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Cold, callous and untreatable? Not all psychopaths fit the stereotype, says new study

Many mask unmanageable emotion, can be helped with right therapy

Movie villains from Norman Bates to Hannibal Lecter have popularized the notion of the psychopath as cold, cruel, lacking in empathy and beyond the reach of treatment.

A new study in the Journal of Abnormal Child Psychology suggests that this monolithic view, shared by some treatment professionals, is not only wrong but prevents many diagnosed with psychopathy, or precursors of it, from receiving therapies that could help them live happier, more productive lives.

The study focused on 150 male and female youth housed in juvenile detention centers, aged 11 to 17, who were classified as callous and unemotional, or CU, exhibiting severe anti-social behaviors that put them at risk of developing psychopathic traits as adults.

While some in the research sample did fit the classic definition of psychopathy, a significant subgroup did not, said Tim Stickle, professor of Psychology at the University of Vermont, who co-authored the paper with Andrew Gill, a graduate student at the university.

"They appear callous and unemotional to others but are actually very distressed, have high levels of anxiety, higher levels of depression, higher levels of emotion," he said. "We think of these harmful, antisocial, aggressive kids as being immune to fear, immune to negative feelings, but in fact we're showing a whole group of them are not only not immune, but are very susceptible."

The hopeful implication, said Stickle, is that this set of psychological issues is treatable with approaches such as cognitive behavioral therapy and dialectical behavior therapy that teach strategies for managing emotions.

Conventional treatments for aggression and psychopathy emphasize rewards and punishments to change unwanted behaviors. "There is an opportunity to do things differently and more effectively," Stickle said.

Savings of \$3 million over lifetime

Effectively treating youth at risk of developing psychopathy as adults has value on a societal as well as an individual level. "Untreated callous unemotional traits put these youth at risk for becoming lifelong criminals," Stickle said.

Preventing one high risk youth from developing lifelong antisocial behavior will save approximately \$3 million across the youth's lifetime, according to a study conducted in 2007.

Other recent studies have confirmed that this emotionally distressed subgroup also exists among adults with psychopathic traits.

Key advance: a comprehensive diagnostic test that reveals differences

The study's ability to identify subgroups within the CU research sample was made possible by the psychological testing instruments the researchers used, which gathered information from subjects on a wide variety of personality and emotional traits.

Psychopathy is usually identified with a far narrower checklist of traits and behaviors. "It's not just one characteristic that allows clear identification of who falls in which group; it takes a wide range of traits," Stickle said.

The multidimensional testing tools the study employed should be widely adopted in the future, said Stickle, to ensure that those in the secondary psychopathy subgroup receive the appropriate therapy. "Using a wide range of measures of emotional experience and expression is very important to clearly identify who these individuals are so they can be helped," he said.

Girls more vulnerable

The study is first to find that CU girls are especially likely to fall within the group that suffers from significant emotional distress and unregulated negative feeling. "These traits are particularly prevalent in adolescent females in the juvenile justice system," Stickle said.

The study also breaks ground in showing that callous and unemotional youth are at risk of developing clinically significant levels of depression.

<http://bit.ly/1y0qRA7>

Kamikaze typhoons spared Japan from Kublai Khan

Evidence of increased typhoon activity around the time of the Mongol attacks

Like any good conqueror, Kublai Khan just wanted to expand his empire. So in the late 13th century, the grandson of Genghis Khan launched a mythic fleet to seize control of Japan. According to Japanese legend, however, the Mongol ships met with typhoons of equally mythic proportions, which quashed their repeated invasions - twice.

These storms, which spared Japan from occupation in 1274 and again in 1281, became known as the "divine wind," or kamikaze, but many scientists and historians have questioned their existence. Now, a new study suggests there may be truth to the tales: researchers recently found evidence of increased typhoon activity around the time of the attacks, including signs that two major storms made landfall not far from the site of Mongol shipwrecks.

Doubts had grown about the kamikaze typhoons in recent decades, partly because events of this size would be unlikely today, says [Kinuyo Kanamaru](#), a geologist at the University of Massachusetts at Amherst (UMass) and an author of the study,

published in *Geology*. So Kanamaru and others, including lead author and UMass colleague [Jonathan Woodruff](#), went looking for hard evidence beneath the waters of Lake Daija on Kyushu, the southernmost of Japan's four main islands.

They picked the site because it sits along the same likely storm track less than 120 kilometers from where archaeologists think the Mongols landed, and for one other reason. "In Japan, people believe in spirits that protect them. Those spirits tend to live in a small lake or a pond or a gigantic tree," Kanamaru says. Because Lake Daija had a legend associated with it - locals believed a serpent inhabited the lake - the researchers hoped it would have a long sedimentary record that might stretch all the way back to the 1200s.

They also hoped it would be a good place to look for evidence of ancient storm surges. With only a thin barrier of beach separating the lake from the ocean, the researchers reasoned that seawater would have washed over the beach during big typhoons, leaving clues in the sediments. In particular, the researchers searched for physical signs of disturbed sediments, as well as changes in the concentration of strontium, which is more enriched in seawater than in the freshwater of the lake.



A new study suggests that a Japanese legend - which holds that "divine wind," or kamikaze, defeated Mongol invaders in the 13th century, as depicted in this 1847 painting by Kikuchi Yōsai - may have some merit. Credit: Public domain.

Their results revealed elevated strontium levels and changes in sediment properties between A.D. 250 and 1600, suggesting that storm surges, and thus typhoons, used to happen more frequently in this part of Japan than they do today. Within this period of heightened typhoon activity, the researchers identified two pronounced storm deposits that dated to the late 1200s. Although they could not constrain the deposits' ages to specific years, the authors suggested the layers might be direct evidence of the kamikaze typhoons of 1274 and 1281.

Kanamaru says it's unlikely the deposits were produced by tsunamis - another way of flooding the lake - because Lake Daija sits on the west coast of Kyushu,

on the opposite side of the island from the faults that might trigger them are also no historical records of tsunamis striking at this time.

"To say that the Mongol invasion was knocked back by hurricanes sounds myth," says [Jonathan Nott](#), a geologist at James Cook University in Australia, who was not involved with the study and reviewed the paper in *Geology*. But he says Woodruff's team seems to have identified evidence of storm surges in the geologic record. "It was very nicely and cleverly done," says [Biu Liu](#), an oceanographer at Louisiana State University who also was involved in the work. "This is a very good way of making these connections. Although the Japanese believed spirits sent the kamikaze typhoons to protect the credit appears to belong to the tropical Pacific, which experienced frequent Niños in the late 13th century. Using complementary studies of historical typhoon activity in China and Japan, scientists have previously found that storm surges toward Japan more often during El Niño-heavy periods and toward China during more dominant La Niña climate states.

This makes the kamikaze events one of the first recorded examples of extreme weather can shape major geopolitical boundaries, Kanamaru says.

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Lower extremity revascularization not effective in majority of nursing home residents

UCSF researchers find most patients still alive gain little, if any, functional

Only a few U.S. nursing home residents who undergo lower extremity revascularization procedures are alive and ambulatory a year after surgery, according to UCSF researchers, and most patients still alive gained little, if any, functional improvement. The study appears in the April 6 issue of *JAMA Internal Medicine*. "Our findings can inform conversations among physicians, patients and families about the risks and expected outcomes of surgery and whether the surgery is likely to allow patients to achieve their treatment goals," said senior author Dr. Peter J. Lee, MD, MS, associate professor of surgery and geriatrics in the Pritzker School of Medicine at UCSF. "Our findings also highlight the importance of carefully considering a prognosis independent of vascular revascularization and assessing the goals of care."

Lower extremity peripheral arterial disease is common among nursing home residents, a substantial number of whom also are at risk for critical limb ischemia. Lower extremity revascularization through stents and other devices is frequently performed to preserve functional independence through limb preservation. However, these procedures have an operative risk, and their benefit in maintaining walking ability is debatable.

In this study, researchers led by Finlayson analyzed Medicare claims data for 2005-2008 for nursing home residents nationwide who underwent lower extremity revascularization, with follow up through 2009. Changes were examined in the residents' ambulatory and functional status after surgery. Also identified were patient and surgery characteristics associated with a composite measure of clinical and functional failure, defined as death or nonambulatory status a year after surgery.

The key findings are:

A total of 10,784 long-term nursing home residents received lower extremity revascularization. The average age was 82 years, and 60 percent had cognitive impairment, 57 percent had congestive heart failure, and 29 percent had renal failure.

Prior to surgery, of the 10,784 residents, 75 percent were not walking, and 40 percent had decline in overall physical functioning.

A year after surgery, 51 percent of these patients had died, and among survivors, 28 percent were nonambulatory and 32 percent had decline in overall physical functioning.

Of the 1,672 residents who were ambulatory before surgery, 63 percent died or now were nonambulatory at one year.

And among 7,188 patients who were nonambulatory prior to surgery, 89 percent died or remained nonambulatory.

As a result, the researchers learned that in patients undergoing lower extremity revascularization, the outcomes in nursing home residents were substantially worse than has been reported in the general population of the same age. These findings are consistent with previous studies that found individuals who are ambulatory prior to this procedure have better outcomes than those who are nonambulatory, and revascularization rarely allows a patient who is nonambulatory to become ambulatory after surgery.

"Among the treatment options, nonoperative symptom management, local wound care, primary amputation and lower extremity revascularization are associated with different risks, benefits and expected outcomes," Finlayson said. "Our findings should be interpreted cautiously; successful relief of pain, healing of wounds and avoidance of major amputation may benefit some of the patients who underwent lower extremity revascularization in the short term."

