
http://scitechdaily.com/aluminum-studs-improve-solar-panel-efficiency/

Aluminum Studs Improve Solar Panel Efficiency

Scientists at the Imperial College London have shown that the efficiency of solar panel designs can be improved by up to 22 percent by covering their surface with aluminum studs.

Most solar cells used in homes and industry are made using thick layers of material to absorb sunlight, but have been limited in the past by relatively high costs. Many new, lower cost designs are limited as their layer of light-absorbing material is too thin to extract enough energy.
In new research, scientists have demonstrated that the efficiency of all solar panel designs could be improved by up to 22 percent by covering their surface with aluminum studs that bend and trap light inside the absorbing layer.
At the microscopic level, the studs make the surface of the solar panels look similar to the interlocking building bricks played with by children across the world.

The study is published in the journal Scientific Reports by scientists from Imperial College London and international collaborators in Belgium, China and Japan.
"In recent years both the efficiency and cost of commercial solar panels have improved but they remain expensive compared to fossil fuels. As the absorbing material alone can make up half the cost of a solar panel our aim has been to reduce to a minimum the amount that is needed," said lead author Dr Nicholas Hylton from the Department of Physics at Imperial College London.
"The success of our technology, in combination with modern anti-reflection coatings, will take us a long way down the path towards highly efficient and thin solar cells that could be available at a competitive price."
Dr Hylton and his colleagues attached rows of aluminum cylinders just 100 nanometers across to the top of the solar panel, where they interact with passing light, causing individual light rays to change course. More energy is extracted from the light as the rays become effectively trapped inside the solar panel and travel for longer distances through its absorbing layer.



A solar panel with rows of aluminum studs and large electrical connections. The studs have been enlarged here but would normally be so small that they are invisible to the naked eye. **Credit: Imperial College London / Nicholas Hylton**

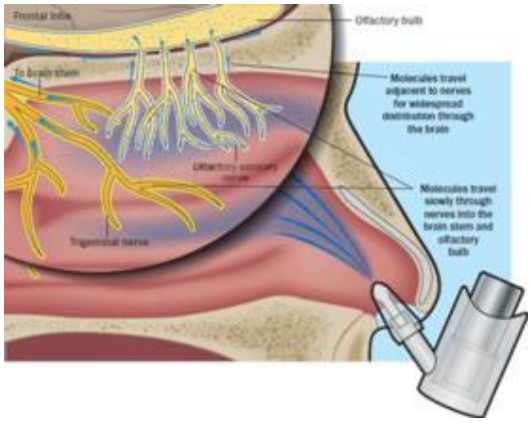
In the past scientists have tried to achieve the light bending effect using silver and gold studs because those materials are known to strongly interact with light, however these precious metals actually reduce the efficiency as they absorb some of the light before it enters the solar panel.
"The key to understanding these new results is in the way the internal structures of these metals interact with light. Gold and silver both have a strong effect on passing light rays, which can penetrate into the tiny studs and be absorbed, whereas aluminum has a different interaction and merely bends and scatters light as it travels past them into the solar cells."
An additional advantage to this solution is that aluminum is cheaper and far more abundant than silver and gold. The future success of this technology opens up the possibility of making flexible solar panels that could be applied to any flat or curved surface, which could be used to power everything from domestic appliances to portable electronics like laptops.
Publication: N. P. Hylton, et al., "Loss mitigation in plasmonic solar cells: aluminium nanoparticles for broadband photocurrent enhancements in GaAs photodiodes," Scientific Reports 3, Article number: 2874; doi:10.1038/srep02874
Source: Simon Levey, Imperial College London

