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Cancer gene unintentionally ends the life of cancer cells, turns off life supporting genes

Discovery triggers rethinking how to unmask cancer vulnerabilities

Myc cancer gene empowers tumor cells to relentlessly divide but simultaneously, provokes a cell suicide process called apoptosis. Myc controls cells by commanding the expression of every tenth of the genes in the nucleus of a tumor cell. However, in spite of more than two decades of intense research, no Myc motivated killer genes have been found. A team of researchers from the University of Wurzburg, Germany, and the University of Helsinki, Finland, discovered that searching (for) Myc motivated killer genes is akin to barking up the wrong tree. The new findings suggest that Myc makes cancer cells vulnerable to cell death by repressing well-being genes, which are essential for maintaining the life of the cells.

Myc is a high-ranking transcriptional commander, which occupies the controller sites of thousands of genes in the genome. It works together with its closest partners, Max and Miz-1, to turn on and off genes, which produce mRNA and then new proteins. These new proteins take care of the cell's energy metabolism and cell division program, and even command cells to die when needed. In cancer, Myc levels and its power becomes overwhelming and the cells start to divide wildly and refuse to die, leading to rapid growth of a tumor mass.

Professor Martin Eilers, from University of Wurzburg and his Ph.D student Katrin Wiese had been working with an experimental mutant version of Myc, which collaborates with Max but refuses to work with the partner Miz-1. These experiments revealed something truly exciting about Myc. Katrin Wiese explains, "Our mutant Myc turned on genes without a hitch but it had difficulties to turn genes off. Even with this handicap, mutant Myc was able to instruct the cells to divide but it could not instruct the cells to die".

Only after these experiments, the researchers realized that a long cultivated idea that Myc kills cells by turning on some killer genes may not be right. Instead, Myc could kill the cells by turning off such genes that cells need to sustain their lives.

To find out what these well-being genes could be, Wiese and Eilers teamed up with Dr Juha Klefström and his Ph.D student Heidi Haikala, working at the University of Helsinki, Finland. The Finnish researchers had used a set of "gene wrenches" called RNAi molecules, to turn off genes of interest, and with these additional experiments the researchers identified tracks leading to a nuclear protein and gene controller protein called SRF.

"It seems that in cancer cells, Myc and its partner Miz-1 invade to gene controller areas where they are not supposed to go. In this situation, Myc and Miz-1 disturb genes, which cells need for their well-being", tells Heidi Haikala. "The well-being genes, when not disturbed, supply cells with bioenergy and nestling connections with other cells. Myc and Miz-1 proteins especially collided with a gene expression controller protein called SRF and, we believe that this clash in the nucleus brings down the well-being genes and makes cancer cells suicidal."

Can these cell death pathways and reactions be exploited in cancer therapies?

The senior researchers of the study, Martin Eilers and Juha Klefström are excited about the concept that Myc's ability to turn off rather than turn on genes is a key to cell death: "It is much easier to bring cellular activities down than up with the existing drugs. These new findings suggest that a drug that brings well-being gene activities further down could significantly boost the killer activity of Myc in tumor cells." The study will be published in EMBO Journal 20th April.

http://www.eurekalert.org/pub_releases/2015-04/kcl-dwa042015.php

Darwin, Wallace, and the overlooked third man

The horticulturist who came up with the concept of 'evolution by natural selection' 27 years before Charles Darwin did should be more widely acknowledged for his contribution, states a new paper by a King's College London geneticist.

The paper, published in the Biological Journal of the Linnean Society, argues that Patrick Matthew deserves to be considered alongside Charles Darwin and Alfred Russel Wallace as one of the three originators of the idea of large-scale evolution by natural selection.

Furthermore, Matthew's version of evolution by natural section captures a valuable aspect of the theory that isn't so clear in Darwin's version - namely, that natural selection is a deductive certainty more akin to a 'law' than a hypothesis or theory to be tested.

Patrick Matthew (1790-1874) was a Scottish landowner with a keen interest in politics and agronomy. He established extensive orchards of apples and pears on his estate at Gourdie Hill, Perthshire, and became adept in horticulture, silviculture and agriculture.

Whilst Darwin and Wallace's 1858 paper to the Linnean Society, On the Origin of Species, secured their place in the history books, Matthews had set out similar ideas 27 years earlier in his book On Naval Timber and Arboriculture. The book, published in 1831, addressed best practices for the cultivation of trees for shipbuilding, but also expanded on his concept of natural selection.

"There is a law universal in nature, tending to render every reproductive being the best possibly suited to its condition that its kind, or that organized matter, is

susceptible of, which appears intended to model the physical and mental or instinctive powers, to their highest perfection, and to continue them so. This law sustains the lion in his strength, the hare in her swiftness, and the fox in his wiles." (Matthew, 1831: 364)

In 1860, Matthew wrote to point out the parallels with his prior work, several months after the publication of On the origin of species. Darwin publically wrote in 1860 "I freely acknowledge that Mr. Matthew has anticipated by many years the explanation which I have offered of the origin of species", while Wallace wrote publically in 1879 of "how fully and clearly Mr. Matthew apprehended the theory of natural selection, as well as the existence of more obscure laws of evolution, many years in advance of Mr. Darwin and myself", and further declared Matthew to be "one of the most original thinkers of the first half of the 19th century". However, both asserted their formulations were independent of Matthew's.

Even if Matthew did not influence Darwin and Wallace, his writings provide a valuable third point of reference on the notion of macroevolution by natural selection, argues the paper's author, Dr Michael Weale. Dr Weale has created a public website to act as an online repository of the writings by Patrick Matthew, including some of his lesser-known work.

Dr Michael Weale, from the Department of Medical and Molecular Genetics at King's College London, said: 'Whilst Darwin and Wallace both deserve recognition for their work, Matthew, the outsider who deduced his idea as part of a grand scheme of a purposeful universe, is the overlooked third man in the story. Matthew's story is an object lesson in the perils of low-impact publishing. Despite its brevity, and to some extent because of it, Matthew's work merits our renewed attention.'

http://www.eurekalert.org/pub_releases/2015-04/uom-ttt041515.php

Telling the time by color

Research by scientists at The University of Manchester reveals that the colour of light has a major impact on how our body clock measures the time of day.

It's the first time the impact of colour has been tested and demonstrates that colour provides a more reliable way of telling the time than measuring brightness.

In research being published on April 17th in the Open Access journal PLOS Biology, the researchers looked at the change in light around dawn and dusk to analyse whether colour could be used to determine time of day. Besides the well-known changes in light intensity that occur as the sun rises and sets they found that during twilight, light is reliably bluer than during the day.

The scientists next recorded electrical activity from the body clock while mice were shown different visual stimuli. They found that many of the cells there were more sensitive to changes in colour between blue and yellow than to changes in brightness.

The scientists then used measurements of the changes in the colour spectra taken from the top of the University's Pariser Building, to construct an artificial sky which recreated the daily changes in colour and brightness.

Mice were placed beneath the sky for several days and their body temperature was recorded. As expected for nocturnal creatures, the highest body temperatures occurred just after night fell when the sky turned a darker blue - indicating that their body clock was working optimally.

When just the brightness of the sky was changed, with no change in the colour, the mice became more active before dusk, demonstrating that their body clock wasn't properly aligned to the day night cycle.

Dr Timothy Brown from the Faculty of Life Sciences led the research: "This is the first time that we've been able to test the theory that colour affects the body clock in mammals. It has always been very hard to separate the change in colour to the change in brightness but using new experimental tools and a psychophysics approach we were successful."

He continues: "What's exciting about our research is that the same findings can be applied to humans. So in theory colour could be used to manipulate our clock, which could be useful for shift workers or travellers wanting to minimise jet lag."

http://www.eurekalert.org/pub_releases/2015-04/acs-uor042015.php

Use of radiotherapy after prostate cancer surgery declining, despite evidence of benefit

Large study finds fewer than 1 in 10 prostate cancer patients with adverse pathologic features after surgery receive radiation therapy

ATLANTA - Despite strong evidence and guidelines supporting its use, post-surgical radiation therapy for prostate cancer patients at risk of recurrence is declining in the United States. The study, published online in the journal European Urology, finds fewer than 10 percent of patients at risk of recurrence received postoperative radiotherapy within six months of surgery in the U.S.

Although radical prostatectomy (RP) is a common curative treatment for localized prostate cancer, about 30% of patients will develop biochemical recurrence after surgery, meaning their prostate-specific antigen (PSA) level will again rise. For some patients with more aggressive cancers, as many as 60% to 70% can experience biochemical recurrence (also called biochemical failure).

Three large randomized prospective clinical trials, two done in Europe and one in the United States, have demonstrated that postoperative radiotherapy (RT) in patients with adverse pathological features reduces risk of PSA recurrence, may

prevent the need for androgen deprivation therapy (ADT), and may reduce metastasis and improve survival.

In the U.S., the American Society for Radiation Oncology (ASTRO) and American Urological Association (AUA) recommend offering adjuvant RT to patients with adverse pathologic features found at the time of surgery.

To investigate how available evidences were being implemented, researchers from the American Cancer Society and Massachusetts General Hospital led by Helmneh Sineshaw, MD, MPH of the American Cancer Society analyzed data from the National Cancer Data Base (NCDB), a national hospital-based cancer registry database that captures data on approximately 70% of newly diagnosed cancer cases in the United States. The study included 97,270 patients between the ages of 18 and 79 diagnosed between 2005 and 2011.

The data showed that receipt of RT after RP decreased steadily between 2005 and 2011, from 9.1% to 7.3%. And while RT use was higher in younger patients and in those at highest risk for recurrence, overall rates of utilization remain low, with fewer than 20% of patients in subgroups most likely to benefit receiving RT.

The authors say declining utilization of RT could be due to multiple factors including patient preference, physician and referral bias, concern for toxicity, lack of a consistent survival benefit seen in the updated randomized trials, or a growing preference for "salvage radiation," done if a patient's PSA rises in the weeks and months after surgery.

Nonetheless, the authors say additional effort is needed to ensure patients are counseled regarding their options and available evidence "The declining trend in the utilization of postoperative RT calls for the attention of clinicians to make appropriate referrals to radiation oncologists or clinical oncologists when appropriate," they write.

Article: Declining Utilization of Radiotherapy for Adverse Features after Radical Prostatectomy: Results from the National Cancer Data Base; European Urology doi: 10.1016/j.eururo.2015.04.003

http://www.eurekalert.org/pub_releases/2015-04/cwru-dsb041715.php

Drugs stimulate body's own stem cells to replace brain cells lost in multiple sclerosis

Approach may offer new way to reverse disability in multiple sclerosis patients

A pair of topical medicines already alleviating skin conditions each may prove to have another, even more compelling use: instructing stem cells in the brain to reverse damage caused by multiple sclerosis.

Led by researchers at Case Western Reserve, a multi-institutional team used a new discovery approach to identify drugs that could activate mouse and human brain stem cells in the laboratory. The two most potent drugs - one that currently treats athlete's foot, and the other, eczema - were capable of stimulating the regeneration of damaged brain cells and reversing paralysis when administered systemically to animal models of multiple sclerosis. The results are published online Monday, April 20, in the scientific journal Nature.

"We know that there are stem cells throughout the adult nervous system that are capable of repairing the damage caused by multiple sclerosis, but until now, we had no way to direct them to act," said Paul Tesar, PhD, the Dr. Donald and Ruth Weber Goodman Professor of Innovative Therapeutics, and associate professor in the Department of Genetics & Genome Sciences at the Case Western Reserve School of Medicine. "Our approach was to find drugs that could catalyze the body's own stem cells to replace the cells lost in multiple sclerosis."

The findings mark the most promising developments to date in efforts to help the millions of people around the world who suffer from multiple sclerosis. The disease is the most common chronic neurological disorder among young adults, and results from aberrant immune cells destroying the protective coating, called myelin, around nerve cells in the brain and spinal cord.

Without myelin, neural signals cannot be transmitted properly along nerves; over time, a patient's ability to walk, hold a cup or even see is inexorably eroded. Current multiple sclerosis therapies aim to slow further myelin destruction by the immune system, but the Case Western Reserve team used a new approach to create new myelin within the nervous system. Their work offers great promise of developing therapies that reverse disabilities caused by multiple sclerosis or similar neurological disorders.

"To replace damaged cells, much of the stem cell field has focused on direct transplantation of stem cell-derived tissues for regenerative medicine, and that approach is likely to provide enormous benefit down the road," said Tesar, also a New York Stem Cell Foundation Robertson Investigator and member of the National Center for Regenerative Medicine. "But here we asked if we could find a faster and less invasive approach by using drugs to activate native stem cells already in the adult nervous system and direct them to form new myelin. Our ultimate goal was to enhance the body's ability to repair itself."

Tesar emphasized that much work remains before multiple sclerosis patients might benefit from the promising approach. Scientists still must find ways to transform the topical medications for internal use and determine their long-term efficacy and potential side effects. That said, using existing, federally approved drugs enhances the likelihood that the compounds can be made safe for human use.

Tesar and his colleagues could zero in on the two catalyzing medications only because of a breakthrough that his laboratory achieved in 2011. Specifically, the

researchers developed a unique process to create massive quantities of a special type of stem cell called an oligodendrocyte progenitor cell (OPC). These OPCs are normally found throughout the adult brain and spinal cord, and therefore inaccessible to study. But once Tesar and his team could produce billions of the OPCs with relative ease, they could begin to test different existing drug formulations to determine which, if any, induced the OPCs to form new myelinating cells.

Using a state-of-the-art imaging microscope, the investigators quantified the effects of 727 previously known drugs, all of which have a history of use in patients, on OPCs in the laboratory. The most promising medications fell into two specific chemical classes. From there, the researchers found that miconazole and clobetasol performed best within the respective classes. Miconazole is found in an array of over-the-counter antifungal lotions and powders, including those to treat athlete's foot. Clobetasol, meanwhile, is typically available by prescription to treat scalp and other skin conditions such as dermatitis. Neither had been previously considered as a therapeutic for multiple sclerosis, but testing revealed each had an ability to stimulate OPCs to form new myelinating cells. When administered systemically to lab mice afflicted with a multiple sclerosis-like disease, both drugs prompted native OPCs to regenerate new myelin.

"It was a striking reversal of disease severity in the mice," said Robert Miller, PhD, a member of the neurosciences faculty at Case Western Reserve who, with Tesar, is a co-senior author of the Nature paper. The two collaborated on this project while Miller also served as Vice President for Research at Case Western Reserve; since June his primary appointments are at the George Washington University School of Medicine and Health Sciences, where he is Senior Associate Dean for Research and Vivian Gill Distinguished Research Chair. "The drugs that we identified are able to enhance the regenerative capacity of stem cells in the adult nervous system. This truly represents a paradigm shift in how we think about restoring function to multiple sclerosis patients."

While the drugs proved to have extraordinary effects on mice, their impact on human patients will not be known fully until actual clinical trials. Nevertheless, Tesar and his team already have added reason for optimism; in addition to the tests with animal cells, they also tested the drugs on human stem cells - and saw the medication prompt a similar response as seen in the mouse cells. Both medications worked well, with miconazole demonstrating the more potent effects.

"We have pioneered technologies that enable us to generate both mouse and human OPCs in our laboratory," said Fadi Najm, MBA, the first author of the study and Research Scientist in the Department of Genetics & Genome Sciences at the Case Western Reserve School of Medicine. "This uniquely positioned us to test if these drugs could also stimulate human OPCs to generate new myelinating cells."

Tesar, who recently received the 2015 International Society for Stem Cell Research Outstanding Young Investigator Award, said investigators next will work to deepen their understanding of the mechanism by which these drugs act. Once these details are clear, researchers will modify the drugs to increase their effectiveness in people.