Other UCSF contributors to the JAMA Internal Medicine study were Michael S. Conte, MD, professor and chief of vascular and endovascular surgery and co-director of the Heart and Vascular Center and Center for Limb Preservation; Kenneth Covinsky, MD, MPH, Edmund G. Brown Distinguished Professorship in Geriatrics at UCSF and San Francisco VA Medical Center geriatrics and palliative medicine service staff physician; Lawrence Oresanya, MD, resident physician of surgery; and Shoujun Zhao, MD, PhD, surgery research specialist. Other contributors were Siqi Gan, MPH, UCLA Fielding School of Public Health; Brant Fries, PhD, Institute of Gerontology and University of Michigan and VA Ann Arbor

Healthcare Systems; and Philip Goodney, MD, MS, Dartmouth Geisel School of Medicine, Dartmouth Institute for Health Policy and Clinical Practice, and the VA Outcomes Group. Funding was provided by the National Institute on Aging/Paul B. Beeson Clinical Scientist Development Award in Aging and the UCSF Claude D. Pepper Older Americans Independence Center.

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Aluminum battery from Stanford offers safe alternative to conventional batteries

Stanford scientists have invented a flexible, high-performance aluminum battery that charges in about 1 minute

Stanford University scientists have invented the first high-performance aluminum battery that's fast-charging, long-lasting and inexpensive. Researchers say the new technology offers a safe alternative to many commercial batteries in wide use today.

"We have developed a rechargeable aluminum battery that may replace existing storage devices, such as alkaline batteries, which are bad for the environment, and lithium-ion batteries, which occasionally burst into flames," said Hongjie Dai, a professor of chemistry at Stanford. "Our new battery won't catch fire, even if you drill through it." Dai and his colleagues describe their novel aluminum-ion battery in "An ultrafast rechargeable aluminum-ion battery," in the April 6 advance online edition of the journal Nature. A video about the battery is available at: <https://youtu.be/ZKICyK7E9IU>

Aluminum has long been an attractive material for batteries, mainly because of its low cost, low flammability and high-charge storage capacity. For decades, researchers have tried unsuccessfully to develop a commercially viable aluminum-ion battery. A key challenge has been finding materials capable of producing sufficient voltage after repeated cycles of charging and discharging.

Graphite cathode

An aluminum-ion battery consists of two electrodes: a negatively charged anode made of aluminum and a positively charged cathode. "People have tried different kinds of materials for the cathode," Dai said. "We accidentally discovered that a simple solution is to use graphite, which is basically carbon. In our study, we identified a few types of graphite material that give us very good performance."

For the experimental battery, the Stanford team placed the aluminum anode and graphite cathode, along with an ionic liquid electrolyte, inside a flexible polymer-coated pouch. "The electrolyte is basically a salt that's liquid at room temperature, so it's very safe," said Stanford graduate student Ming Gong, co-lead author of the Nature study.

Aluminum batteries are safer than conventional lithium-ion batteries used in millions of laptops and cell phones today, Dai added. "Lithium-ion batteries can be a fire hazard," he said. As an example, he pointed to recent decisions by United and Delta airlines to ban bulk lithium-battery shipments on passenger planes.

"In our study, we have videos showing that you can drill through the aluminum battery pouch, and it will continue working for a while longer without catching fire," Dai said. "But lithium batteries can go off in an unpredictable manner - in the air, the car or in your pocket. Besides safety, we have achieved major breakthroughs in aluminum battery performance."

One example is ultra-fast charging. Smartphone owners know that it can take hours to charge a lithium-ion battery. But the Stanford team reported "unprecedented charging times" of down to one minute with the aluminum prototype.

Durability is another important factor. Aluminum batteries developed at other laboratories usually died after just 100 charge-discharge cycles. But the Stanford battery was able to withstand more than 7,500 cycles without any loss of capacity. "This was the first time an ultra-fast aluminum-ion battery was constructed with stability over thousands of cycles," the authors wrote. By comparison, a typical lithium-ion battery lasts about 1,000 cycles.

"Another feature of the aluminum battery is flexibility," Gong said. "You can bend it and fold it, so it has the potential for use in flexible electronic devices. Aluminum is also a cheaper metal than lithium."

Applications

In addition to small electronic devices, aluminum batteries could be used to store renewable energy on the electrical grid, Dai said. "The grid needs a battery with a long cycle life that can rapidly store and release energy," he explained. "Our latest unpublished data suggest that an aluminum battery can be recharged tens of thousands of times. It's hard to imagine building a huge lithium-ion battery for grid storage."

Aluminum-ion technology also offers an environmentally friendly alternative to disposable alkaline batteries, Dai said. "Millions of consumers use 1.5-volt AA and AAA batteries," he said. "Our rechargeable aluminum battery generates about two volts of electricity. That's higher than anyone has achieved with aluminum."

But more improvements will be needed to match the voltage of lithium-ion batteries, Dai added.

"Our battery produces about half the voltage of a typical lithium battery," he said. "But improving the cathode material could eventually increase the voltage and energy density. Otherwise, our battery has everything else you'd dream that a battery should have: inexpensive electrodes, good safety, high-speed charging,

flexibility and long cycle life. I see this as a new battery in its early days. It's quite exciting."

Other co-lead authors of the study affiliated with Stanford are visiting scientists Meng-Chang Lin from the Taiwan Industrial Technology Research Institute, Bingan Lu from Hunan University, and postdoctoral scholar Yingpeng Wu. Other authors are Di-Yan Wang, Mingyun Guan, Michael Angell, Changxin Chen and Jiang Yang from Stanford; and Bing-Joe Hwang from National Taiwan Normal University.

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Working up a sweat - it could save your life

Physical activity that makes you puff and sweat is key to avoiding an early death, a large Australian study of middle-aged and older adults has found

Physical activity that makes you puff and sweat is key to avoiding an early death, a large Australian study of middle-aged and older adults has found.

The researchers followed 204,542 people for more than six years, and compared those who engaged in only moderate activity (such as gentle swimming, social tennis, or household chores) with those who included at least some vigorous activity (such as jogging, aerobics or competitive tennis). They found that the risk of mortality for those who included some vigorous activity was 9 to 13 per cent lower, compared with those who only undertook moderate activity.

"The benefits of vigorous activity applied to men and women of all ages, and were independent of the total amount of time spent being active," said lead author Dr Klaus Gebel from James Cook University's Centre for Chronic Disease Prevention. "The results indicate that whether or not you are obese, and whether or not you have heart disease or diabetes, if you can manage some vigorous activity it could offer significant benefits for longevity."

Co-author Dr Melody Ding from University of Sydney's School of Public Health, said the results indicated that vigorous activities should be more strongly encouraged in clinical and public health guidelines.

The current advice from the World Health Organization - and health authorities in countries including the US, UK and Australia - is for adults to accumulate at least 150 minutes of moderate activity or 75 minutes of vigorous activity per week.

"The guidelines leave individuals to choose their level of exercise intensity, or a combination of levels, with two minutes of moderate exercise considered the equivalent of one minute of vigorous activity," Dr Ding said.

"It might not be the simple two-for-one swap that is the basis of the current guidelines," she said. "Our research indicates that encouraging vigorous activities may help to avoid preventable deaths at an earlier age."

The study classified participants into three groups: those who reported that none of their physical activity was at a vigorous level, and those who reported that up to

30 per cent or more of their activity was at a vigorous level. The mortality rate for those who reported up to 30 per cent vigorous activity, was 9 per cent lower than those who reported no vigorous activity. For those whose exercise routine was vigorous for more than 30 per cent of the time, the rate of mortality was reduced by 13 per cent.

So who should get huffing and puffing, and how much do you need to do?

"Our research indicates that even small amounts of vigorous activity could help reduce your risk of early death," Dr Gebel said.

"For those with medical conditions, for older people in general, and for those who have never done any vigorous activity or exercise before, it's always important to talk to a doctor first. "Previous studies indicate that interval training, with short bursts of vigorous effort, is often manageable for older people, including those who are overweight or obese."

The researchers investigated participants in the Sax Institute's 45 and Up study, which has collected baseline data on more than 267,000 men and women aged 45 and older, in the Australian state of New South Wales. Dr Klaus Gebel is a Senior Research Fellow at the Centre for Chronic Disease Prevention at James Cook University in Cairns. He commenced this study at the University of Sydney, and has completed it in collaboration with a team of University of Sydney researchers including Adrian Bauman, Sesquicentenary Professor of Public Health.

The paper, 'Physical activity and all-cause mortality in middle-aged and older Australians', is published online in the current edition of JAMA Internal Medicine.

<http://nyti.ms/1Ina8uj>

The Mind of Those Who Kill, and Kill Themselves

Recent studies have begun to piece together characteristics shared by many who carry out mass violence; a narcissism, sense of grievance, and desire for infamy

By ERICA GOODE APRIL 6, 2015

He was described, in the immediate aftermath of the Germanwings crash, as a cheerful and careful pilot, a young man who had dreamed of flying since boyhood. But in the days since, it has seemed increasingly clear that Andreas Lubitz, 27, the plane's co-pilot, was something far more sinister: the perpetrator of one of the worst mass murder-suicides in history.

If what researchers have learned about such crimes is any indication, this notoriety may have been just what Mr. Lubitz wanted. The actions now attributed to Mr. Lubitz - taking 149 unsuspecting people with him to a horrifying death - seem in some ways unfathomable, and his full motives may never be fully understood. But studies over the last decades have begun to piece together characteristics that many who carry out such violence seem to share, among them a towering narcissism, a strong sense of grievance and a desire for infamy.

Adam Lankford, an associate professor of criminal justice at the University of Alabama, said that in his research on mass killers who also took their own lives, he has found "a significant number of cases where they mention a desire for fame, glory or attention as a motive."

Before Adam Lanza, 20, the Sandy Hook Elementary School shooter, killed 20 children, six adults and himself in 2012, he wrote in an online forum, "Just look at how many fans you can find for all different types of mass murderers."

Robert Hawkins, 19, who committed suicide after killing eight people at a shopping mall in Omaha in 2007, left a note saying "I'm gonna be famous," punctuating the sentence with an expletive.

And Dylan Klebold, 17, of Columbine High School fame, bragged that the goal was to cause "the most deaths in U.S. history...we're hoping. We're hoping."