http://bit.ly/19UA9L3

Inhaled Stem Cells Might Replace Lost Neurons

Intranasal stem cell therapy may one day treat brain disorders

By Caitlin Shure | Saturday, October 19, 2013



Many diseases of the central nervous system involve the death of neurons—so, theoretically, the replacement of dead cells should improve symptoms of degenerative disorders such as Parkinson's, Huntington's, amyotrophic lateral sclerosis (ALS) and Alzheimer's, as well as stroke and brain tumors. Stem cell therapy may do just that even though evidence of its effectiveness is mixed.
In any cell transplant procedure, the host organ—in this case, the brain—may reject its new additions. Further, it is unclear whether grafted cells can truly integrate into complex neural circuitry. Finally, current procedures require invasive surgical implantation, which can be expensive and risky. The surgery can cause neural inflammation, and the implanted cells may quickly die.
Intranasal administration may address at least some of these issues. Most important, it eliminates the need for surgery. Further, some research suggests that stem cells delivered intranasally are "smart"—they do not spread through the brain indiscriminately but instead target damaged cells.
Although it is difficult to predict when medical practice will adopt stem cell therapy for the brain, animal studies have produced some promising results. In a rat model of Parkinson's, for example, treatment with intranasal stem cells appeared to improve motor function and slow the neurological deterioration associated with the disease.

http://www.eurekalert.org/pub_releases/2013-10/jhm-cm101713.php

'Random' cell movement is directed from within

Clarified role of signal-relay proteins may help explain spread of cancer

Cell biologists at The Johns Hopkins University have teased apart two integral components of the machinery that causes cells to move. Their discovery shows that cellular projections, which act as hands to help a cell "crawl," are apparently always initiated by a network of message-relaying proteins inside the cell. It was already known that in directional movement, the network is activated by sensor proteins on the cell's surface in response to external cues. They now know that in random movement, the messenger network is also causative: It can self-activate spontaneously.

Because cellular movement is necessary for everything from embryo development to wound healing to cancer metastasis, the work is expected to have wide-ranging implications for understanding and manipulating these biological processes, the researchers say. In fact, they note that defects in the messenger protein network have been linked to many types of cancer.

The findings are summarized in a paper published online Oct. 20 in the journal Nature Cell Biology.

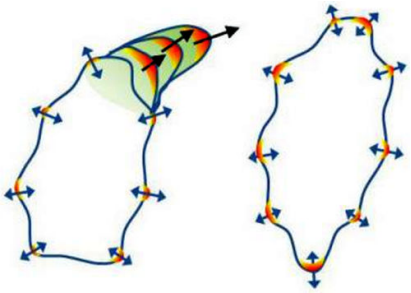


Diagram of a hand-like projection (left) versus the "ruffling" of the cell membrane (right) that occur with and without the activation of the messenger protein network. **Devreotes Lab**

"It was previously thought that messenger proteins were only involved in directional movement: that without them, cells could only move randomly, through the spontaneous formation of these hand-like projections," says Peter Devreotes, Ph.D., professor and director of the Department of Cell Biology at the Johns Hopkins University School of Medicine. "Now we know that even random movement requires the activation of the messenger protein network."

According to Devreotes, a key component of a cell's machinery is a crisscrossing network of protein chains that wrap around the inside edge of the cell, giving it shape and structure and inspiring the name "cytoskeleton." To allow movement, this network must build itself up in a given area of the cell, pushing the cell's membrane outward and creating a hand-like projection that can "grip" the external environment and pull the cell forward. The cytoskeleton, Devreotes says, takes orders from the messenger protein network, which is connected to sensor proteins on the outside of the cell. The sensors detect directional signals coming from other parts of the body and pass them on to the messenger proteins, which in turn call on the cytoskeletal proteins to create a projection in the right direction.

In their experiments, the Devreotes team sought to understand the relationship between each of these components. They began, he says, by bathing their cells in a drug that paralyzes the cytoskeleton. Not surprisingly, the cells wouldn't move, but the spontaneous responses of the messenger network still occurred. Devreotes explains, "You can think of the cell as a row boat with several crewmen and a coxswain, sitting in the rear, steering the rudder and shouting at the crew to keep their movements in sync. If the oars are taken away (i.e., a paralyzed cytoskeleton), the coxswain can yell at the crew as much as he wants but the boat won't move."

Using a combination of genetic and imaging techniques, the team then incapacitated the other components of the system one by one and watched what happened. Inhibiting the messenger proteins (the coxswain) showed that the cytoskeleton has an intrinsic rhythm that "ruffles" the cell membrane every 10 seconds, but there were no projections created, so the cells didn't move. "It's as if the crew can still row without the coxswain but each person is rowing in a different direction so the boat just stays where it is," says Chuan-Hsiang Huang, a co-author of the study.