The team is enthusiastic that optimized versions of these two drugs can be advanced to clinical testing for multiple sclerosis in the future, but Tesar emphasized the danger of trying to use current versions for systemic human administration.

"We appreciate that some patients or their families feel they cannot wait for the development of specific approved medications," Tesar said, "but off-label use of the current forms of these drugs is more likely to increase other health concerns than alleviate multiple sclerosis symptoms. We are working tirelessly to ready a safe and effective drug for clinical use."

While multiple sclerosis is the initial focus for translating this research into the clinic, a number of other disorders involve myelin loss or dysfunction including cerebral palsy, age-related dementia, optic neuritis and schizophrenia. Any drugs developed that enhance myelination in multiple sclerosis also hold promise for benefiting these other disorders.

"The approach from Case Western Reserve University combines cutting-edge stem cell and drug screening technologies to develop new chemical therapeutics for myelin disorders," said Christopher Austin, MD, director of the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH). NCATS researchers performed key external validation experiments as part of the study. "It is clear that the discovery of drugs that control the function of stem cells in the body represents a promising new era in regenerative medicine."

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Joining Tesar and Miller in this research effort were lead author Fadi Najm and contributing authors Mayur Madhavan, Elizabeth Shick, Robert Karl, Daniel Factor, Tyler Miller and Zachary Nevin, the Department of Genetics & Genome Sciences, Anita Zaremba, Christopher Kantor and Alex Sargent, the Department of Neurosciences, Daniela Schlatzer, Center for Proteomics and Bioinformatics, all of Case Western Reserve School of Medicine; Kevin

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http://www.eurekalert.org/pub_releases/2015-04/uomm-gab041715.php

Guideline authored by University of Maryland neurologist advises when to treat a first seizure

Treatment with an antiepileptic medication immediately after a first seizure may reduce the risk of a second seizure in some adults

Washington, DC -A new guideline released today by the American Academy of Neurology (AAN) and the American Epilepsy Society (AES) found that administering an antiepileptic medication immediately after a first seizure reduces the risk of having another seizure within two years. The guideline, authored by Allan Krumholz, MD, a professor of neurology at the University of Maryland School of Medicine and physician at the Maryland Epilepsy Center at the University of Maryland Medical Center, is the first to address treatment of a first seizure in adults. A previous guideline -- also authored by Dr. Krumholz -- addresses how to evaluate a first seizure in adults.

"Determining whether to treat a patient after a first seizure is a complex process, but this guideline supports the use of medication in some cases and could influence standard practice for many physicians," says Dr. Krumholz. "A single seizure could be a sign of epilepsy. Even one seizure is traumatic and can affect many aspects of an individual's life from driving a car to employment options. This guideline clarifies when a person's risk for another seizure warrants medication."

About 150,000 adults have an unprovoked (occurring when an acute brain disturbance cannot be identified as the cause) first seizure in the United States each year, and one in 26 Americans will develop epilepsy -- defined as one or more unprovoked seizures with a high likelihood of recurrence -- in their lifetime.

"This important guideline has important implications for epilepsy patients and healthcare providers across the country and beyond," says E. Albert Reece, MD, PhD, MBA, vice president for Medical Affairs, University of Maryland, and the John Z. and Akiko K. Bowers Distinguished Professor and Dean of the School of Medicine. "Through their research and advanced practice of patient care, our neurology faculty continue to make meaningful contributions to improving outcomes and quality of life for patients facing the challenges of neurological disease."

The guideline states that for adults who have had a first seizure, the risk of another seizure is greatest within the first two years. The risk ranges from about a one-in-five chance, or 21 percent, to nearly a one-in-two chance, or 45 percent.

The risk of another seizure is greatest in those with a previous brain injury such as a stroke, tumor or head trauma. Risk is also high for those with a significant abnormality on imaging tests of the brain, an EEG test result that shows signs of epilepsy or a seizure that occurred during sleep.

According to the guideline, immediate treatment with an antiepileptic medication lowers the risk of another seizure by 35 percent within the first two years. "About half of patients who have a first seizure will never have another seizure, but for the other half, immediate drug therapy may help," says Dr. Krumholz, who stresses that the guideline should be used by physicians to help inform patients of their individual risk of a second seizure and involve them in the decision-making process.

While treatment was shown to provide a short-term benefit, over the longer term of more than three years, treating a first seizure immediately rather than waiting for another seizure to occur is unlikely to increase or decrease the likelihood of remaining seizure-free.

The guideline notes that seven to 31 percent of patients who take an antiepileptic drug will experience a drug side effect; however, these are usually mild and can be reversed when a patient is switched to another drug or the dose is lowered.

The guideline was presented at the AAN's 67th Annual Meeting in Washington, DC and published in the April 21, 2015, issue of Neurology®, the medical journal of the AAN.

http://www.eurekalert.org/pub_releases/2015-04/uob-ofc041715.php

Oldest fossils controversy resolved

New analysis of world-famous 3.46 billion-year-old rocks set to finally resolve long running evolutionary controversy.

New analysis of world-famous 3.46 billion-year-old rocks by researchers from the University of Bristol, the University of Oxford and UWA (the University of Western Australia) is set to finally resolve a long running evolutionary controversy.

The new research, published this week in Proceedings of the National Academy of Sciences USA, shows that structures once thought to be Earth's oldest microfossils do not compare with younger fossil candidates but have, instead, the character of peculiarly shaped minerals.

In 1993, US scientist Bill Schopf described tiny carbon-rich filaments within the 3.46 billion-year-old Apex chert (fine-grained sedimentary rock) from the Pilbara

region of Western Australia, which he likened to certain forms of bacteria, including cyanobacteria.

These 'Apex chert microfossils' - between 0.5 and 20 micrometres wide - soon became enshrined in textbooks, museum displays, popular science books and online reference guides as the earliest evidence for life on Earth. In 1996, these structures were even used to test and help refute the case against 'microfossils' in the Martian meteorite ALH 84001.

Even so, their curious colour and complexity gave rise to some early questions. Gravest doubts emerged in 2002, when a team led by Oxford's Professor Martin Brasier (co-author of this current study) revealed that the host rock was not part of a simple sedimentary unit but rather came from a complex, high-temperature hydrothermal vein, with evidence for multiple episodes of subsurface fluid flow over a long time. His team advanced an alternative hypothesis, stating that these curious structures were not true microfossils but pseudofossils formed by the redistribution of carbon around mineral grains during these hydrothermal events.

Although other research teams have since supported the hydrothermal context of Professor Brasier, the 'Apex microfossil' debate has remained hard to resolve because scientific instrumentation has only recently reached the level of resolution needed to map both chemical composition and morphology of these 'microfossils' at the sub-micrometre scale.

Now Dr David Wacey, a Marie Curie Fellow in Bristol's School of Earth Sciences, in collaboration with the late Professor Brasier, has come up with new high-spatial resolution data that clearly demonstrate that the 'Apex chert microfossils' comprise stacks of plate-like clay minerals arranged into branched and tapered worm-like chains. Carbon was then absorbed onto the edges of these minerals during the circulation of hydrothermal fluids, giving a false impression of carbon-rich cell-like walls.

Dr Wacey and team used transmission electron microscopy to examine ultrathin slices of 'microfossil' candidates, to build up nanoscale maps of their size, shape, mineral chemistry and distribution of carbon.

Dr Wacey said: "It soon became clear that the distribution of carbon was unlike anything seen in authentic microfossils. A false appearance of cellular compartments is given by multiple plates of clay minerals having a chemistry entirely compatible with a high temperature hydrothermal setting.

"We studied a range of authentic microfossils using the same transmission electron microscopy technique and in all cases these reveal coherent, rounded envelopes of carbon having dimensions consistent with their origin from cell walls and sheaths. At high spatial resolution, the Apex 'microfossils' lack all evidence for coherent, rounded walls. Instead, they have a complex, incoherent spiky morphology, evidently formed by filaments of clay crystals coated with iron and carbon."

Before his death Professor Brasier commented: "This research should, at long last, provide a closing chapter for the 'Apex microfossil' debate. Such discussions have encouraged us to refine both the questions and techniques needed to search for life remote in time and space, including signals from Mars or beyond. It is hoped that textbooks and websites will now focus upon recent and more robust discoveries of microfossils of a similar age from Western Australia, also examined by us in the same article."

'Changing the picture of Earth's earliest fossils (3.5-1.9 Ga) with new approaches and new discoveries' *by Martin Brasier, Jonathan Antcliffe, Martin Saunders and David Wacey in PNAS*

http://www.eurekalert.org/pub_releases/2015-04/w-pud042015.php

Providing universal donor plasma to massively bleeding trauma patients is feasible and can save lives

Delivering universal donor plasma to massively hemorrhaging patients can be accomplished consistently and rapidly and without excessive wastage

A recent randomized trial that looked at the feasibility of 2013 guidelines issued by the American College of Surgeons Trauma Quality Improvement Project for trauma resuscitation found that delivering universal donor plasma to massively hemorrhaging patients can be accomplished consistently and rapidly and without excessive wastage in high volume trauma centers. The plasma is given in addition to red blood cell transfusions to optimize treatment.

The 2013 guidelines recommend that universal donor products be immediately available on arrival of severely injured patients, and they represent a major shift in the paradigm of trauma resuscitation and blood product provision that has existed for more than a generation. Those recommendations are currently outside the capabilities of many facilities, due to the expense of maintaining even a small thawed plasma inventory, but they are likely to become the expected standard in the near future.

"We hope the descriptions of the various ways in which centers fulfilled the requirement of delivering blood components to the bedside within 10 minutes inspire other facilities to devise the most effective way for their own circumstances," said Dr. Deborah Novak, lead author of the Transfusion paper.

Injury is the leading cause of death among young adults, and uncontrolled hemorrhage is the most important preventable factor among those who sustain traumatic injury.

http://www.eurekalert.org/pub_releases/2015-04/epfd-uic042015.php

Uranium isotopes carry the fingerprint of ancient bacterial activity

New research shows that the isotopic composition of uranium provides a unique window into microbial activity billions of years into the past

The oceans and other water bodies contain billions of tons of dissolved uranium. Over the planet's history, some of this uranium was transformed into an insoluble form, causing it to precipitate and accumulate in sediments. There are two ways that uranium can go from a soluble to an insoluble form: either through the action of live organisms - bacteria - or by interacting chemically with certain minerals. Knowing which pathway was taken can provide valuable insight into the evolution and activity of microbial biology over Earth's history. Publishing in the journal PNAS, an international team of researchers led by the Ecole Polytechnique Fédérale de Lausanne in Switzerland describes a new method that uses the isotopic composition of uranium to distinguish between these alternative pathways.

The link between bacteria and the rock record is not new. Under certain conditions, bacteria interact biochemically with dissolved ions such as sulfur, or uranium, causing them to become insoluble and precipitate, contributing to their accumulation in oceanic sediments. But for the first time, scientists can determine whether bacteria were active at the time and place the sediments were formed by analyzing tiny amounts of uranium present in sediments.

Picky electron donors

The fact that bacteria and uranium interact at all may sound somewhat surprising. But as Rizlan Bernier-Latmani, the study's principal investigator explains, to complete certain metabolic processes, the bacteria need to get rid of electrons, and dissolved uranium just happens to be capable of taking them up. Uranium is far from being the only metal to which bacteria donate extra electrons. But once it precipitates in its insoluble form, uranium is the only metal known to date that preserves a signal that scientists can analyze to detect whether bacteria were involved in its transformation.

What makes uranium unique is that bacteria are picky when it comes to the atomic weight of the uranium to which they donate electrons. Of the two most abundant uranium isotopes found on earth - uranium-238 and uranium-235 - bacteria seem to prefer the heavier uranium-238. The chemical transformation pathway, by contrast, treats both forms of uranium equally. As a result, a slightly higher ratio between heavy and light isotopes in solid uranium extracted from the ground points at a bacterial transformation process.

The evolution of life

Being able to discriminate between both pathways gives researchers a unique tool to probe into environmental niches occupied by bacteria billions of years ago. Applying their methodology to existing data of Archean sediments from Western Australia, the authors argue that uranium found in oxygen-depleted sediments there was immobilized biologically. Bacteria, they argue, were active there already 2.5 billion years ago when the sediments were formed.

To an environmental biogeochemist like Bernier-Latmani, knowing whether or not bacteria were active at that time and place is exciting, as it could provide new insight into the planet's chemical evolution, for example on the abundance free oxygen in the oceans and the atmosphere. "We have some understanding of how oxygen concentrations in the atmosphere and oceans evolved over time. There is increasing evidence that traces of oxygen were available already billions of years ago in an overall anoxic world - and bacteria existed that indirectly used it. These changes have a direct bearing on the evolution of life and on mass extinctions," she says. In the complex puzzle of the planet's early history, uranium could be holding some of the missing pieces.

The research was carried out in collaboration with researchers from the Institute of Mineralogy at Leibniz University in Hannover, Germany, and the School of Earth and Space Exploration at Arizona State University in Arizona, USA.

http://bit.ly/1Dk2Q2B

Carbon dioxide could be turned into a huge underground battery

What if we transformed carbon dioxide from being a waste product into being a huge battery to help even out our energy supply?

16:23 20 April 2015 by Michael Slezak

We could make carbon storage pay off, while solving problems of intermittent energy supply from renewables. So say Tom Buscheck from the Lawrence Livermore National Laboratory in California and his colleagues who presented a design for this type of energy storage at the European Geosciences Union general assembly last week in Vienna, Austria.

Their design would be able to store the excess energy produced by renewable and conventional power sources when demand is low and, at the same time, lock up the major cause of global warming – carbon dioxide. Carbon capture and storage has been slow to develop, in part because it is an extra cost for energy producers that provides little direct pay-off. "There's no business case to do it," says Jim Underschultz from the University of Queensland in Australia.

"CCS hasn't been utilised because no one has come up with a viable use for that storage," says Buscheck. But if stored CO_2 could be used to hold surplus energy, it may give such technology the economic boost it needs.

"The only way you can decarbonise the fossil-fuel energy systems is if you can devise an approach where the economics makes sense," says Buscheck, who thinks their design, which is funded by the Geothermal Technologies Office at the US Department of Energy, does just that.

Supercritical storage

Buscheck's team proposes storing that excess energy in two forms: pressure and heat. Excess electricity would power a pump that injects supercritical CO_2 – a hybrid state of liquid and gas – into underground brine in sedimentary rocks between 1 and 5 kilometres below the surface. Supercritical CO_2 can drive turbines much more efficiently than steam and can take a lot of squeezing and heating – improving its capacity to store energy.

Another set of pipes tap into the brine in the sedimentary rocks. As the CO_2 is pumped in, it will displace some brine, which is collected at the surface. Surplus energy can also be used to heat the brine and circulate it down into the deep rocks, which are able to store the heat effectively.

When the heated brine comes into contact with the CO_2, it causes it to expand, thereby increasing the pressure of the stored CO_2. The heat energy can be gathered by allowing the CO_2 to depressurise, spinning supercritical CO_2 turbines, which are 50 per cent more efficient than the steam equivalent. The team's modelling suggests that the system could regather up to 96 per cent of the heat stored.

Their approach could help solve a major problem with renewables: intermittent power. Solar and wind can fail to produce power when there is high demand. Similarly, sometimes they produce plenty of energy when demand is lower, and in this case, sources like nuclear, coal and older gas power stations can produce energy at a loss, or simply waste the heat they produce, never turning it into electricity.

The massive batteries that would be required to store the excess are still expensive and not very effective. Storing the energy by using it to pump water uphill – a current state of the art – can also waste a quarter of the energy in the process.