"Directors will be fighting over this story," Mr. Klebold said in a video made before the massacre. If authorities know what might have driven Mr. Lubitz, they have not made it public. Prosecutors said last week that it was now clear that he planned the crash, researching ways to commit suicide and how to operate the cockpit door on his iPad.

Lufthansa, Germanwings's parent airline, has said that Mr. Lubitz suffered in the past from severe depression and had talked to a counselor about suicide during a break in his training. Yet mental health experts who study mass murder-suicides said that depression and thoughts of suicide, which are commonplace, fall far short of explaining such drastic and statistically rare acts.

"People want an easily graspable handle to help understand this, to blame something or scapegoat," said Dr. James L. Knoll, the director of forensic psychiatry at the State University of New York Upstate Medical University.

But to zero in on depression is "a low-yield dead end," he said, adding, "There's something fundamentally different here, aside and apart from the depression, and that's where we need to look."

Serious mental illness, studies of mass killers suggest, is a prime driver in a minority of cases - about 20 percent, according to estimates by several experts. Far more common are distortions of personality - excesses of rage, paranoia, grandiosity, thirst for vengeance or pathological narcissism and callousness.

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"The typical personality attribute in mass murderers is one of paranoid traits plus massive disgruntlement," said Dr. Michael Stone, a forensic psychiatrist in New York who recently completed a study of 228 mass killers, many of whom also killed themselves.

"They want to die, but to bring many others down with them, whether co-workers, bosses, family members or just plain folk who are in the vicinity."

Mr. Lubitz, Dr. Stone noted, now ranks among the deadliest of mass killers, in a league with Adilson Marcelino Alves, who in 1961 killed as many as 500 people in a circus fire in Brazil, or Timothy McVeigh, the Oklahoma City bomber, who killed 168 people and injured more than 680 others.

Dr. J. Reid Meloy, a forensic psychologist who consults on threat assessment for universities and corporations, said perhaps the most salient feature of mass killers was their belief that they had been wronged. "What's become clear over the past 30 years of research is that there's virtually always a personal grievance that will start a person on a pathway to mass murder," Dr. Meloy said.

The target of the grievance, he said, could be a person, a company, an institution or a government, "but it is felt personally and typically involves a major loss or anticipated loss." In Mr. Lubitz's case, whether he knew or cared who would die as result of his actions remains unclear.

"For some people, the targets are very much the purpose of the attack," Dr. Meloy said, referring to mass killers. "I think for other cases, where the purpose of the attack is, for example, primarily to gain notoriety, then the targets in a sense become the means to that end. One could think of them as being collateral damage."

Murder-suicides make up only a small percentage of homicides in the United States, accounting for about 1,000 to 1,500 deaths a year, according to a 1992 epidemiological study. The vast majority are committed by men and most are domestic violence cases: an estranged husband, for example, who kills his wife, girlfriend or lover. Suicides accompanied by the killing of multiple strangers represent an even tinier fraction of homicides over all. But they seem to differ in significant ways from their domestic counterparts, researchers said.

In domestic cases, depression does appear to play a significant role. A recent psychological autopsy study of murder-suicides in Dallas, most of which involved domestic violence, found that 17 of the 18 perpetrators met the diagnostic criteria for major depression or some other form of the illness.

The study, conducted by Dr. Knoll and Dr. Susan Hatters Friedman, a forensic psychiatrist at Case Western, found that a majority of the killers also abused alcohol or drugs. Four had a family history of suicide. The study has been submitted to a scientific journal.

Domestic murder-suicides are almost always impulsive - committed in fits of rage or jealousy, often enabled by the presence of a firearm. In contrast, killers who take groups of strangers as targets plan their crimes carefully, waiting for an opportunity to act. And while domestic murder-suicides are frequently fueled by alcohol, people who plan ahead to kill themselves and others seem concerned about keeping a clear mind for the task ahead.

George Sodini, 48, who killed three people and injured nine others at an aerobics class in a Pittsburgh suburb in 2009, said as much in a blog he kept, detailing his plans.

"I haven't had a drink since Friday at about 2:30," he wrote on Monday, Aug. 3, the day before the massacre. "Total effort needed. Tomorrow is the big day."

An airplane may seem an unusual vehicle for mass murder or self-destruction. But as a pilot's method of choice, several psychiatrists said, it is perhaps not that surprising.

In a study of 85 aircraft suicides from 1965 to the present, Dr. Hatters Friedman and Dr. Chris Kenedi, a psychiatrist at Duke, found that 18 of the crashes appeared to be murder-suicides, 15 perpetrated by pilots. The study looked at general aviation and commercial airline crashes, and included the deliberate crashes by pilots of a Mozambique Airlines jet in 2013 and an EgyptAir plane in 1999.

Malaysia Airlines Flight 370 was not among those studied, although pilot suicide was one theory about the jetliner's disappearance last year.

"Not all of them had a history of mental illness," Dr. Hatters Friedman said of the pilots. "What keeps coming up is family stresses, relationship stress, work stresses, financial stresses." In several cases, the pilots, all men, seemed to be acting on grievances. One crashed a plane into his former mother-in-law's house, another into the offices of the pilot's employer. A third pilot flew a Piper Dakota into a building occupied by the Internal Revenue Service.

Yet few murder-suicides are as chilling as those involving the deliberate crashing of jetliners with hundreds of passengers aboard. In a mall or in a school, Dr. Knoll noted, people can run and take cover. "On a plane, your number of victims is set," he said, "and nobody can go anywhere."

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Middle-aged athletes at low risk for sudden cardiac arrest while exercising

New study in medical journal Circulation also shows those who have a sudden cardiac arrest while playing sports are more likely to survive usually-fatal condition

LOS ANGELES - Middle-aged athletes are at low risk for having a sudden cardiac arrest while playing sports, and those who do have a greater chance of surviving the usually-fatal condition, shows a new Cedars-Sinai Heart Institute study.

"Because there is so much media attention when someone has a sudden cardiac arrest while playing sports, we want to make sure people know that the benefits of exercise far outweigh the risk of having a cardiac arrest," said Sumeet S. Chugh,

M.D., associate director of the Cedars-Sinai Heart Institute and a prominent expert in the diagnosis, treatment and investigation of heart rhythm abnormalities. "Even for middle-aged men, who are more susceptible to heart rhythm disturbances, the risk is quite low."

Although "sudden cardiac arrest" and "heart attack" often are used interchangeably, the terms are not synonymous. Unlike heart attacks (myocardial infarctions), which are typically caused by clogged coronary arteries reducing blood flow to the heart muscle, sudden cardiac arrest is the result of defective electrical activity of the heart. Patients may have little or no warning, and the disorder usually causes instantaneous death.

Sudden cardiac arrest has been blamed for the deaths of journalist Tim Russert and filmmaker John Hughes as well as U.S. Olympic volleyball player Flo Hyman and professional basketball players Pete Maravich and Reggie Lewis.

In the study, published in the medical journal Circulation, investigators studied the 1,247 people aged 35-65 from the Portland, Oregon, metropolitan area who had a sudden cardiac arrest between 2002 and 2013. Results include: Just 5 percent, or 63 people, had a sudden cardiac arrest during sports activities.

Eighty-seven percent of those who had a sudden cardiac arrest while engaged in sports received cardiopulmonary resuscitation.

Fifty-three percent of patients who had a sudden cardiac arrest while not playing sports received cardiopulmonary resuscitation.

The survival rate of 23 percent was markedly higher for those who had a sudden cardiac arrest while exercising compared to just 13 percent for those who had a sudden cardiac arrest during other activities.

Men were seven times more likely than women to have a sports-related sudden cardiac arrest.

"The chance of surviving sudden cardiac arrest is better if the episode occurs while exercising, probably because there are likely to be others around who can do chest compressions until paramedics arrive," said Chugh, the Pauline and Harold Price Chair in Cardiac Electrophysiology Research.

In addition to his leadership role at the Cedars-Sinai Heart Institute, Chugh heads the Oregon Sudden Unexpected Death Study, a comprehensive, 16-hospital, multi-year assessment of cardiac deaths in the 1 million population Portland, Oregon, metropolitan area. The data collected in the study - now ongoing for more than a decade - provides Chugh and his team with unique, community-based information to mine for answers to what causes sudden cardiac arrest. Chugh's Sudden Death Genomics Laboratory at the Cedars-Sinai Heart Institute is funded by two previous grants from the National Heart, Lung, and Blood Institute that also enable ongoing work on solving the mechanisms of sudden cardiac arrest.

"What this study shows is that most middle-aged athletes don't need to worry about sudden cardiac arrest while they are working out," Chugh said. "As our population ages, it's important to know that older people can exercise without worrying about triggering a heart rhythm disturbance."

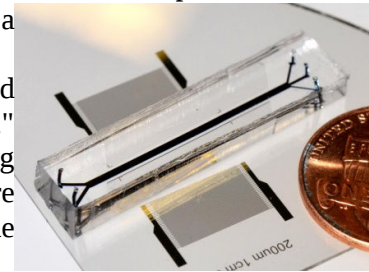
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Sound separates cancer cells from blood samples

Inexpensive, disposable chip separates circulating cancer cells from blood cells for diagnostic, prognostic and treatment purposes

Separating circulating cancer cells from blood cells for diagnostic, prognostic and treatment purposes may become much easier using an acoustic separation method and an inexpensive, disposable chip, according to a team of engineers.

"Looking for circulating tumor cells in a blood sample is like looking for a needle in a haystack," said Tony Jun Huang, professor of engineering science and mechanics. "Typically, the CTCs are about one in every one billion blood cells in the sample."



This is a photograph of an acoustic tweezer device about twice the size of a penny. Two sound transducers move the cells out of the stream for separation. Tony Jun Huang, Penn State

Existing methods of separation use tumor-specific antibodies to bind with the cancer cells and isolate them, but require that the appropriate antibodies be known in advance. Other methods rely on size, deformability or electrical properties. Unlike conventional separation methods that centrifuge for 10 minutes at 3000 revolutions per minute, surface acoustic waves can separate cells in a much gentler way with a simple, low-cost device.