The team expected that when they removed the sensor proteins they would see no movement, based on the old idea that both random and directional cell movement required signaling from these proteins. However, they found instead that the messenger network is "excitable." That is, without the sensor proteins or external cues, the messenger proteins can still work on their own, telling the cytoskeleton to create projections here or there, moving the cells about randomly. "This situation could be compared to a boat without a rudder. The coxswain is there to coordinate the rowing of the crew so the boat does move, but not in any specific direction," explained co-author Ming Tang.

Devreotes says the most exciting implications of this research are those relevant to cancer metastasis. "Several of the messenger proteins that we studied are found in higher quantities during cancer progression, and it is likely that the resulting changes in cell movement are involved in the advancement of the disease," he says. "We now know that we have to create drugs that target the messenger proteins (not just the sensor proteins) in order to entirely immobilize tumor cells."

The other authors of the report are Changji Shi and Pablo Iglesias of The Johns Hopkins University.
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http://www.eurekalert.org/pub_releases/2013-10/wifb-fvw101613.php

Flu virus wipes out immune system's first responders to establish infection

Flu virus is able to infect its host by first killing off the cells of the immune system that are actually best equipped to neutralize the virus.

Written by Matt Fearer

CAMBRIDGE, Mass. Revealing influenza's truly insidious nature, Whitehead Institute scientists have discovered that the virus is able to infect its host by first killing off the cells of the immune system that are actually best equipped to neutralize the virus.

Confronted with a harmful virus, the immune system works to generate cells capable of producing antibodies perfectly suited to bind and disarm the hostile invader. These virus-specific B cells proliferate, secreting the antibodies that slow and eventually eradicate the virus. A population of these cells retains the information needed to neutralize the virus and takes up residence in the lung to ward off secondary infection from re-exposure to the virus via inhalation.

On the surface of these so-called memory B cells are high-affinity virus-specific receptors that bind virus particles to reduce viral spread. While such cells should serve at the body's first line of defense, it turns out that flu virus exploits the specificity of the cells' receptors, using them to gain entry, disrupt antibody production, and ultimately kill the cells. By dispatching its enemies in this fashion, the virus is able to replicate efficiently before the immune system can mount a second wave of defense. This seemingly counter-intuitive pathway to infection is described this week in the journal Nature.

"We can now add this to the growing list of ways that the flu virus has to establish infection," says Joseph Ashour, a co-author of the Nature paper and a postdoctoral researcher in the lab of Whitehead Member Hidde Ploegh. "This is how the virus gains a foothold," adds Ploegh lab postdoc Stephanie Dougan, also a co-author of the study. "The virus targets memory cells in the lung, which allows infection to be established -- even if the immune system has seen this flu before."

Discovering this dynamic of the virus was no small task, in part because virus-specific B cells are found in exceedingly small numbers and are extremely difficult to isolate. To overcome these challenges, Dougan together with students Max Popp and Roos Karssemeijer leveraged a protein-labeling technology developed earlier in the Ploegh lab to attach a fluorescent label to influenza virus, thus identifying flu-specific B cells by their interaction with fluorescent flu micelles. This step was essential because no flu protein can be tagged in the conventional manner with green fluorescent protein (GFP) in the context of an infectious virus. Dougan then introduced the B cells' nuclei into enucleated mouse egg cells via somatic cell nuclear transfer (SCNT) -- a cloning technique she learned in Whitehead Founding Member Rudolf Jaenisch's lab -- to generate a line of mice with virus-specific B cells and cell receptors.

Though complicated, the generation of mice with B cells specific for a known pathogen allowed Dougan and Ashour to track the virus's interactions with the cells in unprecedented fashion. Because the infectious process they discovered is likely not exclusive to influenza virus, these scientists believe their approach could have implications for other viruses as well. "We can now make highly effective immunological models for a variety of pathogens," says Dougan. "This is actually a perfect model for studying memory immune cells."

Adds Ashour: "This is research that could help with rational vaccine design, leading to more effective vaccines for seasonal flu. It might even suggest novel strategies for conferring immunity."

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"Antigen-specific B- cell receptor sensitizes B cells to infection by influenza virus" Nature, October 20, 2013
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