Getting bigger and better

"There is no doubt in my mind that we need to consider hybrid technologies of the sort proposed here," says Peter Cook from the University of Melbourne, Australia. He says the proposal takes a lot of existing ideas and integrates them in a new way, meaning that most of the technology is already proven.

But while this could contribute to reducing atmospheric carbon dioxide, it is unlikely to become a major carbon sink, says Cook.

One site could only store about 8 million tonnes of CO_2 each year for 30 years – about the same amount as produced in one big coal-fired power station, says Buscheck, whose group is now looking for power companies to partner with on a pilot project.

Whether it is possible to scale-up the design remains to be seen, say Cook and Undershultz. Given its complexity, Undershultz says that costs and inefficiencies could add up as they scale it up. And Stuart Haszeldine from the University of Edinburgh, UK, says it would require a really good knowledge of geology to ensure carbon is sealed and does not escape.

http://bit.ly/1OOBMiE

Virus hiding in our genome protects early human embryos

We may owe our survival and complexity to a stowaway virus that springs to life in the very first cells of human embryos.

17:13 20 April 2015 by Andy Coghlan

Not only does the virus seem to protect embryos from other viruses, but it also assists genes when the groundwork is under way for the body plan of a new human.

The finding backs the controversial idea that viruses which took up residence in our DNA millions of years ago may be playing the role of puppet master, quietly influencing our existence and evolution. "We are creatures controlled by viruses," says Luis Villarreal of the University of California at Irvine.

Retroviruses insert their genetic material into the cells of their human or animal host. At first, this causes disease and death. Over time, however, the host evolves resistance to the virus, allowing any DNA that has embedded itself into sperm or egg cells to be passed down to the next generation. The virus is now known as an endogenous retrovirus or ERV – a permanent fixture in the host's genome.

Silent protector

About 9 per cent of our genome is thought to have come about this way. Until recently, these viral relics were largely dismissed as inactive "junk" that ceased to have any impact on their host many thousands of years ago. The discovery that HERVK, the most recent ERV to make itself at home in our DNA – probably around 200,000 years ago – is active in human embryos challenges that notion.

Joanna Wysocka and her colleagues at Stanford University in California made the unexpected find while they were analysing gene activity in 3-day-old human embryos, which are bundles of eight cells. Besides DNA from the parents, they found genetic material from HERVK. "The cells were full of viral protein products, some of which had assembled to form viral-like particles," says Wysocka.

Further experiments revealed that the virus appears to produce a protein that prevents other viruses penetrating the embryo, suggesting it protects the embryo from dangerous circulating viruses, such as influenza. It also seems to play a

crucial role in the genetic activity of the embryonic cells, helping to genetic instructions to the cellular protein factories.

Biological dark matter

Tantalisingly, the stowaway virus might even provide clues to what makes us different from chimpanzees and other non-human primates. Some researchers have previously argued that ERVs may play a key role in how species diverge from each other, by activating different body plans and gene networks that may give one individual an edge over other members of the species.

Wysocka's work backs up this idea, says Patrick Forterre of the Pasteur Institute in Paris. "It shows that the protein products of a relatively 'recent' retrovirus integration are present very early on in the embryo, and could be involved in some critical developmental programmes." The observation that ERVs could also protect the embryo against infection also makes a lot of sense, he says Forterre. "It's as if retroviruses are competing with each other via their human host."

Despite being ubiquitous, viruses are often called the dark matter of biology as their influence frequently goes unnoticed. If DNA is a jungle, then the viruses are the animals and plants that live and adapt within it, says Villarreal, who in 2001 showed that the presence of a viral gene is essential for the formation of the human placenta. "DNA is the habitat, and the viruses are the inhabitants," he says. The most influential viruses are those, like HERVK, that have inserted themselves permanently into our DNA and can be passed on to the next generation.

These viruses have the genetic tools to refashion the hosts' genes, influencing which are active and when, and with which other genes they interact. This means they have the ability to reshape the physical characteristics of their hosts, says Villarreal. "It's a massive dynamic pool of colonising genomes."

Journal reference: Nature, DOI: 10.1038/nature14308

http://bit.ly/1GpnC5z

Dawn Spacecraft Sends First Color Images of Ceres

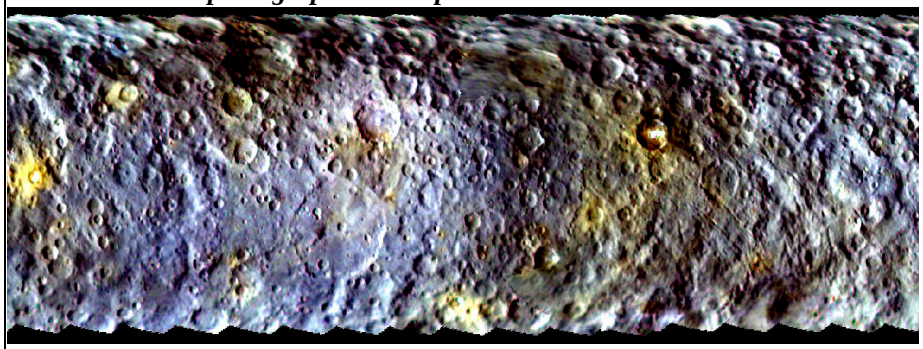
Red and blue tell the tale of a dwarf planet covered in rock and ice

By Marissa Fessenden

Ever since NASA's Dawn spacecraft arrived in orbit around the dwarf planet Ceres in early March, scientists have been eagerly awaiting a flood of data that will hopefully tell researchers more about the origin of the solar system. Now, the team has created the first color photographs of the largest body swinging through space in the asteroid belt between Mars and Jupiter.

For the last month, news from Dawn has been quiet as the spacecraft gently spirals closer Ceres, hidden in the dark side of the dwarf planet. This is, as Robbie Gonzalez at io9.com explains, not because we are trying to sneak up on aliens:

The lack of photos obviously has absolutely nothing to do with the fact t Dawn spacecraft is currently orbiting over Ceres' far-side, i.e. the side facin from the sun, i.e. the side that is, at this very moment, completely shrouded in d and otherwise unphotographable. Nope. That's not it at all.



false-color image of Ceres mimics what human eyes would see **NASA/JPL- Calt**

Earlier this month the probe captured some images, compiled in this vi sunlight illuminating the north pole. Now, to tide people over until the planet's next photoshoot, scientists have rendered Ceres in color. NAS Propulsion Laboratory put together a colorized map of the planetary sur press statement explains how Dawn 'sees' color:

Images taken using blue (440 nanometers), green (550 nanometers) and i (920 nanometers) spectral filters were combined to create the map. The filte assigned to color channels in reverse order, compared to natural color; in othe the short-wavelength blue images were assigned to the red color channel and th wavelength infrared images are assigned to the blue color channel.

At The Conversation, David Rothery, a planetary geoscientist, writes t resulting map — which looks as pock-marked and pebbly as a cartoon din skin — approximates what human eyes would see. Likely, the blue splotc ice and the red areas are relatively bare and rocky. The patchiness of the colors tell the researchers that Ceres was once an active body. Geo processes must have painted its surface with multiple, diverse regions, the report explains.

Even those ruddy areas may just cover ice underneath. As far as research tell, a quarter of the dwarf planet's outer portion is ice and the inside is roc they still have questions. Rothery writes:

Is Ceres' icy shell solid all the way down to the rock, or have lower layers of melted to produce the sort of internal ocean known to exist within some of satellites of Jupiter (Europa) and Saturn (Enceladus)? If there is an internal this could account for plumes of water vapor seen venting from Ceres last yea

Herschel space telescope – not to mention those mysterious white spots seen on the Ceres' surface.

And another unanswered question has to do with a set of mysteroius white spots that gleamed like beacons shining from a crater captured earlier this year. Despite the new images, these glowing dots still offer a tantalizing mystery. "The bright spots continue to fascinate the science team, but we will have to wait until we get closer and are able to resolve them before we can determine their source," says Chris Russell, of the University of California, Los Angeles, in a press statement from NASA.

Dawn will start its first detailed, intensive survey of Ceres on April 23, when it reaches 8,400 miles above the dwarf planet's surface.

http://www.eurekalert.org/pub_releases/2015-04/mcsc-isp041615.php

Immune system protein regulates sensitivity to bitter taste

The bitter taste of illness

PHILADELPHIA - New research from the Monell Center reveals that tumor necrosis factor (TNF), an immune system regulatory protein that promotes inflammation, also helps regulate sensitivity to bitter taste. The finding may provide a mechanism to explain the taste system abnormalities and decreased food intake that can be associated with infections, autoimmune disorders, and chronic inflammatory diseases.

In addition to its role in mediating inflammation, TNF has been implicated in the progression of varied diseases ranging from Alzheimer's disease to cancer.

"Reduced food intake and associated malnutrition is a significant concern that affects the long-term prognosis of many people who are very ill," said senior author Hong Wang, PhD, a molecular biologist at Monell.

"Our findings reveal that bitter taste is regulated by the immune system. Specifically, TNF may make sick people more sensitive to bitterness so that foods taste more bitter and less appetizing."

Wang's research focuses on interactions between the taste and immune systems, with the goal of identifying how taste cell function changes in disease states. As part of this effort, previous research from her laboratory had demonstrated that taste buds contain several immune system proteins, including TNF.

Because TNF is known to suppress food intake, the current study asked whether TNF affects food intake via the taste system. The findings are published online ahead of print in the journal Brain, Behavior, and Immunity.

To examine whether TNF helps regulate taste responses, the researchers first compared taste responses of normal mice to those of mice engineered to be lacking the gene for TNF (TNF knockout mice).

Two different behavioral tests revealed that the TNF knockout mice were less sensitive to bitter-tasting compounds, meaning that they required higher levels of bitterness than normal mice in order to show a response. However, there were no differences in how the two sets of mice responded to sweet, umami, salty, and sour tastes.

To confirm that the behavioral tests reflect a change in taste sensing on the tongue rather than how taste is processed in the brain, the researchers next measured how the chorda tympani nerve, which transmits taste information from the front of the tongue to the brain, responded to the different tastes.

They found that taste nerves from TNF knockout mice showed less activity in response to bitter taste compounds than nerves from normal mice. Again, the response was specific to bitter, with no differences in neural responses to the other taste qualities.

The combined findings indicate a deficit in the ability of the TNF-knockout mice to sense bitter taste. This suggests that TNF regulates bitter taste in normal mice and that elevated TNF levels associated with infection or inflammation may cause foods to taste more bitter.

"I was often sick as a child and still remember the bitter taste in my mouth when I was ill. Because of this, understanding how illness makes foods taste bitter is interesting to me personally," said Wang.

A third study in normal mice revealed that receptors for TNF are located on several types of taste sensing cells within the taste bud, including the cells that contain receptors for bitter taste. This expression pattern suggests that TNF interacts with TNF receptors on bitter taste cells to directly influence how these cells respond to taste stimuli.

"This new research establishes a functional link between the immune and taste systems," said Wang. "An interesting question to consider is whether changing the levels of TNF, perhaps by using inhibitors, can modulate bitter taste sensations."

Other studies will explore how TNF acts on taste cells to regulate bitter taste and whether other inflammatory factors interact with the taste system.

Monell molecular biologist Pu Feng and electrophysiologist Masafumi Jotaki are the paper's co-first authors. Also contributing to the research were Monell scientists Agnes Kim, Jinghua Chai, Nirvine Simon, Minliang Zhou, Alexander Bachmanov, and Liquan Huang. Funding was provided by the Institute of Deafness and Other Communication Disorders (grants R01DC010012, R21DC013177, R01DC00882, and P30DC011735) of the National Institutes of Health and by National Science Foundation grant DBJ-0216310. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the National Science Foundation.

http://www.eurekalert.org/pub_releases/2015-04/b-lbs041715.php

Link between serotonin and depression is a myth, says top psychiatrist

The widely held belief that depression is due to low levels of serotonin in the brain - and that effective treatments raise these levels - is a myth, argues a leading psychiatrist in The BMJ this week.

David Healy, Professor of Psychiatry at the Hergest psychiatric unit in North Wales, points to a misconception that lowered serotonin levels in depression are an established fact, which he describes as "the marketing of a myth."

The serotonin reuptake inhibiting (SSRI) group of drugs came on stream in the late 1980s, nearly two decades after first being mooted, writes Healy. The delay centred on finding an indication.

After concerns emerged about tranquilliser dependence in the early 1980s, drug companies marketed SSRIs for depression, "even though they were weaker than older tricyclic antidepressants, and sold the idea that depression was the deeper illness behind the superficial manifestations of anxiety," he explains. The approach was an astonishing success, "central to which was the notion that SSRIs restored serotonin levels to normal, a notion that later transmuted into the idea that they remedied a chemical imbalance."

In the 1990s, no one knew if SSRIs raised or lowered serotonin levels, he writes; they still don't know. There was no evidence that treatment corrected anything, he argues.

He suggests that the myth "co-opted" many, including the complementary health market, psychologists, and journals. But above all the myth co-opted doctors and patients, he says. "For doctors it provided an easy short hand for communication with patients. For patients, the idea of correcting an abnormality has a moral force that can be expected to overcome the scruples some might have had about taking a tranquilliser, especially when packaged in the appealing form that distress is not a weakness."

Meanwhile more effective and less costly treatments were marginalised, he says.

He stresses that serotonin "is not irrelevant" but says this history "raises a question about the weight doctors and others put on biological and epidemiological plausibility." Does a plausible (but mythical) account of biology and treatment let everyone put aside clinical trial data that show no evidence of lives saved or restored function, he asks? Do clinical trial data marketed as evidence of effectiveness make it easier to adopt a mythical account of biology?

These questions are important, he says. "In other areas of life the products we use, from computers to microwaves, improve year on year, but this is not the case for medicines, where this year's treatments may achieve blockbuster sales despite being less effective and less safe than yesterday's models."

"The emerging sciences of the brain offer enormous scope to deploy any amount of neurobabble. We need to understand the language we use. Until then, so long, and thanks for all the serotonin," he concludes.

http://www.eurekalert.org/pub_releases/2015-04/uovh-sct042115.php

Surprising contributor to Rett syndrome identified

Cells meant to maintain health worsening neurodevelopmental disorder's progression

The immune system is designed to protect us from disease. But what if it was malfunctioning? Would it make a disease worse? That appears to be the case with Rett syndrome, a neurodevelopmental disorder, and possibly in other neurological disorders as well, new research from the University of Virginia School of Medicine has found.

UVA's discovery suggests that immune cells bearing a mutation in the Rett gene, MeCP2, cannot perform their normal function and are instead amplifying the disease. By identifying a new role of the immune system in the disorder, through cells known as "macrophages," the UVA team has opened up an exciting new pathway to targeting the disease therapeutically.

Rett syndrome, until recently classified as a severe case of autism-spectrum disorder, affects girls almost exclusively. Children with the disease develop normally at first, but then symptoms begin to appear -- children lose their acquired cognitive and motor skills, develop seizures and experience breathing problems. Scientists previously linked the condition with a mutation of the MeCP2 gene within brain cells called neurons. UVA's discovery, however, shows that a lack of that gene in immune cells has disastrous consequences that reach beyond the brain.

"These immune cells may be functioning OK when there is no problem, but the moment there is any sort of problem in any tissue, to respond they need this gene," said Jonathan Kipnis, PhD, of the UVA Department of Neuroscience and director of UVA's Center for Brain Immunology and Glia. "And without this gene, macrophages not only do not respond properly. They respond abruptly, and they start to produce molecules that are further damaging the tissue. ... Cells which are supposed to maintain tissue are killing that tissue."