Acoustic-based separations are potentially important because they are non-invasive and do not alter or damage cells. However, in order to be effective for clinical use, they also need to be rapidly and easily applicable.

"In order to significantly increase the throughput for capturing those rare CTCs, device design has to be optimized for much higher flow rates and longer acoustic working length," said Ming Dao, principal research scientist, materials science and engineering, Massachusetts Institute of Technology. "With an integrated experimental/modeling approach, the new generation of the device has improved cell sorting throughput more than 20 times higher than previously achieved and made it possible for us to work with patient samples."

The researchers worked both experimentally and with models to optimize the separation of CTCs from blood. They used an acoustic-based microfluidic device

so that the stream of blood could continuously pass through the device for separation. Using the differential size and weight of the different cells they chose appropriate acoustic pressures that would push the CTCs out of the fluid stream and into a separate channel for collection. They report their results today (Apr. 6) in the Proceedings of the National Academy of Sciences.

Tilted-angle standing surface acoustic waves can separate cells using very small amounts of energy. The power intensity and frequency used in this study are similar to those used in ultrasonic imaging, which has proven to be extremely safe, even for fetuses. Also, each cell experiences the acoustic wave for only a fraction of a second. In addition, cells do not require labeling or surface modification. All these features make the acoustic separation method, termed acoustic tweezers, extremely biocompatible and maximize the potential of CTCs to maintain their functions and native states.

If two sound sources are placed opposite each other and each emits the same wavelength of sound, there will be a location where the opposing sounds cancel each other. Because sound waves have pressure, they can push very small objects, so a cell or nanoparticle will move with the sound wave until it reaches the location where there is no longer lateral movement, in this case, into the fluid stream that moves the separated cells along.

The researchers used two types of human cancer cells to optimize the acoustic separation - HELA cells and MCF7 cells. These cells are similar in size. They then ran an experiment separating these cells and had a separation rate of more than 83 percent. They then did the separation on other cancer cells, ones for which the device had not been optimized, and again had a separation rate of more than 83 percent.

"Because these devices are intended for use with human blood, they need to be disposable," said Huang. "We are currently figuring out manufacturing and mass production possibilities."

Physicians could use the devices to monitor how patients reacted to chemotherapy, for initial diagnosis and for determining treatment and prognosis.

"This work, involving a highly cross-disciplinary group of medical doctors, engineers, computational biologists, and device experts, has led to the design and development of a label-free platform for identifying and separating CTCs while preserving the integrity of the cell," said Subra Suresh, president, Carnegie Mellon University and part of the research team. "It promises to offer new avenues for basic research into the pathology and metastasis, and for clinical diagnosis of rare tumor cells."

Other researchers working on this project include Peng Li, postdoctoral fellow; Zhangming Mao, graduate student; Yuchan Chen, graduate student; and Po-Hsun Huang, graduate

student, all in engineering science and mechanics at Penn State. Also on the project were Lanlan Zhou, former graduate student in Hematology-Oncology, Penn State Hershey Cancer Institute; Wafik S. El-Deiry, former professor of medicine, Penn State College of Medicine; Joseph J. Drabick, professor of medicine, Penn State College of Medicine; Cristina I. Truica, director, Breast Medical Oncology, Penn State Hershey Cancer Institute and Zhangli Peng, postdoctoral fellow at MIT now assistant professor of aerospace and mechanical engineering, University of Notre Dame.

The National Institutes of Health and the National Science Foundation supported this work.

http://www.eurekalert.org/pub_releases/2015-04/epfd-pav040215.php

Purging a virus from organ transplants

Researchers have discovered the molecular switch that allows HCMV to either lie dormant or reactivate its infection

Human cytomegalovirus (HCMV) is an extremely common virus, which as other members of the herpes virus family causes life-long infections in humans. Most individuals are exposed to HCMV during childhood, yet symptoms can be easily fought off by a healthy immune system. However, infections can be life-threatening for individuals with defective immunity, for instance newborn babies, people with AIDS, or those taking immunosuppressive drugs following organ transplantation. Scientists at École Polytechnique Fédérale de Lausanne (EPFL) have discovered the molecular switch that allows HCMV to either lie dormant or reactivate its infection. The switch can be manipulated with simple drugs to force the virus out of dormancy, making it easy to target with antivirals. Published in eLife, the study shows how HCMV could be fought in high-risk patients and purged from organs before transplantation.

HCMV infects 60% of the population in industrialized countries, and almost everybody in less affluent places. This virus persists for life by hiding in blood-making ("hematopoietic") stem cells, where it lies dormant and goes completely unrecognized. It occasionally reactivates in the descendance of these hematopoietic stem cells, but these bouts are rapidly tamed by the immune system. However, in people whose immune system has been compromised, e.g. by AIDS, and organ transplant recipients who have to take immunosuppressive drugs, HCMV reactivation can cause devastating symptoms.

Throwing the switch

The lab of Didier Trono at EPFL discovered a protein that switches HCMV between dormancy and reactivation. They found this protein to be bound to the HCMV genome in latently infected hematopoietic stem cells and, upon a variety of external stimuli, to undergo a modification that allows for viral activation.

Furthermore, the researchers were able to control this switch with a drug called chloroquine, usually used against malaria. When they treated hematopoietic stem cells containing dormant HCMV with chloroquine, the virus reactivated and

became exposed, opening the door to maneuvers aimed at eliminating virus-infected cells.

The simplicity of the study's design underlies its enormous significance. On one hand, it sheds light on the molecular mechanism by which HCMV becomes dormant in hematopoietic stem cells, possibly offering insights into similar infections by other herpes viruses. On the other hand, the study provides a straightforward method for forcing HCMV out of dormancy in infected tissue. Coupled with a simultaneous dose of an antiviral, this could become a standard regimen for eradicating HCMV from high-risk patients and purging it from tissue before transplantation.

Trono's team is now testing the method's efficiency in purging HCMV from cells to be used for bone marrow transplantation. Following that step, the group will be developing the first trials in humans.

This work was supported by grants from the Swiss National Science Foundation and the European Research Council.

Rauwel B, Jang SM, Cassano M, Kapopoulou A, Barde I, Trono D. Release of Human Cytomegalovirus from latency by KAP1/TRIM28 phosphorylation switch. eLife <http://dx.doi.org/10.7554/eLife.06068>

<http://read.bi/1CPZuYv>

Potions and polls: Tanzanian albinos terrified after attacks
Their limbs hacked off and babies and children abducted or killed, albinos in Tanzania live in fear
Emile Costard, AFP

Dar es Salaam (AFP) - Their limbs hacked off and babies and children abducted or killed, albinos in Tanzania live in fear of another horrific spate of attacks against them ahead of elections in October.

Albino body parts are boiled up in foul human potions for witchcraft in the east African nation, and reports of killings have increased as local politicians order their spells in the belief that the expensive brews will secure poll victory.

"Local political leaders believe in the power of witchdoctors and think that it could help them to win elections," said Vicky Ntetema, director of Under The Same Sun, an organisation defending the rights of albinos in Tanzania.

With an entire corpse selling for as much as \$75,000 (70,000 euros), Ntetema claims the high price is an indication that "some political and economic elites" could be involved in albino murders.

In one recent attack, a six-year-old albino boy's hand was chopped off with a machete and his mother assaulted as she tried to protect him.

At least 76 albinos have been murdered since 2000 with their dismembered body parts selling for hundreds of dollars, according to United Nations experts.

A further 34 albinos have survived after having parts of their bodies hacked off, and grave robbers have dug up at least 15 more albinos, seeking buried limbs and bodies.

Forced to flee

Sengerema Simon, a 28-year-old man with albinism, was forced to flee his village in Tanzania's northern Tabora region fearing he would be attacked and cooked.

"In the village, I often heard people just call me 'the albino', then one day men I did not know called me by my name, saying they were going to do business... I was very scared," he told AFP. Unemployed, he now ekes out a living in the commercial capital Dar es Salaam with help from the Tanzania Albinism Society.

Albinism is a hereditary genetic condition which causes a total absence of pigmentation in the skin, hair and eyes. It affects one Tanzanian in 1,400, often as a result of inbreeding, experts say. Tanzania is home to some 49 million people.

Many attacks take place in northwestern Tanzania among the Sukuma people, the country's largest ethnic group and one with a long belief in witchcraft.

But experts say a thriving informal mining industry has also driven the killings, with prospectors desperate for anything that could help them strike it rich.

"The murders are connected to gold and diamond miners' efforts to secure lucky charms for finding minerals and protection against danger while mining," a 2010 report by the British-based Journal of Modern African Studies said.

In Africa, albinos generate a mixture of fear and fascination: some are stigmatised for their different colour, others treated almost as "divine figures," said Giorgio Brocco, an expert at Germany's Free University of Berlin.

"In some part of Africa, some ethnic groups originally believed that people with albinism disappeared instead of dying - or that they are gods," Brocco said.

Stigma from birth

Not in Tanzania, however, where they have "mostly been discriminated against" because they cannot so easily take part in farming, as their skin burns in the fierce sun, Brocco added.

That stigma begins at birth, said Josephat Torner, 32, who has albinism and works for the country's Albino Society. "When I was born, the community wanted to poison me. People thought I was a bad omen for the village... but my mother stopped them and saved my life." Torner recalls how growing up he was ostracised for his looks. "Children didn't want to play with me because they thought I could contaminate them, even my own brothers didn't touch my clothes for the same reasons," he said.

Campaigners say that education and raising awareness are vital in changing beliefs and prejudice. "You may apply for a post of employment... you may have

all the qualifications and experience, but you will never get employed because of negative attitudes," said Kondo Seif, who works for Under the Same Sun.

Seif, a top student at the University of Dar es Salaam, says he was denied a scholarship and teaching post after studying "because of my condition."

Still Seif is optimistic that attitudes are slowly changing, at least in urban areas. "Bad reactions in a restaurant or a bar were very common in the past but not so much now," he said.

In March, Tanzanian police rounded up hundreds of witchdoctors in a bid to stem the albino murders. But campaigners such as Torner - who travels regularly around remote northern regions to raise awareness about albinism - say that in the long-term, it will be education that will "eliminate the false beliefs."

http://www.eurekalert.org/pub_releases/2015-04/ncfa-ses040315.php

Sun experiences seasonal changes, new research finds

Quasi-annual variations may hold clues to space weather

BOULDER -The Sun undergoes a type of seasonal variability with its activity waxing and waning over the course of nearly two years, according to a new study by a team of researchers led by the National Center for Atmospheric Research (NCAR). This behavior affects the peaks and valleys in the approximately 11-year solar cycle, sometimes amplifying and sometimes weakening the solar storms that can buffet Earth's atmosphere.

The quasi-annual variations appear to be driven by changes in the bands of strong magnetic fields in each solar hemisphere. These bands also help shape the approximately 11-year solar cycle that is part of a longer cycle that lasts about 22 years.

"What we're looking at here is a massive driver of solar storms," said Scott McIntosh, lead author of the new study and director of NCAR's High Altitude Observatory. "By better understanding how these activity bands form in the Sun and cause seasonal instabilities, there's the potential to greatly improve forecasts of space weather events."

The overlapping bands are fueled by the rotation of the Sun's deep interior, according to observations by the research team. As the bands move within the Sun's northern and southern hemispheres, activity rises to a peak over a period of about 11 months and then begins to wane.

The quasi-annual variations can be likened to regions on Earth that have two seasons, such as a rainy season and a dry season, McIntosh said.

The study, published this week in Nature Communications, can help lead to better predictions of massive geomagnetic storms in Earth's outer atmosphere that sometimes disrupt satellite operations, communications, power grids, and other technologies.

The research was funded by NASA and the National Science Foundation, which is NCAR's sponsor.

A "jet stream" in the Sun

The new study is one of a series of papers by the research team that examines the influence of the magnetic bands on several interrelated cycles of solar magnetism. In a paper last year in Astrophysical Journal, the authors characterized the approximately 11-year sunspot cycle in terms of two overlapping parallel bands of opposite magnetic polarity that slowly migrate over almost 22 years from high solar latitudes toward the equator, where they meet and terminate.

McIntosh and his co-authors detected the twisted, ring-shaped bands by drawing on a host of NASA satellites and ground-based observatories that gather information on the structure of the Sun and the nature of solar flares and coronal mass ejections (CMEs). These observations revealed the bands in the form of fluctuations in the density of magnetic fuel that rose from the solar interior through a transition region known as the tachocline and on to the surface, where they correlated with changes in flares and CMEs.

In the new paper, the authors conclude that the migrating bands produce seasonal variations in solar activity that are as strong as the more familiar 11-year counterpart. These quasi-annual variations take place separately in both the northern and southern hemispheres.

"Much like Earth's jet stream, whose warps and waves have had severe impact on our regional weather patterns in the past couple of winters, the bands on the Sun have very slow-moving waves that can expand and warp it too," said co-author Robert Leamon, a scientist at Montana State University. "Sometimes this results in magnetic fields leaking from one band to the other. In other cases, the warp drags magnetic fields from deep in the solar interior, near the tachocline, and pushes them toward the surface."

The surges of magnetic fuel from the Sun's interior catastrophically destabilize the corona, the Sun's outermost atmosphere. They are the driving force behind the most destructive solar storms.

"These surges or 'whomps' as we have dubbed them, are responsible for over 95 percent of the large flares and CMEs - the ones that are really devastating," McIntosh said.

The quasi-annual variability can also help explain a cold-war era puzzle: why do powerful solar flares and CMEs often peak a year or more after the maximum number of sunspots? This lag is known as the Gnevyshev Gap, after the Soviet scientist who first reported it in the 1940s. The answer appears to be that seasonal changes may cause an upswing in solar disturbances long after the peak in the solar cycle.

Researchers can turn to advanced computer simulations and more detailed observations to learn more about the profound influence of the bands on solar activity. McIntosh said this could be assisted by a proposed network of satellites observing the Sun, much as the global networks of satellites around Earth have helped advance terrestrial weather models since the 1960s.

"If you understand what the patterns of solar activity are telling you, you'll know whether we're in the stormy phase or the quiet phase in each hemisphere," McIntosh said. "If we can combine these pieces of information, forecast skill goes through the roof."

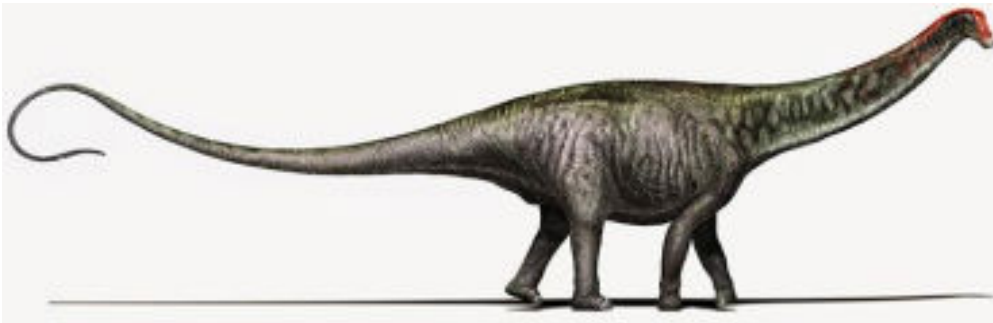
The solar magnetic activity band interaction and instabilities that shape quasi-periodic variability Scott W. McIntosh, Robert J. Leamon, Larisza D. Krista, Alan M. Title, Hugh S. Hudson, Pete Riley, Jerald W. Harder, Greg Kopp, Martin Snow, Thomas N. Woods, Justin C. Kasper, Michael L. Stevens, and Roger K. Ulrich Nature Communications

<http://bit.ly/1NQzWxt>

Back to Brontosaurus? The Dinosaur Might Deserve Its Own Genus After All

The popular name could be pulled back out of the scientific wastebasket, based on new analysis of dozens of related dinosaurs

By [Brian Switek](#) smithsonian.com



Welcome back, Brontosaurus? (Davide Bonadonna, CC- BY NC SA)

It may be one of the most famous dinosaurs of all time. The trouble is that shortly after being discovered, the Jurassic creature fell into an identity crisis. The name for the long-necked, heavy-bodied herbivore [Brontosaurus excelsus](#) - the great "thunder lizard" - was tossed into the scientific wastebasket when it was discovered that the dinosaur wasn't different enough from other specimens to deserve its own distinct genus.

But now, in a paleontological twist, *Brontosaurus* just might be back. A new analysis of dinosaur skeletons across multiple related species suggests that the original thunder lizard is actually unique enough to resurrect the beloved moniker,

according to researchers in the U.K. and Portugal. "We didn't expect this at all at the beginning," says study co-author [Emmanuel Tschopp](#) of the Universidade Nova de Lisboa. At first, Tschopp had been working only with Octávio Mateus of the Museu da Lourinhã to update the family tree of diplodocid dinosaurs.

But when it started looking like *Brontosaurus* might be real after all, they asked Roger Benson at the University of Oxford to join their team and run a statistical analysis on their findings. "Roger's calculations gave the same results," Tschopp says. "*Brontosaurus* should be valid."

The name *Brontosaurus excelsus* was coined by Yale paleontologist Othniel Charles Marsh, who described the species in an 1879 paper with the mundane title "[Notice of New Jurassic Reptiles](#)." His description is based on an enormous partial skeleton exhumed from the 150-million-year-old rock of Como Bluff, Wyoming. This "monster" of a dinosaur added to Marsh's rapidly growing fossil collection, which already included similar species. Just two years earlier, Marsh had named *Apatosaurus ajax* - the "deceptive lizard" - from a partial skeleton found in the Jurassic rock of Colorado. *Brontosaurus* quickly gained fame because it was among the first dinosaurs the public encountered. An [illustration of its skeleton](#) "was the first dinosaur restoration to get a wide circulation," points out North Carolina Museum of Natural Sciences historian [Paul Brinkman](#). This "helped spread the popularity of *Brontosaurus* in an era before dinosaurs proliferated widely in natural history museums." And once museums started to put up skeletons of *Brontosaurus* - the first was assembled in New York City in 1905 - the dinosaur's popularity only grew.



An old-school drawing of Brontosaurus excelsus graces a [1900s trading card](#) from a French chocolate manufacturer. Public domain, via AlphaGalileo

But as anyone who has strolled through an up-to-date museum hall knows, the name *Brontosaurus* was eventually abandoned. In 1903, paleontologist Elmer Riggs found that most of the traits that seemed to distinguish Marsh's two specimens had to do with differences in growth, and it was more likely that the skeletons belonged to the same genus. Since it was named first, *Apatosaurus* had priority over *Brontosaurus*. Despite the extreme similarity between Marsh's skeletons, Riggs recognized that they differed just enough to be regarded as

different species. Therefore *Apatosaurus ajax* would remain in place, and *Brontosaurus* was changed to *Apatosaurus excelsus*. It took a while for museums to follow suit, but by the 1970s everyone finally got on board with the shift. Bringing *Brontosaurus* back from scientific obsolence would be the equivalent of [restoring Pluto](#) to the status of planet. And much like the drawn-out debate over the extraterrestrial body, the status of *Brontosaurus* relies on definitions and the philosophy of how scientists go about making divisions in a messy natural world. To navigate the ever-growing number of dinosaur species, paleontologists look to a discipline called cladistics. In short, scientists pore over dinosaur skeletons to score a set of subtle characteristics, such as the way a flange of bone is oriented. Computer programs sort through those traits to create a family tree based upon who shares which characteristics. However, different researchers might pick different characteristics and score them in different ways, so any single result is a hypothesis that requires verification from other researchers independently generating the same results.