The discovery points to the immune system as a promising target for slowing the progression of Rett syndrome. Unlike most brain cells, which are never replaced, the immune system can be easily manipulated or even replaced entirely via a bone-marrow transplant. "I don't think you could cure this disease without fixing the neurons, but fixing neurons is a really tall order," said researcher Jim Cronk, the lead author of a new paper outlining the findings. "So our tact is to look at

what else is going on here and what else can we do to help. What's feasible with the tools that are available?"

The researchers identified the role of the immune system after contemplating the scope of the Rett symptoms. "Many organs are suffering from this disease - guts, bones, muscles, heart," Kipnis said. "And we said, wait a second, we see that MeCP2 plays a very important role in microglia. Microglia are brain macrophages [immune cells]. What about other macrophages? Each tissue has its own macrophages - and their No. 1 goal is to ensure homeostasis of tissue. If macrophages are impaired, then every tissue may be suffering."

The work, a close collaboration between the Kipnis lab and the lab of Vladimir Litvak, PhD, of the University of Massachusetts Medical School, has been published online by the journal Immunity.

Kipnis hailed Cronk's important contributions to the work, noting that Cronk is a student in UVA's Medical Scientist Training Program.

http://www.bbc.com/news/health-32333161

Gene therapy: 'Tame HIV' used to cure disease

The lives of six boys with a deadly genetic disease have been transformed by a pioneering treatment to correct errors in their DNA, say doctors.

By James Gallagher Health editor, BBC News website

A defective immune system in Wiskott-Aldrich syndrome leaves people vulnerable to infections and bleeding. A British and French study, published in JAMA, used tamed HIV to correct the defects. One child who needed a wheelchair can now move freely, while symptoms have improved in the other patients. The syndrome affects up to 10 children in every million born and almost exclusively affects boys. Even tiny bumps and scrapes can lead to wounds that are slow to close in patients.

Eczema is common, they face repeat infections including pneumonia as well as some cancers and autoimmune diseases. It all stems from an error in the genetic code that contains the building instructions for a key element in the immune system - a protein called WAS.

Therapy

The main treatment is a bone marrow transplant - but that is an option only when the donor is a close tissue match, such as a sibling. The trial at Great Ormond Street Hospital, in London, and Necker Children's Hospital, in France, removed part of the children's bone marrow. It was purified in the laboratory to find the cells that regenerate the immune system and a tamed version of HIV was used to "infect" the cells with the correct DNA.

The corrected bone marrow cells were then put back into the children.

In six out of seven boys, the therapy was a success. It reversed symptoms and massively cut the number of nights spent in hospital. One French child with severe autoimmune disease no longer needs a wheelchair. Another died from a drug-resistant herpes infection acquired before the therapy started.

Daniel Wheeler, who is now 15 and from Bristol, was the first British patient.

His older brother died from the same condition when he was two-and-a-half.

Their mum Sarah told the BBC News website: "Daniel was in and out of hospital, he had frequent infections of ear, chest, flare-ups and bruised joints, lots of operations. "He was in education as much as we could, we didn't wrap him in cotton wool, but his sickness rate was very high. "We were anxious. We never knew what would happen in the long-term, we still don't really but, touch wood, it has been a success."

Prof Adrian Thrasher, from Great Ormond Street Hospital, told the BBC News website: "I think it is very significant, it is another clear and powerful demonstration that a gene therapy approach is an effective one. "And that we can begin to think of these, alongside conventional transplantation, as alternative options particularly where transplant is going to be complicated. "What we hope, and the evidence is certainly suggestive of this, is that the therapeutic effect will last for a very substantial amount of time, such that the patients should not need another treatment and so therefore we hope that it will be lifelong."

Prof Ian Alexander from the Gene Therapy Research Unit at Sydney's Children's Medical Research Institute in Australia said although the work was promising, it was "still early days". "The gene therapy field remains in its infancy, with the vast majority of its genuine promise yet to be realised."

Analysis

By James Gallagher, Health editor, BBC News website

The promise of gene therapy being able to cure a wide range of diseases has never been realised.

All medicine, even paracetamol, has risks and the early days of tinkering with the genetic code threw up huge dangers.

Several trials were abandoned as patients developed leukaemia when the modification turned healthy cells cancerous.

But those trials did show one thing - the underlying principle worked.

Safer methods, such as using modified HIV, have been developed in the past decade.

There is now hope that some of the early optimism could soon be justified.

The first commercially available gene therapy was approved in 2012 for people who are unable to properly digest fats.

Gene therapy could be about to come in from the cold.

http://www.eurekalert.org/pub_releases/2015-04/uonc-cdd042215.php

Cirrhosis deaths drop 41 percent from 2002 to 2012

A new study by UNC researchers has found dramatic improvements in the survival of patients with cirrhosis and liver failure supporting improved treatment strategies for patients with cirrhosis and concurrent bacterial infections.

The study analyzed more than 780,000 hospitalizations of patients with cirrhosis from 2002 to 2010 and found that inpatient mortality decreased steadily during that period despite increases in patient age and the necessity for more complex medical care. The study used the Health Care Cost and Utilization Project National Inpatient Sample, the largest sampling of U.S. hospitals to date.

Monica Schmidt, MPH, research associate at the UNC Liver Center and doctoral candidate at the Gillings School of Global Public Health, is lead author of the study, which is published in the May 2015 issue of the journal, Gastroenterology.

"While the number of cirrhosis hospitalizations increased during the sample period, the rate of hospital deaths fell by 41 percent, " Schmidt said. "In addition, the decline in mortality for cirrhosis patients dropped significantly compared to non-cirrhotic patients. Increased awareness of disease management and earlier diagnosis for cirrhosis-related complications may have led to better survival rates."

Coauthoring and overseeing the study were A. Sidney Barritt, MD, MSCR, assistant professor of medicine, Eric Orman, MD, MSCR, assistant professor of medicine and Paul H. Hayashi, MD, MPH, associate professor of medicine in UNC's Division of Gastroenterology and Hepatology.

"These data are encouraging because there has been a lot of research effort put into improving inpatient cirrhosis care over the years, and it appears it may be paying off," Hayashi said.

Liver disease, or cirrhosis, is the eighth-leading cause of death in the U.S. and often requires hospitalization for complications that can include bleeding, confusion, cancer and susceptibility to bacterial infections.

Cirrhosis-related admissions to hospitals continue to grow. Care of cirrhosis patients is complex and often managed by a team of gastroenterologists, hepatologists, intensivists and nephrologists. The study targeted all causes and forms of liver cirrhosis.

While the decline in patient deaths was good news, the study found that cirrhosis patients do much worse than other patients with sepsis (bacterial infections). The mortality risk for infections actually increased over time, despite the ongoing "surviving sepsis campaign." The increased risk for cirrhosis patients may be related to abnormal blood-flow issues and immune responses that could hinder survival.

The study suggests that improving cirrhosis care may be leading to better overall survival, but notes that rising mortality risks for sepsis suggest a more tailored approach is needed for treating sepsis in patients with cirrhosis. The study's authors suggest that these data can help in setting appropriate quality care indicators and setting guideline use as well as determining adjusted mortality risk and use of palliative care.

http://www.eurekalert.org/pub_releases/2015-04/uons-cm-042115.php

Cloth masks -- dangerous to your health?

The widespread use of cloth masks by healthcare workers may actually put them at increased risk of respiratory illness and viral infections and their global use should be discouraged, according to a UNSW study.

The results of the first randomised clinical trial (RCT) to study the efficacy of cloth masks were published today in the journal BMJ Open.

The trial saw 1607 hospital healthcare workers across 14 hospitals in the Vietnamese capital, Hanoi, split into three groups: those wearing medical masks, those wearing cloth masks and a control group based on usual practice, which included mask wearing. Workers used the mask on every shift for four consecutive weeks.

The study found respiratory infection was much higher among healthcare workers wearing cloth masks. The penetration of cloth masks by particles was almost 97% compared to medical masks with 44%.

Professor Raina MacIntyre, lead study author and head of UNSW's School of Public Health and Community Medicine, said the results of the study caution against the use of cloth masks. "Masks are worn to protect from infection during pandemics and outbreaks, especially when there are no drugs or vaccines available for protection," Professor MacIntyre said.

"Masks are especially important for frontline doctors and nurses, as their protection from infection is key to maintaining the ability to tackle a pandemic effectively. "We should be cautious about cloth mask use in healthcare settings, particularly high-risk situations such as emergency departments, intensive care, paediatric or respiratory wards."

Cloth masks remain widely used globally because they are a cheaper option especially in areas where there are shortages of protective equipment, including in Asian countries, which have historically been affected by emerging infectious diseases, as well as in West Africa, which was the epicentre of the recent Ebola epidemic.

The authors speculate that the cloth masks' moisture retention, their reuse and poor filtration may explain the increased risk of infection.

Professor MacIntyre, who has completed the largest body of clinical trial research on respiratory protection in health workers internationally, said emerging infectious diseases are not constrained within geographical borders.

"Effective controls of outbreaks and pandemics at the origin impacts us directly, so it is important for global disease control that the use of cloth masks be discouraged in high-risk situations," she said.

"Despite more than half the world using cloth masks, global disease control guidelines, including those from the World Health Organisation, fail to clearly specify conditions of their use. "These guidelines need to be updated to reflect the higher infection risk posed by cloth masks, as found in our study."

Professor MacIntyre said the study's results pointed to the effectiveness of medical masks, in addition to the harm caused by cloth masks.

"Additional research is urgently needed to build on our study's findings."

The trial was a collaboration between researchers in Australia and the National Institute for Hygiene and Epidemiology in Vietnam and was funded by an Australian Research Council Linkage Grant.

A separate expert review by Professor MacIntyre published in the British Medical Journal earlier this month found that the lack of research on facemasks and respirators is reflected in varied and sometimes conflicting global policies and guidelines.

http://www.eurekalert.org/pub_releases/2015-04/aga-uil042215.php

Updates in liver disease research: Do you want the good or bad news?

Important research updates on the most deadly forms of liver disease.

Bethesda, MD - The May issues of AGA's journals -- Clinical Gastroenterology and Hepatology and Gastroenterology -- highlight important research updates on the most deadly forms of liver disease. Here's what you need to know:

Researchers confirm that NAFLD worsens heart disease.

One specific cardiovascular disease risk factor -- psychological distress -- is linked to death from liver disease in a large, general population sample.

Improvements in cirrhosis care have contributed to a 41 percent decrease in inpatient mortality.

NAFLD Worsens Cardiovascular Disease

Cardiovascular disease is the leading cause of death both in the general population and in patients with NAFLD. A new study in Clinical Gastroenterology and Hepatology[1] confirms that NAFLD is responsible for worsening of the cardiovascular risk factor profile, even in the absence of diabetes. This finding is based on a case-control study, which found that NAFLD causes increased serum levels of laboratory markers of cardiovascular risk. This information is important to better define the "at-risk" population, allowing for personalized management approaches in such individuals.

Psychological Distress Linked to Liver Disease Mortality

A novel new study in Gastroenterology[2] finds that psychological distress, which includes symptoms of anxiety and depression, is linked to subsequent liver disease mortality. This large, general population sample was the first study of its kind, and while this study is not able to confirm direct cause and effect, it does provide evidence that requires further consideration in future studies.

Decrease in In-Patient Cirrhosis Deaths

In some positive news, researchers report in Gastroenterology[3] that, in the U.S., inpatient mortality for cirrhosis patients has decreased steadily from 2002 through 2010, despite increasing age and medical complexity. Based on this representative sample of U.S. hospitalized patients with cirrhosis, the absolute rate of dying in the hospital fell steadily by 41 percent from 9.1 percent in 2002 to 5.4 percent in 2010. The decline in mortality for cirrhosis patients was significantly larger compared to non-cirrhotic patients, suggesting that the improvement in cirrhosis survival may be due to better cirrhosis-specific care that extends beyond general improvements in inpatient care. This is welcomed news considering that cirrhosis is the eighth leading cause of death in the U.S., which often requires hospitalizations due to severe complications.

[1] *Siddiqui, M. Shadab, et al., Severity of Nonalcoholic Fatty Liver Disease and Progression to Cirrhosis Are Associate With Atherogenic Lipoprotein Profile, Clinical Gastroenterology and Hepatology, 13(5): 1000-1008.e3, http://www.cghjournal.org/article/S1542-3565(14)01467-0/abstract*

[2] *Russ, Tom C., et al., Association Between Psychological Distress and Liver Disease Mortality: a Meta-analysis of Individual Study Participants, Gastroenterology, 148(5): 958-966.e4, http://www.gastrojournal.org/article/S0016-5085(15)00195-X/abstract*

[3] *Schmidt, Monica, et al., Decreasing Mortality Among Patients Hospitalized with Cirrhosis in the United States From 2002 through 2010, Gastroenterology, 148(5): 967-977.e2, http://www.gastrojournal.org/article/S0016-5085(15)00117-1/abstract*

http://www.eurekalert.org/pub_releases/2015-04/osu-aap042215.php

Autism and prodigy share a common genetic link

Study involved families that had both prodigies and people with autism

COLUMBUS, Ohio - Researchers have uncovered the first evidence of a genetic link between prodigy and autism. The scientists found that child prodigies in their sample share some of the same genetic variations with people who have autism. These shared genetic markers occur on chromosome 1, according to the

researchers from The Ohio State University and Nationwide Children's Hospital in Columbus.

The findings confirm a hypothesis made by Joanne Ruthsatz, co-author of the study and assistant professor of psychology at Ohio State's Mansfield campus.

In a previous study, Ruthsatz and a colleague had found that half of the prodigies in their sample had a family member or a first- or second-degree relative with an autism diagnosis. "Based on my earlier work, I believed there had to be a genetic connection between prodigy and autism and this new research provides the first evidence to confirm that," Ruthsatz said.

The new study appears online in the journal Human Heredity.

While this study provides a solid basis for identifying a linkage, there is a lot more to be learned, said co-author Christopher Bartlett, a principal investigator at Nationwide Children's Hospital and associate professor of pediatrics at Ohio State. "We haven't identified the mutations, but we found that there's something in this region of chromosome 1 that is the same with both prodigies and their family members with autism," Bartlett said.

These findings are the first step toward answering the big question, Ruthsatz said. "We now know what connects prodigy with autism. What we want to know is what distinguishes them. We have a strong suspicion that there's a genetic component to that, as well, and that's the focus of our future work," she said.

The Human Heredity study involved five child prodigies and their families that Ruthsatz has been studying, some for many years. Each of the prodigies had received national or international recognition for a specific skill, such as math or music. All took tests to confirm their exceptional skills.

The researchers took saliva samples from the prodigies, and from between four and 14 of each prodigy's family members. Each prodigy had between one and five family members in the study who had received a diagnosis on the autism spectrum. DNA was extracted from the saliva and the researchers sequenced the exome - the segment of DNA containing the 1 to 2 percent of genes that make proteins. (This is less expensive and complex than sequencing the entire genome.) The researchers plan to follow up with full genome sequencing, which will reveal more information about genetic mutations that the prodigies share with people with autism.

"What we found here was just an indication that there's something similar in the genetic makeup of prodigies and their family members with autism. There's a lot more that needs to be studied," Bartlett said.

In her earlier work, Ruthsatz found that while both prodigies and people with autism share better than average scores on tests that measure attention to detail, prodigies scored higher among those two groups. And prodigies really excelled when it came to working memory, with all that she studied scoring in the 99th percentile.

"We believe that there may some gene or genes for working memory that may be a key part of helping to create prodigies," Ruthsatz said. "Prodigies seem to have some protective genes that are saving them from the deficits associated with autism and only allowing the talent you see in savants to shine through. That's what we're looking to identify."

In the meantime, the researchers caution that they haven't found any "smoking gun." "The testing we did here wouldn't help anyone tell if he or she was going to be a prodigy or have autism," Bartlett said. "We didn't find the exact genes or mutations involved. It is a good start, but it is just a start."