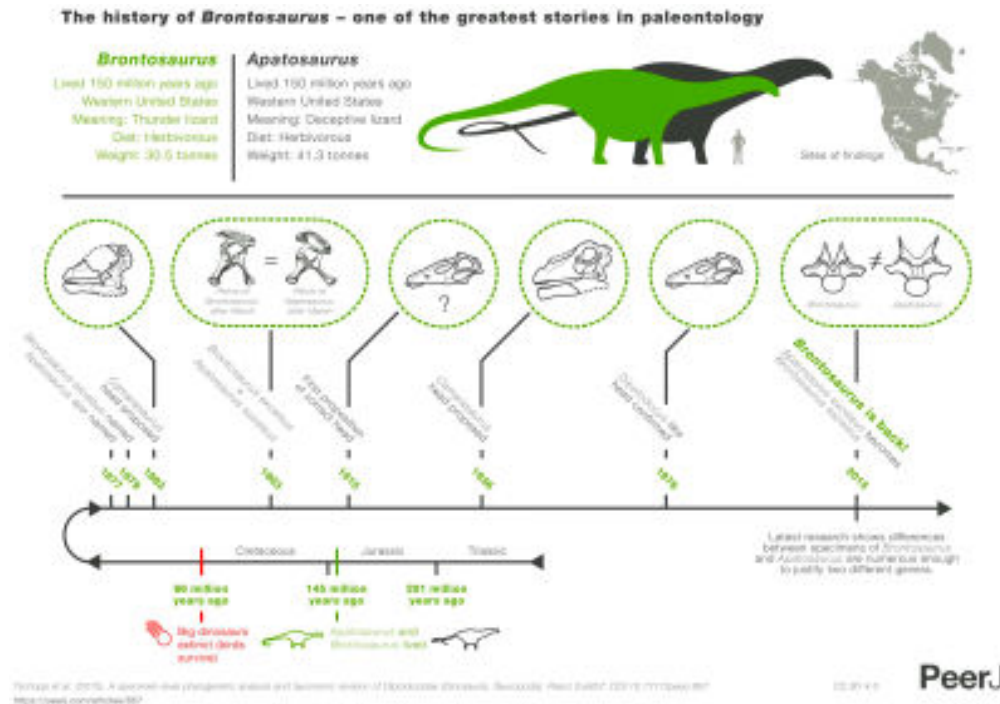
Here's where *Brontosaurus* stomps in. Tschopp and colleagues had set out to create a revised family tree of diplodocid dinosaurs - huge sauropods found from the western United States to Portugal - with a special emphasis on sorting out how many species of *Diplodocus* and *Apatosaurus* there were. The researchers scored 477 anatomical landmarks across 81 individual dinosaurs. While the general shape of the tree supported what other paleontologists had previously proposed, there was a surprise in store: The bones Marsh originally called *Brontosaurus* seem to stand apart from the two *Apatosaurus* species, the team [reports today in PeerJ](#).

Most of the differences the researchers identified were subtle anatomical features, but there are some broader traits, Tschopp says. "The most obvious and visual feature would be that *Apatosaurus* has a wider neck than *Brontosaurus*," he says, adding that despite the title "thunder lizard," *Brontosaurus* was not quite as robust as *Apatosaurus*.

These results came from two *Brontosaurus* skeletons: the one Marsh used to coin the name, and a second that could confidently be referred to as the same species. There are more possible *Brontosaurus* bones out there, and Tschopp studied many of them in preparation for the current study. But because the skeletons were incomplete, the bones popped up in various positions on the family tree. Now, with the new diplodocid tree in hand, Tschopp says he plans to take a second look at these bones to see whether they truly group with *Brontosaurus* or something else.

What remains unclear is whether *Brontosaurus* is here to stay. Southern Methodist University paleontologist [Louis Jacobs](#) praises the new study. "Numerous new sauropods have been discovered and named in the last couple of decades, new techniques have been developed, and we simply have a more sophisticated understanding of sauropods now," he says. The potential resurrection comes out of this burgeoning understanding. In short, Jacobs says, "good for them, and bully for *Brontosaurus*!"

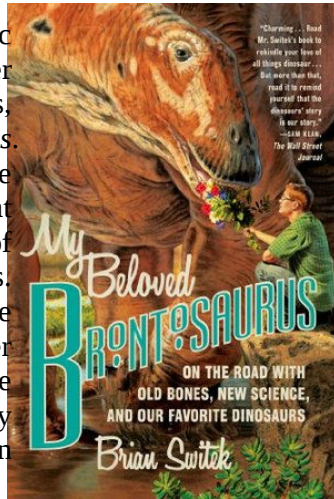
[John Whitlock](#) of Mount Aloysius College is more reserved. "For me the issue is how you want to define genera and species in dinosaur paleontology," Whitlock says. Some researchers will look at this study and conclude that *Brontosaurus* should still be an *Apatosaurus* because of their close relationship, forming what paleontologists call [a monophyletic group](#), while others will emphasize the diversity. There's no standard rule for how such decisions should be made. "I think we are going to start seeing discussion about not only how much change is enough to split a monophyletic group but, more importantly, how do we compare characters and character states?" Whitlock says. "That's going to be a fun debate to be a part of, and I'm excited about it."



An infographic traces the history of *Brontosaurus* and *Apatosaurus*. (StudioAM, CC BY 4.0)

The fate of *Brontosaurus* now relies upon whether other paleontologists will be able to replicate the results, as well as what those researchers think about the threshold for when dinosaurs merit different names.

Other dinosaurs are held in the same taxonomic tension. While some researchers recognize the slender tyrannosaur *Gorgosaurus libratus* as a unique genus, for example, others see it as a species of *Albertosaurus*. But the battle for *Brontosaurus* stands apart. The name has become a totem of the extinct creatures that continue to [ignite our imaginations](#) with scenes of Jurassic titans ambling over fern-carpeted floodplains. We've kept the name *Brontosaurus* alive because the hefty herbivore is an emissary to a past we can never visit, but that we can still connect to through the dinosaur's magnificent bones. Protocol will ultimately dictate the dinosaur's title, but in spirit if not in science, those old bones will always be *Brontosaurus*.



[My Beloved Brontosaurus: On the Road with Old Bones, New Science, and Our Favorite Dinosaurs](http://www.eurekalert.org/pub_releases/2015-04/uoca-nsh040615.php)

http://www.eurekalert.org/pub_releases/2015-04/uoca-nsh040615.php

New study hints at spontaneous appearance of primordial DNA DNA fragments may have guided their own growth into repeating chemical chains long enough to act as a basis for primitive life

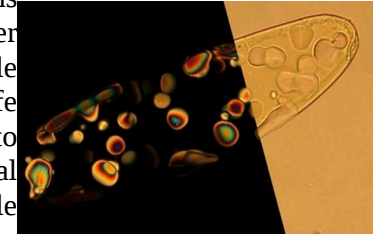
The self-organization properties of DNA-like molecular fragments four billion years ago may have guided their own growth into repeating chemical chains long enough to act as a basis for primitive life, says a new study by the University of Colorado Boulder and the University of Milan.

While studies of ancient mineral formations contain evidence for the evolution of bacteria from 3.5 to 3.8 billion years ago - just half a billion years after the stabilization of Earth's crust - what might have preceded the formation of such unicellular organisms is still a mystery. The new findings suggest a novel scenario for the non-biological origins of nucleic acids, which are the building blocks of living organisms, said CU-Boulder physics Professor Noel Clark, a study co-author.

A paper on the subject led by Tommaso Bellini of the University of Milan was published in a recent issue of Nature Communications. Other CU-Boulder co-authors of the study include Professor David Walba, Research Associate Yougwooo Yi and Research Assistant Gregory P. Smith. The study was funded

by the Grant PRIN Program of the Italian Ministries of Education, Universities and Research and by the U.S. National Science Foundation.

The discovery in the 1980's of the ability of RNA to chemically alter its own structure by CU-Boulder Nobel laureate and Distinguished Professor Tom Cech and his research team led to the development of the concept of an "RNA world" in which primordial life was a pool of RNA chains capable of synthesizing other chains from simpler molecules available in the environment. While there now is consensus among origin-of-life researchers that RNA chains are too specialized to have been created as a product of random chemical reactions, the new findings suggest a viable alternative, said Clark.



The image shows a droplet of condensed nano-DNA and within it smaller drops of its liquid crystal phase which show up in polarized light on the left. The liquid crystal droplets act as 'micro-reactors'. Noel Clark, University of Colorado

The new research demonstrates that the spontaneous self-assembly of DNA fragments just a few nanometers in length into ordered liquid crystal phases has the ability to drive the formation of chemical bonds that connect together short DNA chains to form long ones, without the aid of biological mechanisms. Liquid crystals are a form of matter that has properties between those of conventional liquids and those of a solid crystal - a liquid crystal may flow like a liquid, for example, but its molecules may be oriented more like a crystal.

"Our observations are suggestive of what may have happened on the early Earth when the first DNA-like molecular fragments appeared," said Clark.

For several years the research group has been exploring the hypothesis that the way in which DNA emerged in the early Earth lies in its structural properties and its ability to self-organize. In the pre-RNA world, the spontaneous self-assembly of fragments of nucleic acids (DNA and RNA) may have acted as a template for their chemical joining into polymers, which are substances composed of a large number of repeating units.

"The new findings show that in the presence of appropriate chemical conditions, the spontaneous self assembly of small DNA fragments into stacks of short duplexes greatly favors their binding into longer polymers, thereby providing a pre-RNA route to the RNA world," said Clark.

The CU-Boulder authors are part of the Soft Materials Research Center (SMRC) headquartered on campus, one of 12 Materials Research and Science Engineering Centers selected by the National Science Foundation for funding in February 2015. The CU-Boulder center was founded with a \$12 million NSF grant over six years. Clark is the SMRC center director and Walba is the associate director.

Other paper co-authors include the University of Milan's Tommaso P. Fraccia, Giuliano Zanchetta and Elvezia Paraboschi and the University of Parma's Giorgio Dieci. Parma University is located in Parma, Italy.