Other co-authors on the study were Stephen Petrill, professor of psychology at Ohio State; and Ning Li and Samuel Wolock of Nationwide Children's Hospital.

Support for the study came from the Marci and Bill Ingram Research Fund for Autism Spectrum Disorders.

http://www.eurekalert.org/pub_releases/2015-04/uoq-dc042215.php

'Exciting discovery' could aid frontline spinal injury treatment

Scientists a step closer to treating harmful inflammation after spinal cord injury

Rapid treatment with a new anti-inflammatory could have a major impact on recovery from spinal cord injury, University of Queensland researchers have found.

UQ School of Biomedical Sciences' Dr Marc Ruitenberg and PhD student Ms Faith Brennan said they made the discovery during laboratory trials with an experimental drug.

Ms Brennan said that excessive inflammation caused additional damage in spinal cord injuries and hindered recovery. "We found that a molecule called C5aR exacerbates inflammation and tissue damage after spinal cord injury," she said.

"Our study shows that drugs inhibiting C5aR can improve recovery when administered early after injury. "This exciting discovery could form the basis for new frontline therapies to treat patients with spinal cord trauma."

Dr Ruitenberg said there was a critical time window for this new treatment. "What we also discovered is that this molecule, C5aR, has multiple roles and is also needed for repair processes undertaken by astrocytes, a specialised type of cell in the spinal cord," he said. "Astrocytes normally multiply in response to injury, which is an essential process to form a barrier between damaged and healthy tissue."Any long-term interference with this process could therefore make things worse. "Our challenge was to find out how long treatment with the new drug could be continued before its beneficial effects were lost, and also to understand why this occurred so that adverse side-effects could be prevented."

SpinalCure Australia CEO Mr Duncan Wallace, whose organisation supports the UQ research, said the study was a great step towards developing an effective treatment for spinal cord injury. "It takes us closer to the day when a spinal cord injury is no longer a life sentence," he said. The research is published in the Journal of Neuroscience (The Complement Receptor C5aR Controls Acute Inflammation and Astrogliosis following Spinal Cord Injury) on 22 April 2015.

http://www.eurekalert.org/pub_releases/2015-04/cu-sda042115.php

Scientists discover asthma's potential root cause and a novel treatment

Previously unproven role of the calcium sensing receptor (CaSR) in causing asthma

Published today in Science Translational Medicine journal, Cardiff University researchers, working in collaboration with scientists at King's College London and the Mayo Clinic (USA), describe the previously unproven role of the calcium sensing receptor (CaSR) in causing asthma, a disease which affects 300 million people worldwide.

The team used mouse models of asthma and human airway tissue from asthmatic and non-asthmatic people to reach their findings.

Crucially, the paper highlights the effectiveness of a class of drugs known as calcilytics in manipulating CaSR to reverse all symptoms associated with the condition. These symptoms include airway narrowing, airway twitchiness and inflammation - all of which contribute to increased breathing difficulty.

"Our findings are incredibly exciting," said the principal investigator, Professor Daniela Riccardi, from Cardiff University School of Biosciences. "For the first time we have found a link between airways inflammation, which can be caused by environmental triggers - such as allergens, cigarette smoke and car fumes - and airways twitchiness in allergic asthma.

"Our paper shows how these triggers release chemicals that activate CaSR in airway tissue and drive asthma symptoms like airway twitchiness, inflammation, and narrowing. Using calcilytics, nebulized directly into the lungs, we show that it is possible to deactivate CaSR and prevent all of these symptoms."

Dr Samantha Walker, Director of Research and Policy at Asthma UK, who helped fund the research, said: "This hugely exciting discovery enables us, for the first time, to tackle the underlying causes of asthma symptoms. Five per cent of people with asthma don't respond to current treatments so research breakthroughs could be life changing for hundreds of thousands of people.

"If this research proves successful we may be just a few years away from a new treatment for asthma, and we urgently need further investment to take it further through clinical trials. Asthma research is chronically underfunded; there have only been a handful of new treatments developed in the last 50 years so the importance of investment in research like this is absolutely essential."

While asthma is well controlled in some people, around one-in-twelve patients respond poorly to current treatments. This significant minority accounts for around 90% of healthcare costs associated with the condition.

According to Cardiff University Professor Paul Kemp, who co-authored the study, the identification of CaSR in airway tissue means that the potential for treatment of other inflammatory lung diseases beyond asthma is immense. These include chronic obstructive pulmonary disease (COPD) and chronic bronchitis, for which currently there exists no cure. It is predicted that by 2020 these diseases will be the third biggest killers worldwide.

Professor Riccardi and her collaborators are now seeking funding to determine the efficacy of calcilytic drugs in treating asthmas that are especially difficult to treat, particularly steroid-resistant and influenza-exacerbated asthma, and to test these drugs in patients with asthma.

Calcilytics were first developed for the treatment of osteoporosis around 15 years ago with the aim of strengthening deteriorating bone by targeting CaSR to induce the release of an anabolic hormone. Although clinically safe and well tolerated in people, calcilytics proved unsuccessful in treating osteoporosis.

But this latest breakthrough has provided researchers with the unique opportunity to re-purpose these drugs, potentially accelerating the time it takes for them to be approved for use asthma patients. Once funding has been secured, the group aim to be trialling the drugs on humans within two years.

"If we can prove that calcilytics are safe when administered directly to the lung in people, then in five years we could be in a position to treat patients and potentially stop asthma from happening in the first place," added Professor Riccardi.

The study was part-funded by Asthma UK, the Cardiff Partnership Fund and a BBSRC 'Sparking Impact' award.

http://www.eurekalert.org/pub_releases/2015-04/eaft-cph042215.php

Chili peppers hold promise of preventing liver damage and progression

Capsaicin shown to inhibit progression of liver injury and demonstrates anti-fibrotic potential

Austria, Vienna: Results revealed today at the International Liver Congress™ 2015 show that the daily consumption of capsaicin, the active compound of chilli peppers, was found to have beneficial effects on liver damage. In the study, capsaicin was found to reduce the activation of hepatic stellate cells (HSCs) in

mice models. HSCs are the major cell type involved in liver fibrosis, which is the formation of scar tissue in response to liver damage.

The mice were split into two groups and received capsaicin in their food:

After three days of bile duct ligation (BDL) in which the common bile duct is obstructed, leading to bile accumulation and liver fibrosis

Before and during chronic carbon tetrachloride treatment (CCl4). CCl4 is an inorganic compound that was widely used in fire extinguishers, as a precursor to refrigerants and as a cleaning agent. It is now known to be one of the most potent hepatotoxins

The study demonstrates that capsaicin partially improved liver damage in the BDL mice and inhibited further progression of the injury. In the second group of CCl4-treated mice, capsaicin prevented livers from injury development but did not reduce the fibrosis when it was already established.

These results support the need for further investigation into capsaicin for the treatment and prevention of liver injury and fibrosis.

http://www.eurekalert.org/pub_releases/2015-04/eaft-prs042215.php

Preliminary results show Civacir prevents recurrence of hepatitis C in liver transplants

Phase III data demonstrate prophylactic efficacy of Civacir® in patients who undergo antiviral therapy prior to transplantation

Vienna, Austria - New data from an ongoing Phase III trial revealed today at The International Liver CongressTM 2015 show that the use of hepatitis C immune globulin (HCIG, Civacir®) can effectively prevent hepatitis C virus (HCV) recurrence in patients following a liver transplant (LT). The data demonstrate that intravenous Civacir given both peri- and post-LT prevents HCV-reinfection in patients who also received antiviral therapy (AVT) before their transplant operation.

Civacir is a hepatitis C immune globulin (HCIG) produced from pooled plasma from hundreds of screened donors who have high antibody titers against HCV. In this trial, patients received AVT before their LT and those in the active treatment groups received 16 infusions of Civacir in the peri- and immediate post-LT period for 10 weeks. The control group received current standard of care (no treatment) post-LT.

The preliminary results suggest that Civacir provides an effective alternative approach as compared to current standard of care to prevent HCV recurrence in post-LT patients. Civacir was well tolerated with no drug-related serious adverse events observed during the study.

Hepatitis C virus (HCV) remains the leading cause for liver transplantation (LT) and recurrent HCV disease is the most frequent cause of graft loss. Prevention of recurrence independent of genotype and severity of cirrhosis is highly desirable because it simplifies post-LT management.

http://www.eurekalert.org/pub_releases/2015-04/eaft-hrd042215.php

Herbal remedy derived from milk thistle demonstrates efficacy in non-alcoholic steatohepatitis

Silymarin results in resolution of non-alcoholic steatohepatitis and improvement in fibrosis

Vienna, Austria: Results from a double-blind, placebo-controlled study of silymarin, which is derived from the milk thistle plant, have shown that this herbal remedy may be a useful treatment option for non-alcoholic steatohepatitis (NASH).

An interim analysis of the study, revealed today at The International Liver Congress™ 2015, shows a significantly higher percentage of patients experienced NASH resolution and improvement in fibrosis after 48 weeks of treatment with silymarin compared to placebo.

NASH occurs when the liver becomes inflamed due to the accumulation of fat. Over time, persistent inflammation can lead to the formation of fibrous scar tissue in the liver and around its blood vessels, which can eventually cause cirrhosis.

A total of 64 patients (silymarin = 30, placebo = 34) with biopsy-proven NASH had completed the study at the time of interim analysis. Silymarin has already demonstrated anti-oxidant, anti-inflammatory and anti-fibrotic properties, and these latest study results show that it may be a useful treatment for NASH.

http://www.bbc.com/news/health-32425666

Newborn baby Teddy was UK's youngest ever organ donor

A newborn baby, who lived for less than two hours, became Britain's youngest-ever organ donor last year.

Doctors at the University Hospital of Wales, Cardiff, carried out the pioneering surgery three minutes after Teddy Houlston died on April 22. His kidneys were then used to save an adult's life in Leeds. His parents, Mike Houlston and Jess Evans, from Cardiff, say they want people to know his story and see his face, saying: "We are so proud of him". In an interview with told the Daily Mirror, Mr Houlston said: "He lived and died a hero. It's impossible to explain how proud we are of him."

'Soul destroying'

Ms Evans was carrying twins when she was told - 12 weeks into her pregnancy - that one was fatally ill. Teddy had anencephaly, a rare and lethal abnormality which prevents the brain and skull from developing. Babies with the condition either die in the womb, are stillborn or live for just seconds, minutes or hours after

birth. Ms Evans told the Mirror that the news of Teddy's condition was "soul-destroying".

Though doctors offered the couple the option of an abortion, Ms Evans said: "We thought that even if we had a moment with him, or 10 minutes, or an hour, that time was the most precious thing that we would ever experience." As they continued with the pregnancy, the couple decided that they wanted to donate their baby's organs. Ms Evans said: "Organ donation was something I've always felt quite strongly about ever since I was a child."

In an interview with the BBC, Mr Houlston said they were initially told a transplant was not possible because it had never been done before.

But he said hearing the news that the transplant from Teddy had gone to plan had left them with a feeling of joy, saying: "We never doubted him".

"He is still very much a part of our family today, we talk of him every day, our children talk of him, our families do, we always remember him, he is with us all the time," Ms Evans added.

The success of the transplant "helped us grieve", she said, adding: "Knowing that he was able to do such good, more good than most of us will ever do in our lifetime - it is just overwhelming how proud we are of him."

'Precious minutes'

Retrieving organs from children for transplant is rare, it is particularly unusual from newborn babies - and unheard of in those with anencephaly.

Yet his kidneys would have been fully functional in the womb.

Angharad Griffiths, a specialist nurse from NHS Blood and Transplant who helped complete the transplant, said told BBC Radio 4's Today programme she had "every belief" that a similar transplant could be successfully carried out in the future. She said the transplant had been "challenging", particularly as they did not know if Teddy would be born alive. Her team monitored Teddy throughout his short life, before performing the transplant minutes after he died.

The couple have encouraged people to sign the NHS Organ Donor Register

Being present throughout Teddy's life was "a privilege", she said, saying his life was "an hour-and-a-half of pure joy".

"There was some sadness in the room naturally, [his parents] knew they were going to lose their baby, they knew he would pass away, but they were overjoyed that he had been born alive and they had those precious minutes with him and they spent those precious minutes enjoying him and his life," she added.

Analysis

By Philippa Roxby, health reporter, BBC News website

The process of matching a donor's organs to a recipient on the transplant waiting list is a complex one. Depending on the organs donated, the needs of the people waiting, their tissue type, overall health and location, the organs are offered to the most appropriate patient on the waiting list.

In this case, Teddy's kidneys - which were unaffected by the rare brain disease he had - will be able to grow inside another living body, making them suitable for donation to an adult, as well as a small baby.

Teddy lived for 100 minutes after he was born. After he died, doctors would have moved quickly to perform the rare and intricate operation to remove his kidneys and use them to save another life.

His case puts the focus back on neo-natal organ donation as a way of increasing the number of organ donors in the future. There are currently around 7,000 patients on the organ transplant waiting list in the UK.

'Heroism'

The Mirror said that the family visited Teddy's grave on Wednesday - on what would have been his first birthday - with his surviving twin, Noah.

Ms Evans said: "Although he wasn't with us very long, and we brought him into the world knowing there was no hope of a life for him, we are incredibly proud of his heroism."

"We hope Teddy's story will inspire families who find themselves in the position of losing a child."

The couple are encouraging anyone who is not on the NHS Organ Donor Register to sign up.

They are also raising money for the charity 2 Wish Upon a Star, which aims to improve bereavement services for parents who lose babies or children.

Earlier this year, doctors at the Imperial College NHS Trust in London revealed that a six-day-old baby girl's kidneys and liver cells had been given to two separate recipients after her heart stopped beating.

At the time, it had been thought she was the youngest organ donor in the UK.

http://bit.ly/1HDGTC7

Papyrus Reveals Ancient Egyptian Hangover Cure

Trying to ease a bad hangover? Wearing a necklace made from the leaves of a shrub called Alexandrian laurel would do the job, according to a newly translated Egyptian papyrus.

by Rossella Lorenzi

The “drunken headache cure” appears in a 1,900-year-old text written in Greek and was discovered during the ongoing effort to translate more than half a million scraps of papyrus known as the Oxyrhynchus Papyri.

Housed at Oxford University’s Sackler Library, the enormous collection of texts contains lost gospels, works by Sophocles and other Greek authors, public and

personal records and medical treatises dating from the first century AD to the sixth century A.D.

The key ingredient listed to treat the hangover — the slow growing evergreen Danae racemosa — wasn't exactly known for its medical properties.

The plant was used in Greek and Roman times to crown distinguished athletes, orators and poets.

Whether stringing its leaves and wearing the strand around the neck had any effect to relieve headaches in alcohol victims isn't known.

The improbable hangover remedy is part of a newly published volume containing about 30 medical papyri found at Oxyrhynchus. The documents were translated by researchers at the University of Oxford and University College London.

The new book, the 80th to be released during the century-old ongoing translation effort, represents "the largest single collection of medical papyri to be published," according to an introductory note by Vivian Nutton, a professor at University College London.

The Oxyrhynchus Papyri were unearthed in 1898 from a Greco-Roman dump in the ancient Egyptian town of Oxyrhynchus, about 100 miles south of Cairo.

The city flourished after the conquest of Egypt by Alexander the Great in 332 B.C., remained prominent in Roman and Byzantine times, but began to decline after the Arab conquest in 641 A.D.

The collection is the result of the Oxyrhynchus inhabitants's habit of throwing their trash in the desert. The dumps remained covered by sand until 1896, when Oxford archaeologists Bernard Grenfell and Arthur Hunt began excavating the area.

Apart from the hangover remedy, the latest batch of newly translated papyri include complex treatments for hemorrhoids, toothache, and various eye conditions, Live Science reported.

One recipe for treating rheum, a mucus discharged from the eyes, uses a concoction of copper flakes, antimony oxide, white lead, washed lead dross, starch, dried roses, rain water, gum Arabic, poppy juice and a plant called Celtic spikenard, known today to have anti-fungal and anti-bacterial properties.

A papyrus fragment also contains a gruesome description of eye surgery, providing a first person account of an everted eyelid (turned inside out) treatment. Translated by Cambridge scholar Marguerite Hirt, the text reads:

"The eye … I began … by the temple … the other from the temple … to remove with a small round-bladed knife … the edge of the eyelid from outside … from within until I scooped out."

http://bit.ly/1b1qrFx

Scientists agree: Coffee naps are better than coffee or naps alone

If you're feeling sleepy and want to wake yourself up - and have 20 minutes or so to spare before you need to be fully alert - there's something you should try.

It's more effective than drinking a cup of coffee or taking a quick nap. It's drinking a cup of coffee and then taking a quick nap. This is called a coffee nap.

It might sound crazy: conventional wisdom is that caffeine interferes with sleep. But if you caffeinate immediately before napping and sleep for 20 minutes or less, you can exploit a quirk in the way both sleep and caffeine affect your brain to maximize alertness. Here's the science behind the idea.

How a coffee nap works

To understand a coffee nap, you have to understand how caffeine affects you. After it's absorbed through your small intestine and passes into your bloodstream, it crosses into your brain. There, it fits into receptors that are normally filled by a similarly-shaped molecule, called adenosine.

Adenosine is a byproduct of brain activity, and when it accumulates at high enough levels, it plugs into these receptors and makes you feel tired. But with the caffeine blocking the receptors, it's unable to do so. As Stephen R. Braun writes in Buzz: the Science and Lore of Alcohol and Caffeine, it's like "putting a block of wood under one of the brain's primary brake pedals."

"it takes about 20 minutes for caffeine to hit your brain"

Now, caffeine doesn't block every single adenosine receptor - it competes with adenosine for these spots, filling some, but not others.

But here's the trick of the coffee nap: sleeping naturally clears adenosine from the brain. If you nap for longer than 15 or 20 minutes, your brain is more likely to enter deeper stages of sleep that take some time to recover from. But shorter naps generally don't lead to this so-called "sleep inertia" - and it takes around 20 minutes for the caffeine to get through your gastrointestinal tract and bloodstream anyway.

So if you nap for those 20 minutes, you'll reduce your levels of adenosine just in time for the caffeine to kick in. The caffeine will have less adenosine to compete with, and will thereby be even more effective in making you alert.

Experiments show coffee naps are better than coffee or naps

Scientists haven't directly observed this going on in the brain after a coffee nap - it's all based on their knowledge of how caffeine, adenosine, and sleep each affect the brain independently.

But they have directly observed the effects of coffee naps, and experiments have shown they're more effective than coffee or naps alone in maximizing alertness.

"people who took a coffee nap committed fewer errors in a driving simulator"

In a few different studies, researchers at Loughborough University in the UK found that when tired participants took a 15-minute coffee nap, they went on to commit fewer errors in a driving simulator than when they were given only coffee, or only took a nap (or were given a decaf placebo). This was true even if they had trouble falling asleep, and just laid in bed half-asleep during the 15 minutes.

Meanwhile, a Japanese study found that people who took a caffeine nap before taking a series of memory tests performed significantly better on them compared to people who solely took a nap, or took a nap then washed their faces or had a bright light shone in their eyes. They also subjectively rated themselves as less tired.

Interestingly, there's even some evidence that caffeine naps can help people go for relatively long periods without proper sleep. As part of one study, 24 young men went without proper sleep for a 24-hour period, taking only short naps. 12 of them, who were given just a placebo, performed markedly worse on a series of cognition tests, compared to their baseline scores. 12 others, who had caffeine before their naps, managed scores roughly the same as their baselines for the entire day.

How to take a coffee nap

Taking a coffee nap is pretty straightforward. First, drink coffee. Theoretically, you could drink another caffeinated beverage, but tea and soda have generally have much less caffeine than coffee, and energy drinks are disgusting. Here's a good database of the amount of caffeine in many types of drinks.

You need to drink it quickly, to give yourself a decently long window of time to sleep as it's going through your gastrointestinal tract and entering your bloodstream. If it's tough for you to drink a lot of hot coffee quickly, good options might be iced coffee or espresso.

Right after you're finished, immediately try to go to sleep. Don't worry if it doesn't come easily - just reaching a tranquil half-asleep stage can be helpful.

Finally, make sure to wake up within 20 minutes, so you don't enter the deeper stages of sleep, and you're awake when the caffeine is just starting to hit your brain.

http://www.eurekalert.org/pub_releases/2015-04/tl-tls042215.php

The Lancet: Scientists announce final trial results of the world's most advanced malaria vaccine

First malaria vaccine candidate to reach phase 3 clinical testing is partially effective in young African children up to 4 years after vaccination

The first malaria vaccine candidate (RTS,S/AS01) to reach phase 3 clinical testing is partially effective against clinical disease in young African children up to 4 years after vaccination, according to final trial data, published in The Lancet. The results suggest that the vaccine could prevent a substantial number of cases of clinical malaria, especially in areas of high transmission.

The findings reveal that vaccine efficacy against clinical and severe malaria was better in children than in young infants, but waned over time in both groups. However, protection was prolonged by a booster dose, increasing the average number of cases prevented in both children and young infants.

Brian Greenwood, corresponding author and Professor of Clinical Tropical Medicine at London School of Hygiene & Tropical Medicine in the UK explains, "Despite the falling efficacy over time, there is still a clear benefit from RTS,S/AS01. An average 1363 cases of clinical malaria were prevented over 4 years of follow-up for every 1000 children vaccinated, and 1774 cases in those who also received a booster shot. Over 3 years of follow-up, an average 558 cases were averted for every 1000 infants vaccinated, and 983 cases in those also given a booster dose." [1]

"Given that there were an estimated 198 million malaria cases in 2013, this level of efficacy potentially translates into millions of cases of malaria in children being prevented."[1]

The RTS,S/AS01 vaccine was developed for use in sub-Saharan Africa where malaria still kills around 1300 children every day [2]. There is currently no licensed vaccine against malaria anywhere in the world.

The phase 3 randomised trial enrolled 15459 young infants (aged 6 to 12 weeks at first vaccination) and children (5 to 17 months at first vaccination) from 11 sites across seven sub-Saharan African countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique and United Republic of Tanzania) with varying levels of malaria transmission. In 2014, initial phase 3 results at 18 months showed vaccine efficacy of about 46% against clinical malaria in children and around 27% among young infants [3].

In this study, members of the RTS,S Clinical Trials Partnership followed up the infants and children for a further 20 to 30 months, respectively, and assessed the impact of a fourth booster dose. Participants were each vaccinated three times with RTS,S/AS01 with or without a booster dose 18 months later, or given four doses of a comparator vaccine (control group).

In children who received 3 doses of RTS,S/AS01 plus a booster, the number of clinical episodes of malaria at 4 years was reduced by just over a third (36%). This is a drop in efficacy from the 50% protection against malaria seen in the first year (see table 1).

Importantly, without a booster dose, significant efficacy against severe malaria was not shown in this age group. However, in children given a booster dose,

overall protective efficacy against severe malaria was 32%, and 35% against malaria-associated hospitalisations.

In infants who received 3 doses of RTS,S/AS01 plus a booster, the vaccine reduced the risk of clinical episodes of malaria by 26% over 3 years follow-up. There was no significant protection against severe disease in infants (see table 3).

Meningitis occurred more frequently in children given RTS,S/AS01 (11 children in the group who received the booster dose and 10 in those who did not) than in those given the control vaccine (1 child). RTS,S/AS02 produced more adverse reactions than the control vaccines. Convulsions following vaccination, although uncommon, occurred more frequently in children who received RTS,S/AS01 than in controls. The incidence of other serious adverse events was similar in all groups of participants.

According to Professor Greenwood, "The European Medicines Agency (EMA) will assess the quality, safety, and efficacy of the vaccine based on these final data. If the EMA gives a favorable opinion, WHO could recommend the use of RTS,S/AS01 as early as October this year. If licensed, RTS,S/AS01 would be the first licensed human vaccine against a parasitic disease."[1]

Writing in a linked Comment, Vasee Moorthy and Jean Marie Okwo-Bele, from the Department of Immunization, Vaccines and Biologicals at WHO in Geneva, Switzerland say, "The donor community would need to coordinate any financing for the RTS,S/AS01 vaccine carefully, should it reach that stage. In particular, funding must not be redirected away from meeting adequate access to artemisinin-combination treatments, rapid diagnostic tests, longlasting insecticidal nets, and other malaria control measures already in place in certain settings."

NOTES TO EDITORS:

This study was funded by GlaxoSmithKline Biologicals SA and the PATH Malaria Vaccine Initiative.

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

[2] http://www.who.int/malaria/media/world_malaria_report_2014/en/

[3] Vaccine efficacy is the reduction in the incidence of a disease (the number of new cases that occur in a population in a given period) among trial participants who receive the vaccine compared to the incidence among participants who do not receive the vaccine.

http://www.eurekalert.org/pub_releases/2015-04/tjnj-oaw042215.php

Oophorectomy associated with decrease in breast cancer death in women with cancer, BRCA1 mutation

Removal of the ovaries, a procedure known as an oophorectomy, was associated with a 62 percent reduction in breast cancer death in women diagnosed with breast cancer and carrying a BRCA1 gene mutation, according to an article published online by JAMA Oncology.

Women who carry a germline mutation in either the BRCA1 or BRCA2 gene face a lifetime risk of breast cancer of up to 70 percent. Once they are diagnosed with breast cancer, they face high risks of both second primary breast and ovarian cancers. Other studies of BRCA gene mutation carriers have reported reduced mortality associated with oophorectomy for women with a history of breast cancer, according to the study background.

Steven A. Narod, M.D., and Kelly Metcalfe, Ph.D., of the Women's College Research Institute, Toronto, Canada, and coauthors sought to confirm these earlier observations in a group of women with BRCA1 and BRCA2 gene mutations and early-stage breast cancer. Their study included 676 women, of whom 345 underwent oophorectomy after being diagnosed with breast cancer, while 331 women retained both ovaries.

The study found 20-year survival for the entire group was 77.4 percent. In the entire group, there was a 56 percent reduction in breast cancer death associated with oophorectomy. Undergoing an oophorectomy was associated with a significant reduction (62 percent) in breast cancer death in women with a BRCA1 mutation but not in women with a BRCA2 mutation because the 43 percent reduction authors found was not statistically significant.

In addition there were nine deaths from ovarian cancer in the group of women who did not have oophorectomies. The authors found a 65 percent reduction in all-cause mortality associated with oophorectomy in their analysis.

According to the study results, oophorectomies were performed an average of six years after breast cancer diagnosis. For the 70 BRCA1 carriers for whom the oophorectomy was performed within two years of breast cancer diagnosis, there was a 73 percent reduction in death compared with women with a BRCA1 mutation who never underwent oophorectomy. The authors note the protective effect of oophorectomy on deaths from breast cancer was apparent immediately after diagnosis and lasted for 15 years.

"It is important that follow-up studies be performed on women who undergo oophorectomy as part of their initial treatment, in particular, those women who undergo oophorectomy in the first year after diagnosis. It is also important that our observations be confirmed in other study populations. Further data are needed, in particular for BRCA2 carriers in order to confirm the benefit of oophorectomy in this population," article concludes.

Editor's Note: ***Adjuvant Oophorectomy in Treatment of Early-Stage BRCA Mutation-Positive Breast Cancer***

In a related editor's note, Mary L. Disis, M.D., editor-in-chief of JAMA Oncology, writes: "The results provide a validation of the role of oophorectomy in conveying both a disease-free and overall survival benefit for BRCA1 mutation carriers. Oophorectomy

after the primary diagnosis of breast cancer significantly reduced breast cancer-specific mortality in women with BRCA1 mutations but not in BRCA2 mutation carriers. In the entire group, oophorectomy was particularly effective for survival benefit in women with estrogen receptor-negative breast cancer. ... The data reported here are compelling and suggest that the potential of oophorectomy should become part of the treatment discussion at the time of diagnosis for BRCA mutation carriers with early-stage breast cancers."

(JAMA Oncol. Published online April 16, 2015. doi:10.1001/jamaoncol.2015.0658. Available pre-embargo to the media at http://media.jamanetwork.com.)

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http://bit.ly/1E6I8Y3

First human embryos genetically modified – more will come

The prospect of genetically engineering humans has come a step closer, with the publication of the first paper to describe efforts to modify embryos.

14:49 23 April 2015 by Michael Le Page

There is a long way to go before we can safely tinker with our genes, but at least one group in the US and four in China are aiming to edit human embryos: this will be the first of many studies.

The work was done using a gene editing technique called CRISPR (pronounced "crisper").

The idea of gene editing is to make specific changes in a particular gene, just as you might correct a spelling mistake. Gene editing has been around for decades, but in organisms other than mice it used to be difficult, expensive and time-consuming.

The CRISPR method – the name refers to characteristic sets of repeating chunks of DNA known as "clustered regularly interspaced short palindromic repeats" – developed in just the past few years, has changed all that, allowing biologists to achieve in weeks what used to take years.

The ease, speed and cheapness of CRISPR has made it possible for more people to experiment with gene editing. Last month, it was reported that a handful of teams are trying to modify human embryos using the method. Now one of those teams, led by Junjiu Huang at the Sun Yat-sen University in Guangzhou, China, has published its results.

Rejected eggs

"Because ethical concerns preclude studies of gene editing in normal embryos," the team writes, the researchers used human eggs that had been fertilised by two sperm rather than one.

These "polyspermic" eggs may develop for a few days but never develop normally and are discarded by fertility clinics.

Huang's team then attempted to modify one of the genes coding for the oxygen-carrying blood protein haemoglobin. Mutations in this gene cause the disease beta-thalassemia, itself a target for previous gene-editing attempts. The team injected the various snippets of RNA and DNA needed for CRISPR into the polyspermic eggs. One of the DNA sequences was a "template" for the desired changes to the gene, intended to guide the repair process.

Of the 86 eggs injected, just four were successfully modified – an efficiency rate far lower than required to make human germline gene editing a practical prospect. The others either did not survive, or were not successfully modified.

Missing the target

There were also changes to genes other than the globin gene. Such "off-target" alterations are a big concern, because they could cause serious illnesses.

It should be possible to reduce the number of off-target changes by refining the CRISPR method. However, it will probably never be possible to completely eliminate them. So if gene editing were ever to be used for modifying inherited human genetic material, it would be essential to check embryos for any off-target effects before implanting them in the mother-to-be.

In theory, this can be done by removing a single cell from a developing embryo and sequencing its DNA – a method already sometimes used during IVF to ensure embryos don't carry serious disease mutations, called preimplantation genetic diagnosis.

Living mosaics

However, Huang and his colleagues found what could be a serious problem: the embryos were a mixture of modified and unmodified cells – so-called genetic mosaics. That means the results of preimplantation genetic testing could be misleading.

On the face of it, these findings are not encouraging for those hoping to use gene editing to correct hereditary diseases in children. However it is too soon to draw sweeping conclusions. The low efficiency and the mosaicism could be a result of using flawed eggs. There might also be a specific problem with their approach – the paper was published just a day after being received by the journal, so it has not yet been thoroughly scrutinised by independent researchers. What's more, CRISPR is still a new method, so it is likely to be improved greatly in the coming years.