<http://bit.ly/1Psnzv6>

Amazing Discovery: Nearly Extinct Bird Found Breeding in Japan

Higashijima hides an incredible secret

By John R. Platt

Higashijima Island doesn't look like much from the sky. This tiny, uninhabited scrap of land 1,000 kilometers south of the coast of Japan is only a few hectares in size. The eastern half of the island consists of rocky outcroppings, while the western half contains small plots of grassland and shrubs. Nothing about Higashijima appears all that notable.

But Higashijima hides an incredible secret. The island is the only known home to the incredibly rare Bryan's shearwater (*Puffinus bryani*), a bird that until recently was feared to be extinct.

The Bryan's shearwater was only discovered four years ago, when scientists examined two nearly 50-year-old museum samples originally collected in Hawaii and the Midway Atoll. Previously thought to be a little shearwater (*P. assimilis*), DNA testing revealed the sample to be a previously unknown species. But even the revelation of the new species didn't answer questions about where the tiny birds bred or if they even still existed.

A few more clues emerged in 2012. With the genetic and morphological descriptions of Bryan's shearwaters in hand, scientists reexamined six previously unidentified birds found in the Ogasawara archipelago (also known as the Bonin Islands) between 1997 and 2011. Even though the five of the six carcasses had been heavily munched on by invasive rats, researchers were able to identify them as the newly discovered species.

But no new sightings came after 2011. Had rats wiped this species out before we even knew it existed?

Now we know. This February a team from the Forestry and Forest Products Research Institute (FFPRI) in Japan visited Higashijima in the Ogasawara archipelago. After hearing a high-pitched chirp, they started combing through the island's three hectares of grass and shrubs.

That's when they found them. All told, the researchers discovered 10 Bryan's shearwaters, including one that was sitting on an underground nest. They briefly captured and measured four of the birds, photographed some of them, captured a few seconds of video, and then left them to continue with their mysterious ways.

Higashijima appears relatively safe for the 150-gram birds, as Japan's Ministry of the Environment has already completed a rat-eradication project there. However a new threat has already started to emerge. The island contains invasive plants, which the FFPRI worries could choke off the native plants the birds depend upon for shelter. The organization is starting a project to remove the plant before it causes more damage the islands.

Meanwhile, they'll keep looking for more Bryan's shearwaters on other islands in the archipelago. Will the researchers find more? Will the birds that we know about remain on Higashijima or do they still fly 4,000 kilometers to Midway every year? What will it take to protect them? Those and other questions remain to be answered.

http://www.eurekalert.org/pub_releases/2015-04/si-fft040315.php

Food for thought: Master protein enhances learning and memory *Physical and mental activities rely on a single metabolic protein, ERRγ, that controls the flow of blood and nutrients throughout the body*

LA JOLLA - Just as some people seem built to run marathons and have an easier time going for miles without tiring, others are born with a knack for memorizing things, from times tables to trivia facts. These two skills—running and memorizing—are not so different as it turns out.

Salk scientists and collaborators have discovered that physical and mental activities rely on a single metabolic protein that controls the flow of blood and nutrients throughout the body, as reported in the journal *Cell Metabolism*. The new study could point to potential treatments in regenerative and developmental medicine as well as ways to address defects in learning and memory.

"This is all about getting energy where it's needed to 'the power plants' in the body," says Ronald Evans, director of Salk's Gene Expression Laboratory and senior author of the new paper, published April 7, 2015. "The heart and muscles need a surge of energy to carry out exercise and neurons need a surge of energy to form new memories."

Energy for muscles and brains, the scientists discovered, is controlled by a single protein called estrogen-related receptor gamma (ERRγ). Evans' research group has previously studied the role of ERRγ in the heart and skeletal muscles. In 2011, they discovered that promoting ERRγ activity in the muscle of sedentary mice increased blood supply to their muscles and doubled their running capacity. ERRγ, they went on to show, turns on a whole host of muscle genes that convert fat to energy.

Thus, ERRγ became known as a master metabolic switch that energized muscle to enhance performance. Although studies had also shown that ERRγ was active in the brain, researchers didn't understand why—the brain burns sugar and ERRγ

was previously shown to only burn fat. So the team decided to look more closely at what the protein was doing in brain cells.

By first looking at isolated neurons, Liming Pei, lead and co-corresponding author of the paper, found that, as in muscle, ERR γ activates dozens of metabolic genes in brain cells. Unexpectedly, this activation related to sugar instead of fat. Neurons that lacked ERR γ could not ramp up energy production and thus had a compromised performance.

"We assumed that ERR γ did the same thing throughout the body," says Evans. "But we learned that it's different in the brain." ERR γ , they now conclude, turns on fat-burning pathways in muscles and sugar-burning pathways in the brain.

Evans and his collaborators noticed that ERR γ in live mice was most active in the hippocampus—an area of the brain that is active in producing new brain cells, is involved in learning and memory and is known to require lots of energy. They wondered whether ERR γ had a direct role in learning and memory. By studying mice lacking ERR γ in the brain, they found a link.

While mice without the protein had normal vision, movement and balance, they were slower at learning how to swim through a water maze - and poor at remembering the maze on subsequent trials - compared to mice with normal levels of ERR γ . "What we found is that mice that missing ERR γ are basically very slow learners," says Pei. Varying levels of ERR γ could also be at the root of differences between how individual humans learn, he hypothesizes. "Everyone can learn, but some people learn and memorize more efficiently than others, and we now think this could be linked to changes in brain metabolism."

A better understanding of the metabolism of neurons could help point the way to improved treatments for learning and attention disorders. And possibly, revving up levels of ERR γ could even enhance learning, just as it enhances muscle function. "What we've shown is that memories are really built on a metabolic scaffold," says Evans. "And we think that if you want to understand learning and memory, you need to understand the circuits that underlie and power this process."

Other researchers on the study were Yangling Mu, Mathias Leblanc, William Alaynick, Matthew Pankratz, Tiffany W. Tseng, Samantha Kaufman, Ruth T. Yu, Michael Downes, Samuel L. Pfaff, and Fred H. Gage, all of the Salk Institute for Biological Studies; Liming Pei of the University of Pennsylvania; Grant D. Barish of Northwestern University; Christopher Liddle of the University of Sydney; and Johan Auwerx of Ecole Polytechnique Federale de Lausanne.

The work was supported by the Howard Hughes Medical Institute, the National Institutes of Health, the Leona M. and Harry B. Helmsley Charitable Trust, the Ellison Medical Foundation and Glenn Foundation for Medical Research, the Children's Hospital of Philadelphia and the Penn Medicine Neuroscience Center.

<http://bit.ly/1Pso0FF>

When Peanut Allergy Comes from a Blood Transfusion ***A Canadian boy picked up new allergies when he received donor plasma***

April 7, 2015 |By Dina Fine Maron

The origin of a food allergy usually remains a mystery. Not so for an eight-year-old boy who received a blood transfusion unexpectedly brimming with antibodies against salmon and peanuts—two foods he had routinely consumed in the past. A few weeks after receiving transfusions, when he had a serious allergic reaction within 10 minutes of eating salmon and another after he ate a chocolate peanut butter cup, his doctors soon identified the source of the problem. Although transfusion-borne allergies are not unheard of, they are extremely rare.

"Allergies are so common in the population so we would anticipate that the rate of such events might be higher, and yet they have only been documented a few times in the literature," says Julia Upton, an allergist at the Hospital for Sick Children in Toronto who wrote about this incident in the Canadian Medical Association Journal. In prior donor-linked allergy cases, a patient developed new allergies to foods, drugs or other allergens like grass following a transfusion from a donor who harbored such allergies. Fortunately, each time the allergies were short-lived and dissipated after several months because the patients did not produce the allergen antibodies themselves. With this patient, too, the allergies faded over several months.

"We've had two such cases reported to Canadian Blood Services in the past decade, and we distribute over a million blood components for transfusion every year," says Robert Skeate, Canadian Blood Services' associate medical director for eastern Canada. But even though the transference of allergen antibodies via transfusion is apparently rare, the principle behind it makes sense. Clinicians purposefully transfer antibodies to give patients protection against infections, so it is not surprising that other antibodies could be transferred and cause ripple effects, Upton says. Large amounts of immunoglobulin-E (IgE) antibodies remain in blood products even after storage of more than a month. Typically, fresh frozen plasma will contain the largest amount of the antibodies, followed by platelets and then red cells because all three blood components contain plasma, which can contain antibodies.

Still, multiple events must come together for a patient to have this rare allergic reaction. First, the blood donor must have high levels of IgE antibodies—those that react against allergens. Second, a substantial amount of blood product must be given to the patient. Then, in order to detect the new allergy, the patient would have to be exposed to the specific allergen the antibodies would react against within a few months of receiving the transfusion. That window is tight, because

passively acquired antibodies will naturally fade after a few months and the transient allergy will disappear. IgE is estimated to have a half-life of just a few hours or days, but once it enters the body and binds to cells, it can remain detectable for weeks or months and cause allergic reactions.

Blood donors in the U.S. and Canada are not usually screened for allergies or asked to defer donation if they have a history of allergy. With this case, Canadian Blood Services officials traced the problematic blood product back to a donor with several allergies, checked to see if any more of that person's blood was in the donor pool (it was not) and barred that person from making future donations. This incident provided "sufficient reason to think it may happen again in the future," so Canadian Blood Services took this step as a precaution, Skeate says.

Typically, blood donors are only asked if they are currently experiencing any allergy symptoms at the time of donation (and asked not to donate if the answer is "yes"). That protocol makes sense, Upton says. Even if donors submitted to allergy blood tests, the results would not be definitive—they could pick up high levels of IgE antibodies but that person, or any recipients of their blood, may not have any actual reaction to the allergens in the real world. With that in mind, Upton and her co-authors are not calling for any changes in blood donation policy. "It would be very difficult to reduce the risk of such a rare reaction without substantial blood donor loss, and that's one reason the policy is the way it is," she says. Still, if doctors are on the lookout for the development of allergies after a blood transfusion, then the field will likely get a better sense of how common this effect is, she says.

http://www.eurekalert.org/pub_releases/2015-04/uoc--mhb040815.php

Mars has belts of glaciers consisting of frozen water

Mars has distinct polar ice caps, but Mars also has belts of glaciers at its central latitudes in both the southern and northern hemispheres.