But should this kind of research be done at all? That depends on whether you think modifying the inheritable DNA of the human germline is acceptable. Some have called for a moratorium on this kind of work, and according to Huang, the

paper was rejected by the journals Science and Nature in part because of ethical concerns.

Polls in various countries, however, indicate that there is actually substantial public support – sometimes over 50 per cent – for using germline modification to prevent genetic diseases.

The efficiency of gene editing can vary greatly across both species and cell types. So to find out whether any method is safe and effective it is necessary to try it in human embryos.

Journal reference: Protein Cell, DOI: 10.1007/s13238-015-0153-5

http://nyti.ms/1Ki1M5A

Chinese Scientists Edit Genes of Human Embryos, Raising Concerns

The experiment with human embryos was dreaded, yet widely anticipated.

By GINA KOLATA APRIL 23, 2015

Scientists somewhere, researchers said, were trying to edit genes with a technique that would permanently alter the DNA of every cell so any changes would be passed on from generation to generation.

Those concerns drove leading researchers to issue urgent calls in major scientific journals last month to halt such work on human embryos, at least until it could be proved safe and until society decided if it was ethical.

Now, scientists in China report that they tried it.

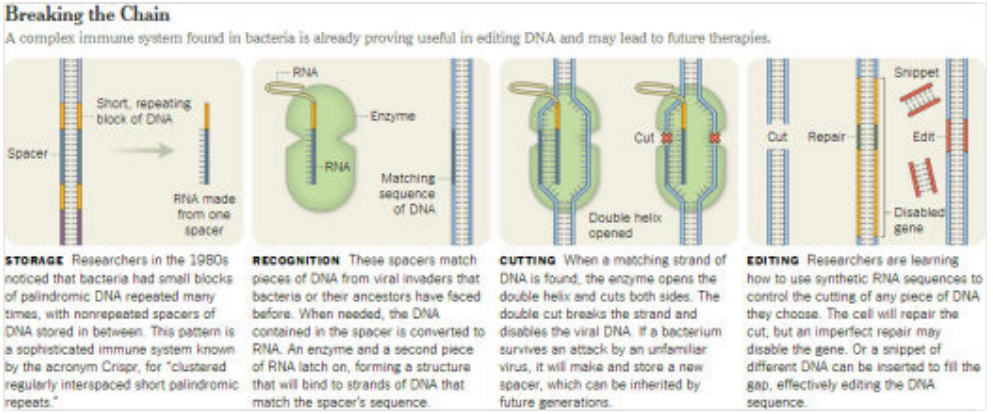
The experiment failed, in precisely the ways that had been feared.

The Chinese researchers did not plan to produce a baby — they used defective human embryos — but did hope to end up with an embryo with a precisely altered gene in every cell but no other inadvertent DNA damage. None of the 85 human embryos they injected fulfilled those criteria. In almost every case, either the embryo died or the gene was not altered. Even the four embryos in which the targeted gene was edited had problems. Some of the embryo cells overrode the editing, resulting in embryos that were genetic mosaics. And speckled over their DNA was a sort of collateral damage — DNA mutations caused by the editing attempt.

“Their study should give pause to any practitioner who thinks the technology is ready for testing to eradicate disease genes during I.V.F.,” said Dr. George Q. Daley, a stem cell researcher at Harvard, referring to in vitro fertilization. “This is an unsafe procedure and should not be practiced at this time, and perhaps never.”

David Baltimore, a Nobel laureate molecular biologist and former president of the California Institute of Technology, said, “It shows how immature the science is,” adding, “We have learned a lot from their attempts, mainly about what can go wrong.”

But some researchers worry that this paper is just an initial sally and that attempts will continue with clinical applications in mind. They fear the result will be the birth of babies whose every cell has been altered by scientists in a rush to be first. This could happen well before researchers know enough about the consequences of editing genes, before they know how to edit safely and before society can debate if such procedures are even acceptable.



Sources: Nature; Addgene By The New York Times

Gene editing uses a method called Crispr that has rapidly become a research stalwart. It exploits a system that bacteria use to protect themselves from viruses and allows researchers to cut out selected genes and insert new ones.

A pressing question, said Rudolf Jaenisch, an M.I.T. biology professor, is why anyone would want to edit the genes of human embryos to prevent disease. Even in the most severe cases, involving diseases like Huntington’s in which a single copy of a mutated gene inherited from either parent is enough to cause the disease with 100 percent certainty, editing poses ethical problems. Because of the way genes are distributed in embryos, when one parent has the gene, only half of the parent’s embryos will inherit it. With gene editing, the cutting and pasting has to start immediately, in a fertilized egg, before it is possible to know if an embryo has the Huntington’s gene. That means half the embryos that were edited would have been normal — their DNA would have been forever altered for no reason.

“It is unacceptable to mutate normal embryos,” Dr. Jaenisch said. “For me, that means there is no application.”

Noting the many unresolved questions about gene editing of human embryos, a group of leading American researchers recently published a paper in the journal Science calling for a moratorium on doing such work for clinical purposes. They pointed out that current knowledge about genes and their interactions was limited

and that changing a disease gene in an embryo that then develops into a baby could have unintended consequences that would be inherited by all of that person's progeny.

A recent paper in the journal Nature made similar points. In it, Edward Lanphier of Sangamo Biosciences in Richmond, Calif., and his colleagues wrote: "In our view, genome editing in human embryos using current technologies could have unpredictable effects on future generations. This makes it dangerous and ethically unacceptable."

The new paper, he said, is "a bull's-eye example of the two issues we were concerned about." It shows that the technology is not ready for editing genes of human embryos, he said. But, he added: "As that work goes on, if one, five, 12, 100 labs are doing it, the process could get effective. That is what we want to slow down until we have an opportunity to discuss whether it should be done."

In their new paper, published in the online journal Protein & Cell, Junjiu Huang and Canquan Zhou and colleagues at Sun Yat-sen University in Guangzhou say they obtained human embryos from a fertility clinic. None could have developed normally because they had extra chromosomes, so they had been donated for research. The investigators used the Crispr method to try to edit a gene that, when mutated, causes beta thalassemia, a serious blood disorder. Their goal was to alter that gene and only that gene in every cell of the developing embryo.

The Chinese researchers point out that in their experiment gene editing almost certainly caused more extensive damage than they documented; they did not examine the entire genomes of the embryo cells.

Dr. Daley notes that when cloning techniques were developed, there was an international consensus that it would be unacceptable to clone a human being. Nonetheless, some researchers tried. He worries that something similar will happen with gene editing. "This type of intervention would achieve worldwide acclaim," Dr. Daley said. "I think that is the sort of deranged motivation that sometimes prompts people to do things."

http://www.bbc.com/news/science-environment-32432693

Mammoth genome sequence completed

An international team of scientists has sequenced the complete genome of the woolly mammoth.

By Pallab Ghosh Science correspondent, BBC News

A US team is already attempting to study the animals' characteristics by inserting mammoth genes into elephant stem cells. They want to find out what made the mammoths different from their modern relatives and how their adaptations helped them survive the ice ages. The new genome study has been published in the journal Current Biology.

Dr Love Dalén, at the Swedish Museum of Natural History in Stockholm, told BBC News that the first ever publication of the full DNA sequence of the mammoth could help those trying to bring the creature back to life. "It would be a lot of fun (in principle) to see a living mammoth, to see how it behaves and how it moves," he said. But he would rather his research was not used to this end. "It seems to me that trying this out might lead to suffering for female elephants and that would not be ethically justifiable."

Dr Dalén and the international group of researchers he is collaborating with are not attempting to resurrect the mammoth. But the Long Now Foundation, an organisation based in San Francisco, claims that it is.

Now, with the publication of the complete mammoth genome, it could be a step closer to achieving its aim. On its website, the foundation says its ultimate goal is "to produce new mammoths that are capable of repopulating the vast tracts of tundra and boreal forest in Eurasia and North America. "The goal is not to make perfect copies of extinct woolly mammoths, but to focus on the mammoth adaptations needed for Asian elephants to live in the cold climate of the tundra.

Could the mammoth become a familiar sight across parts of the the world once again?

The foundation is supporting a team based at Harvard University, which is using genetic engineering techniques to insert mammoth genes into living elephant cells. So far, the foundation says it has placed mammoth genes involved in blood, fat and hair into elephant stem cells in order to study the effects of these genes.

The researchers hope to produce mammoth red blood cells to see how much oxygen they might have carried and so learn more about the physiology of the animals. Similar tests, they claim, can be done to investigate how their fat and hair grew. The Long Now Foundation's stated aim is to insert synthetically created mammoth genetic material inside an elephant egg, which it would then place in a zoo elephant. It believes that cloning attempts can begin by 2018.

Many experts, however, believe that there are considerable obstacles in the way of creating a mammoth in this way. Among them is Prof Beth Shapiro, of the University of California, Santa Cruz, who has written a book called How to Clone a Mammoth.

"There is an enormous difference between having a cell living in a dish in a lab whose genome contains a few changes and having a living animal that is a little bit mammoth-like," she told BBC News.

De-extinction

"We'd have to use that cell to create an embryo, get an embryo into a maternal host, and establish a pregnancy and hope that pregnancy was successful."

Prof Shapiro is opposed to what is known in the field as "mammoth de-extinction".

"Elephants do not fare well in captivity, struggle with assisted reproduction, and should be allowed to make more elephants.

"Secondly, elephants are highly social creatures and there is no reason to suspect that mammoths were not. One mammoth would be necessarily alone in the world. It could not be released into the freedom of the Arctic until there were many of them. Until we can make many mammoths without using elephants, to my mind it is ethically unsound."

Dr Dalén and his colleagues sequenced the mammoth genome in order to learn more about what happened when the creature went extinct around 4,000 years ago on Russia's Wrangel Island. They compared the DNA of one of the last creatures to have lived with one that lived 45,000 years ago when mammoths were more commonplace.

The study showed that the population on Wrangel Island was so small that the animals became inbred for the last 5,000 years of their existence. Dr Dalén cannot say categorically that inbreeding was the cause or contributed to their eventual demise because it doesn't always have a negative effect, but he thinks that his study makes this a distinct possibility. "When we look at modern animals we know that most animals that are inbred suffer from it. So we think it is likely that it had some sort of negative effect," he said.

The genetic data also showed that there was a dip in the mammoth population 300,000 years ago. "We were very surprised by this," Dr Dalén said. "It seems like there was an ancient bottleneck. It was before modern humans were in this region and we are not entirely sure what caused it. A good bet is that it was due to a past change in climate."

Prof Shapiro believes that there is much more to come from the new mammoth DNA. "We'll probably find answers to questions that we've yet to think of. Genomes are rich sources of information, and we have only tapped the surface of that information," he said.

http://bit.ly/1HH8zYk

This Stroke of Genius Could Allow You to Write With Your Brain

Not Impossible Labs has developed a breakthrough approach to communication

By Elizabeth Quill Smithsonian Magazine

The notion of a nefarious power somehow dictating what individuals say and do by tampering with their brains is, for the moment at least, still fictional. But there's a less diabolical kind of mind control and it's very real, as Mick Ebeling is In his Venice, California, laboratory he is developing a device that will permit disabled people to write with their minds—no pencil strokes or keystrokes required. Called the Brainwriter, it combines new, low-cost headsets that monitor the brain's electrical activity with eye-tracking technology and open-source software. By thinking about a single idea or word, a person can command a computer cursor to enter writing mode, the equivalent of putting pen to paper. Then, as the eyes move, the cursor traces their path on-screen.

"I like to see things that are not supposed to be done, be done," says Ebeling, co-founder of the hopeful-sounding company Not Impossible. He's not an engineer himself—he's a film and TV producer—so he recruits technical experts to help him solve real-world problems. "Help one, help many" is one of his mantras. For instance, Ebeling and his team 3-D-printed prosthetic arms for amputees in South Sudan, starting with a teenage boy named Daniel.

Brainwriter was inspired by an L.A. graffiti artist named Tony Quan (tag name Tempt One), who is afflicted by amyo-trophic lateral sclerosis and no longer has control over his muscles.

At first, Ebeling and his crew fashioned a device out of plastic eyeglasses, a coat hanger and a hacked-open PlayStation 3 camera. "Steve Jobs would roll over in his grave if he saw our stuff," Ebeling says.

In this version, Quan blinked to enter writing mode and select his drawing tools. But as his condition worsened, he could no longer control the device with his blinks.

So the next step was to tap into brain waves, monitored via electroencephalogram. A focusing brain produces a particular EEG pattern, which the computer software recognizes and processes the same way it processes the click of a mouse.

Still in the testing phase, Brainwriter will give patients with paralysis a new way to communicate, more efficient than the current method of spelling out words letter by letter. In later iterations, it might be adapted for people with no control over their eye movements.

"Mick will unashamedly and unabashedly say that our solution is not the end word," says David Putrino (left), a neuroscientist who works with Not Impossible. "Our solution is a lesson that it can be done."

Ebeling predicts that someday soon similar technologies will not only help disabled people but will also enhance the way everyone communicates. Ordinary baseball caps studded with EEG sensors will be sold at the mall.

You won't necessarily compose a sonnet with them, but you'll be able to perform simple actions, like making a dinner reservation.

While other developers hack the brain to make a toy robot walk or control a video game, Ebeling strives for a technology more akin to the telephone. "Just being able to convey information," he says, "is huge."

http://www.eurekalert.org/pub_releases/2015-04/usgs-msc042315.php

Map shows content and origins of the nation's geologic basement

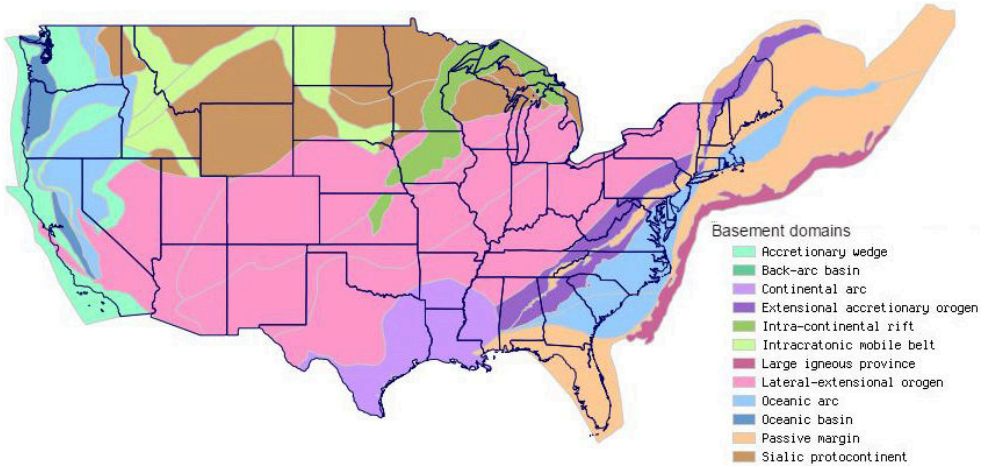
A map showing the many different pieces of Earth's crust that comprise the nation's geologic basement is now available from the U.S. Geological Survey.

This is the first map to portray these pieces, from the most ancient to recent, by the events that influenced their composition, starting with their origin.

This product provides a picture of the basement for the U.S., including Alaska, that can help scientists produce regional and national mineral resource assessments, starting with the original metal endowments in source rocks.

"Traditionally, scientists have assessed mineral resources using clues at or near the Earth's surface to determine what lies below," said USGS scientist Karen Lund, who led the project.

"This map is based on the concept that the age and origins of basement rocks influenced the nature and location of mineral deposits. It offers a framework to examine mineral resources and other geologic aspects of the continent from its building blocks up," said Lund.



Map showing basement domains according to generalized original crust types. (High resolution image) **USGS**

More than 80 pieces of crust have been added to the nation's basement since the Earth began preserving crust about 3.6 billion years ago. These basement domains had different ages and origins before they became basement rocks, and this map includes these as key factors that determined their compositions and the original metals that may be available for remobilization and concentration into ore deposits.

The map further classifies the basement domains according to how and when they became basement, as these events also influence the specific metals and deposit types that might be found in a region.

Users can identify domains potentially containing specific metals or deposit types. They can configure the companion database to show the construction of the U.S. through time.

The map also provides a template to correlate regional to national fault and earthquake patterns.

The map is also available on a separate site, where users can combine data and overlay known mineral sites or other features on the domains.

Basement rocks are crystalline rocks lying above the mantle and beneath all other rocks and sediments. They are sometimes exposed at the surface, but often they are buried under miles of rock and sediment and can only be mapped over large areas using remote geophysical surveys.

This map was compiled using a variety of methods, including data from national-scale gravity and aeromagnetic surveys.

Crustal rocks are modified several times before they become basement, and these transitions alter their composition. Basement rocks are continental crust that has been modified by a wide variety of plate tectonic events involving deformation, metamorphism, deposition, partial melting and magmatism.

Ultimately, continental crust forms from pre-existing oceanic crust and overlying sediments that have been thus modified.

It is not only the myriad processes that result in varying basement rock content but also the time when these processes occurred during the Earth's history.

For example, because the Earth has evolved as a planet during its 4.5 billion year history, early deposit types formed when there was less oxygen in the atmosphere and the thin crust was hotter.

The ancient domains are now more stable and less likely to be altered by modern processes that could cause metals to migrate.

By contrast, basement rocks that formed out of crust that is less than one billion years old have origins that can be interpreted according to the present-day rates and scales of plate tectonic processes that reflect a more mature planet with a thicker crust.

By incorporating ancient to modern processes, this map offers a more complete and consistent portrait of the nation's geologic basement than previous maps and presents a nationwide concept of basement for future broad-scale mineral resource assessments and other geologic studies.

http://bit.ly/1E7JkdL

Japan Plans a Trip to the Moon by 2018

The lander will use information from Japan's moon-orbiting satellite to stick the landing

By Marissa Fessenden

The moon has seen many spacecraft by now. The former Soviet Union, the U.S. and most recently, China have all touched down on the surface of our satellite. Now, Japan plans to be the next in line for lunar exploration. They recently announced a plan to launch a probe in 2018.

The Japan Aerospace Exploration Agency (JAXA), divulged the plan to an expert panel, including members of the cabinet and the Education, Culture, Sports, Science and Technology Ministry on Monday.

"This is an initial step and a lot of procedures are still ahead before the plan is formally approved," a JAXA spokesperson told reporters.

Japan hopes to be able to accomplish the feat better and for less money than the three nations who have already landed on the lunar surface, reports Yomiuri Shimbun for *The Japan News*. The newest moon lander will have the advantage of the latest technology and experience, especially when compared to landings in the 1960s, but that doesn't mean Japan is taking it easy.

Other moon probes have landed within several kilometers of the target site, but the so-called "SLIM" probe would aim to land within 100 meters (approximately 328 feet) of its target. Shimbun reports that the mission will photograph the moon's surface as it descends and then access data gathered by the Kaguya lunar orbiter, also known as SELENE, launched in 2007, to make adjustments. Then the probe will come in for a soft landing - something that is notoriously difficult to achieve.

The panel tjat announced the mission estimated that development costs would be somewhere between ¥10 billion to ¥15 billion (about $84 million to $130 million), Shimbun writes.

Rae Botsford End reports for *Space Flight Insider*:

Yet the lunar mission is not set in stone. "This is an initial step and a lot of procedures are still ahead before the plan is formally approved," said a JAXA official.

If it occurs, the mission will use a probe called Smart Lander for Investigating Moon (SLIM), and it will likely be carried aboard JAXA's solid-fuel Epsilon rocket, a design that has only seen one launch to date. Its maiden flight in September 2013 brought the SPRINT-A satellite, later called Hisaki, to orbit. Epsilon is a smaller and less expensive follow-on to the retired M-V (or Mu-5) rocket.

The probe's mission will be far more serious that Japanese beverage manufacturer Otsuka's plan to send a powdered sports drink to the moon. SLIM will test soft-landing techniques that could be used by manned lunar missions in the future.

With China's fifth lunar probe set for launch in 2017, a lunar lander from India in the works, and all the previous landings, the moon could soon seem downright crowded.

http://www.eurekalert.org/pub_releases/2015-04/tau-tas042415.php

Texas A&M study finds we think better on our feet, literally

Preliminary results show 12 percent greater on-task engagement in classrooms with standing desks

A study from the Texas A&M Health Science Center School of Public Health finds students with standing desks are more attentive than their seated counterparts. In fact, preliminary results show 12 percent greater on-task engagement in classrooms with standing desks, which equates to an extra seven minutes per hour of engaged instruction time.

The findings, published in the International Journal of Health Promotion and Education, were based on a study of almost 300 children in second through fourth grade who were observed over the course of a school year. Engagement was measured by on-task behaviors such as answering a question, raising a hand or participating in active discussion and off-task behaviors like talking out of turn.

Standing desks - also known as stand-biased desks - are raised desks that have stools nearby, enabling students to sit or stand during class at their discretion. Mark Benden, Ph.D., CPE, associate professor at the Texas A&M Health Science Center School of Public Health, who is an ergonomic engineer by trade, originally became interested in the desks as a means to reduce childhood obesity and relieve stress on spinal structures that may occur with traditional desks. Lessons learned from his research in this area led to creation of Stand2Learn™, an offshoot company of a faculty-led startup that manufactures a classroom version of the stand-biased desk.

Benden's previous studies have shown the desks can help reduce obesity - with students at standing desks burning 15 percent more calories than students at traditional desks (25 percent for obese children) - and there was anecdotal evidence that the desks also increased engagement. The latest study was the first designed specifically to look at the impact of classroom engagement.

Benden said he was not surprised at the results of the study, given that previous research has shown that physical activity, even at low levels, may have beneficial effects on cognitive ability.

"Standing workstations reduce disruptive behavior problems and increase students' attention or academic behavioral engagement by providing students with a different method for completing academic tasks (like standing) that breaks up the monotony of seated work," Benden said.

"Considerable research indicates that academic behavioral engagement is the most important contributor to student achievement. Simply put, we think better on our feet than in our seat."

The key takeaway from this research, Benden said, is that school districts that put standing desks in classrooms may be able to address two problems at the same time: academic performance and childhood obesity.

Additional Texas A&M researchers involved with the study, which was funded by the National Institutes of Health, were Hongwei Zhao, Ph.D., professor of epidemiology and biostatistics at the Texas A&M School of Public Health; Jamilia Blake, Ph.D., assistant professor of educational psychology at the Texas A&M College of Education; and Marianela Dornhecker, doctoral student in educational psychology at the Texas A&M College of Education. Monica Wendel, Dr.P.H., associate dean for public health practice at the University of Louisville, also contributed to the research.

http://www.eurekalert.org/pub_releases/2015-04/luhs-hhc041615.php

How hospitals can improve outcomes of weekend surgeries

More nurses, electronic medical records among resources that help overcome 'weekend effect'

Studies have shown that patients who undergo surgeries on weekends tend to experience longer hospital stays and higher mortality rates and readmissions.

For the first time, a new study has identified five resources that can help hospitals overcome this "weekend effect": Increased nurse-to bed ratio; full adoption of electronic medical records; inpatient physical rehabilitation; a home-health program; and a pain management program.

"Specific hospital resources can overcome the weekend effect seen in urgent general surgery procedures," senior author Paul Kuo, MD, MS, MBA, first author Anai Kothari, MD, and colleagues reported. The study was released April 25, 2015, in a podium presentation at the American Surgical Association meeting in San Diego. Several reasons have been proposed to explain the weekend effect, including reduced staffing and resources and fewer experienced doctors and nurses working on weekends.

Loyola researchers hypothesized that boosting hospital resources before, during and after surgery could overcome the weekend effect. They tested their hypothesis in patients undergoing three types of urgent surgeries that could not be delayed until weekdays: appendectomies, hernia repairs and gall bladder removals.

The researchers examined records of 126,666 patients at 117 Florida hospitals participating in a data base program sponsored by the U.S. Agency for Healthcare Research and Quality. Florida was picked because of its large, diverse population. To determine characteristics of individual hospitals, the patient data were linked to the American Hospital Association Annual Survey database.

Of the 21 hospital resources researchers examined, five were found to help overcome the weekend effect after controlling for patient characteristics:

Hospitals with increased nurse-to-bed ratios were 1.44 times more likely to overcome the weekend effect. Seventeen hospitals that overcame the weekend effect had a median nurse-to-bed ratio of 1.3, compared with a nurse-to-bed ratio of 1.1 among 41 hospitals with a persistent weekend effect.

Hospitals with home health programs were 2.37 times more likely to overcome the weekend effect. In such programs, skilled caregivers check on patients after they are discharged, providing wound care, administering medications, etc.

Hospitals that fully adopted electronic medical records were 4.74 times more likely to overcome the weekend effect.

Hospitals with inpatient physical rehabilitation programs were 1.03 times more likely to overcome the weekend effect. Such programs identify patients who require additional physical conditioning prior to discharge or need extra resources at home.

Hospitals with pain management programs were 1.48 times more likely to overcome the weekend effect.

Researchers plan to conduct a follow-up study of hospitals in California, which also has a large, diverse population.

The study was conducted by Loyola's predictive analytics program, which mines large data sets to predict health outcomes. In addition to the weekend effect study, researchers are studying, for example, how many rectal cancer operations a hospital needs to perform for the best results, and whether having a trauma department confers a beneficial "halo effect" on patient outcomes across the board.

Large new databases, electronic medical records and more powerful computers are enabling researchers to conduct such studies. "We're now able to ask and answer a broad range of questions that could significantly help improve patient care and reduce costs," Dr. Kuo said. Dr. Kuo heads Loyola's analytics group, One to Map Analytics. (One-to-map is a common computer command in analytics research.)

Dr. Kuo is the John P. Igini professor and chair of the Department of Surgery of Loyola University Chicago Stritch School of Medicine. The study is titled, "Components Of Hospital Perioperative Infrastructure Can Overcome The Weekend Effect In Urgent General Surgery Procedures." In addition to Dr. Kuo and Dr. Kothari, other co-authors are Matthew Zapf; Robert Blackwell, MD; Victor Chang; Zhiyong Mi, PhD; and Gopal Gupta, MD.

The complete manuscript of this study and its presentation at the American Surgical Association's 135th Annual Meeting, April 2015, in San Diego, California, is anticipated to be published in the Annals of Surgery pending editorial review.

http://bit.ly/1EEK7WN

Liquid mercury found under Mexican pyramid could lead to king's tomb

Researcher reports 'large quantities' of the substance under ruins of Teotihuacan in discovery that could shed light on city's mysterious leaders

Alan Yuhas in New York

An archaeologist has discovered liquid mercury at the end of a tunnel beneath a Mexican pyramid, a finding that could suggest the existence of a king's tomb or a ritual chamber far below one of the most ancient cities of the Americas.

Mexican researcher Sergio Gómez announced on Friday that he had discovered "large quantities" of liquid mercury in a chamber below the Pyramid of the Feathered Serpent, the third largest pyramid of Teotihuacan, the ruined city in central Mexico.

Gómez has spent six years slowly excavating the tunnel, which was unsealed in 2003 after 1,800 years. Last November, Gómez and a team announced they had found three chambers at the tunnel's 300ft end, almost 60ft below the the temple. Near the entrance of the chambers, they a found trove of strange artifacts: jade statues, jaguar remains, a box filled with carved shells and rubber balls.

Visitors look at the archaeological area of the Quetzalcoatl (Feathered Serpent) Temple near the Pyramid of the Sun at the Teotihuacan archaeological site, north of Mexico City. **Photograph: Henry Romero/Reuters**

Slowly working their way down the broad, dark and deep corridor beneath the pyramid, battling humidity and now obliged to wear protective gear against the dangers of mercury poisoning, Gómez and his team are meticulously exploring the three chambers.

Mercury is toxic and capable of devastating the human body through prolonged exposure; the liquid metal had no apparent practical purpose for ancient Mesoamericans. But it has been discovered at other sites. Rosemary Joyce, a professor of anthropology at the University of California, Berkeley, said that archaeologists have found mercury at three other sites, two Maya and one Olmec, around Central America.

Gómez speculated to Reuters that the mercury could be a sign that his team is close to uncovering the first royal tomb ever found in Teotihuacan after decades of excavation – and centuries of mystery surrounding the leadership of the cryptic but well-preserved city.

The mercury may have symbolized an underworld river or lake, Gómez postulated, an idea that resonated with Annabeth Headreck, a professor at the University of Denver and the author of works on Teotihuacan and Mesoamerican art.

The shimmering, reflective qualities of liquid mercury may have resembled "an underworld river, not that different from the river Styx," Headrick said, "if only in the concept that it's the entrance to the supernatural world and the entrance to the underworld."

"Mirrors were considered a way to look into the supernatural world, they were a way to divine what might happen in the future," she said. "It could be a sort of river, albeit a pretty spectacular one."

Joyce said that archaeologists know that scintillation fascinated the ancient people generally, and that the liquid mercury may have held been regarded as "somewhat magical … there for ritual purposes or symbolic purposes."

Headrick said that mercury was not the only object of fascination: "a lot of ritual objects were made reflective with mica," a sparkling mineral likely imported to the region.

In 2013 archaeologists using a robot found metallic spheres which they dubbed "disco balls" in an un-excavated portion of the tunnel, near pyrite mirrors. "I wish I could understand all the things these guys are finding down there," Headrick said, "but it's unique and that's why it's hard."

Water was also precious to many of the people of Mesoamerica, who knew of underground water systems and lakes that could be accessed through caves. Teotihuacan once had springs as well, though they are now dried out.

Joyce said the ancient Mesoamericans could produce liquid mercury by heating mercury ore, known as cinnabar, which they also used for its blood-red pigment.

The Maya used cinnabar to decorate jade objects and color the bodies of their royalty, for instance; the people of Teotihuacan – for whom archaeologists have not agreed on a name – have not left any obvious royal remains for study.

The discovery of a tomb could help solve the enigma of how Teotihuacan was ruled, and Joyce said that the concentration of artifacts outside the tunnel chambers could be associated with a tomb – or a set of ritual chambers.

A royal tomb could lend credence to the theory that the city, which flourished between 100-700AD, was ruled by dynasties in the manner of the Maya, though with far less obvious flair for self-glorification.

But a royal tomb cold also hold the remains of a lord, which may fit with a competing idea about the city. Linda Manzanilla, a Mexican archaeologist acclaimed by many of her peers, contends that the city was ruled by four lords and notes that the city lacks a palace or apparent depiction of kings on its many murals.

Headrick suggested yet more fluid models, in which strong lineages or clans traded rule but never cemented into dynasties, or in which the rulers relied on agreements with the military to maintain power, and authority was vested more in an office than a family. Ancient Teotihuacan was a city with familiar factions vying for influence: the elite, the military, the merchants, the priests and the people.

For now, the archaeologists and anthropologists continue digging and deducing. Gomez says he hopes excavation of the chambers to be complete by October, and Headrick said that archeologists are looking at the city from new angles. Some are trying to decipher the paintings and hieroglyphics around the city, others trying to parse what may be a writing system without verbs or syntax.

Then there are the thousands of artifacts, some unprecedented and bizarre, that Gomez and his fellows are disinterring from beneath the pyramid. “It’s quite the mystery,” Headrick said. “It’s fun.”