A thick layer of dust covers the glaciers, so they appear as surface of the ground, but radar measurements show that underneath the dust there are glaciers composed of frozen water. New studies have now calculated the size of the glaciers and thus the amount of water in the glaciers. It is the equivalent of all of Mars being covered by more than one meter of ice. The results are published in the scientific journal, Geophysical Research Letter.

Several satellites orbit Mars and on satellite images, researchers have been able to observe the shape of glaciers just below the surface. For a long time scientists did not know if the ice was made of frozen water (H₂O) or of carbon dioxide (CO₂) or whether it was mud.

Using radar measurements from the NASA satellite, Mars Reconnaissance Orbiter, researchers have been able to determine that it is water ice. But how thick is the

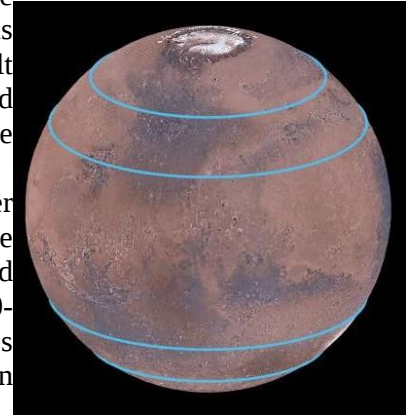
ice and do the glaciers resemble glaciers on Earth? A group of researchers at the Niels Bohr Institute have now calculated this using radar observations combined with ice flow modelling.

Data combined with modelling

"We have looked at radar measurements spanning ten years back in time to see how thick the ice is and how it behaves. A glacier is after all a big chunk of ice and it flows and gets a form that tells us something about how soft it is. We then compared this with how glaciers on Earth behave and from that we have been able to make models for the ice flow," explains Nanna Bjørnholt Karlsson, a postdoc at the Centre for Ice and Climate at the Niels Bohr Institute at the University of Copenhagen.

Nanna Bjørnholt Karlsson explains that earlier studies have identified thousands of glacier-like formations on the planet. The glaciers are located in belts around Mars between the latitudes 300-500 - equivalent to just south of Denmark's location on Earth. The glaciers are found on both the northern and southern hemispheres.

Mars distinct polar ice caps, but Mars also has belts of glaciers at its central latitudes -- between the blue lines between the latitudes 300-500 in both the southern and northern hemispheres. A thick layer of dust covers the glaciers, so they appear as the surface of the ground, but radar measurements show that there are glaciers composed of frozen water underneath the dust. Mars Digital Image Model, NASA/Nanna Karlsson



From some locations on Mars they have good detailed high-resolution data, while they only have more sparse data from other areas. But by supplementing the sparse data with information about the flow and form of the glaciers from the very well studied areas, they have been able to calculate how thick and voluminous the ice is across the glacier belts.

Could cover the entire planet

"We have calculated that the ice in the glaciers is equivalent to over 150 billion cubic meters of ice - that much ice could cover the entire surface of Mars with 1.1 meters of ice. The ice at the mid-latitudes is therefore an important part of Mars' water reservoir," explains Nanna Bjørnholt Karlsson.

That the ice has not evaporated out into space could actually mean that the thick layer of dust is protecting the ice. The atmospheric pressure on Mars is so low that water ice simply evaporates and becomes water vapour. But the glaciers are well protected under the thick layer of dust.

http://www.eurekalert.org/pub_releases/2015-04/uoer-sa040715.php

Research shows alternating antibiotics could make resistant bacteria beatable

Pioneering new research has unlocked a new technique to help combat the rise of antibiotic-resistant bacteria, that cause debilitating and often life-threatening human illness.

Researchers from the University of Exeter has shown that the use of 'sequential treatments' - using alternating doses of antibiotics - might offer effective treatment against bacterial infection. Crucially, the research also demonstrates this technique for administering treatment also reduces the risk of the bacteria becoming resistant to antibiotics, and so maintaining the long-term effectiveness of the drugs. The collaborative international research, led by Professor Robert Beardmore from the University of Exeter and funded by EPSRC, is published in leading scientific journal PLOS Biology on Wednesday 8 April.

The research indicates that drug treatments with two antibiotics can be designed to kill bacteria at dosages that would ordinarily cause rapid development of drug resistance and sustained bacterial growth, when administered alone or in combination.

The researchers used a test-tube model of a bacterial infection to show that, even in bacteria that already harbour drug resistance genes, sequential treatments could deal with the bacteria, even when much higher doses of single drugs or mixtures of two drugs failed to do so.

"Our study finds a complex relationship between dose, bacterial population densities and drug resistance," said lead author, Professor Beardmore. "As we demonstrate, it is possible to reduce bacterial load to zero at dosages that are usually said to be sub lethal and, therefore, are assumed to select for increased drug resistance."

The researchers also discovered that, although sequential treatments didn't suppress the rise of all drug resistance mutations in the bacteria, one drug would 'sensitize' the bacteria to the second drug, and therefore reduce the risk of resistance occurring.

Study co-author Dr Ayari Fuentes-Hernandez said: "Research has concentrated for decades on synergistic drug cocktails. We believe 'sequential synergies' might be just as potent if we look for them, this research will therefore be of interest to the pharma and dwindling antibiotic discovery communities."

While bacteria are masters at adapting to antibiotic challenge, this research suggests that there is a way to use this adaptation against them. The fluctuating environments created by well-designed sequential treatments can sensitize

bacteria and render them susceptible to concentrations of antibiotics that would normally induce drug resistance and continued existence.

EPSRC-funded researcher, Dr Jessica Plucain, said that although extensive further work is now needed to will be needed before sequential treatments make it in to the clinic, the research demonstrates that they can be effective even when using drug doses below their maximal potency.

She said: "One outcome of this highly surprising result will be to set in motion a series of studies to determine ways of using antibiotics not only in combination, but sequentially and with the potential for lower dosages than is currently thought possible."

<http://www.bbc.com/news/science-environment-32219494>

Multiple studies address riddles of the Moon's origin

The planet that collided with the early Earth might have been made of similar stuff

By Jonathan Webb Science reporter, BBC News

The Moon may have been formed by a collision between Earth and an object that was strikingly similar in composition to our own planet. This could help resolve why Earth and Moon rocks are much more similar than we would expect from this "giant impact hypothesis". The study is one of three published in the prestigious journal Nature. Two further research papers in the issue report subtle, previously unseen differences in lunar rocks. Scientists say they paint a consistent - and much clearer - picture of our satellite's history.

The modelling study, done by researchers from Israel and France, precisely simulates the turmoil of the early, inner Solar System and quantifies the variety of collisions that might have occurred. In its early stages, the proto-Earth would have been subjected to a string of brutal collisions with other wannabe planets.

According to our best understanding, the last of these was a cataclysmic tangle with a planetary body just ten times lighter than Earth - and the resulting debris eventually clumped together to make the Moon.

Insufficiently alien

The problem is that most of what became the Moon should have come from the imposter - and based on our existing knowledge of what was flying where at that time, that imposter was thought to be a very different type of planet.

"So if the impactor had a different composition from the Earth, we should expect the Moon to have a different composition," Dr Hagai Perets, one of the study's authors, told the Nature podcast. But this is not the case.

"They are almost identical. This is one of the major challenges for this really beautiful giant impact hypothesis," said Dr Perets, from the Technion-Israel Institute of Technology.

This is why a study made headlines in 2014 when it pinpointed some tiny differences between Earth and Moon rocks.

What Dr Perets and his colleagues found in their new simulations was that the impactor planet might, in fact, have been made of surprisingly similar stuff to the Earth - leaving only the sort of subtle differences that we do see in lunar material.

Sisters in space - how similar are the Earth and the Moon?

"What we found is that many of these impactors on a planet have very similar composition to that of the planets they impact - as similar as what we measure between the Earth and the Moon," Dr Perets explained.

Specifically, the models indicated a 20% chance that the impact could have been between such similar proto-planets. These odds give our prevailing "origins story" for the Moon a fighting chance, Dr Perets said.

"[Now] I am even more confident about the giant impact hypothesis."

Violent veneer

A different challenge to our current ideas about the Moon relates to what happened subsequently. To explain certain details in the Earth's make-up, scientists have proposed that both the Earth and Moon amassed a large amount of extra matter - a so-called "late veneer" - during a subsequent period when they were bombarded by huge numbers of meteorites.

And just like the original giant impact, this process should also have left a trail of evidence that had not been detected until now.

Even if, as the French-Israeli study now suggests, the Earth and Moon got started from very similar building blocks, this bombardment should have had a much bigger effect on the bulkier, heavier Earth with its much stronger gravity, shifting the balance of its ingredients away from that of the Moon.

The two new investigations of lunar rocks, one from the US and one from Germany, find support for that shift for the first time, by analysing samples from the Apollo missions with new levels of precision.

Both teams looked specifically at traces of tungsten within small chunks of the Moon that they borrowed from Nasa, and found a small but tell-tale difference compared to Earth rock. The ratio of the metal's different isotopes was altered.

Two teams of researchers examined moon rocks collected by the Apollo missions. Importantly, the ratios measured by the two teams match - and the difference fits what might be expected if the Earth collected a bigger "veneer" from the bombardment.

"The small, but significant, difference in the tungsten isotopic composition between Earth and the Moon perfectly corresponds to the different amounts of material gathered by Earth and the moon post-impact," said Prof Richard Walker from the University of Maryland, one of the authors on the US study.

Considering the three studies in total, Dr Matthias Willbold from the University of Manchester told the BBC he was impressed and excited.

"They all tell the same story - it all falls into place," said Dr Willbold, a planetary scientist who has also investigated the late veneer idea using tungsten ratios.

"It's quite striking. [The lunar rock studies] mention that it is quite baffling that the Earth and Moon have the same starting composition, before the bombardment.

"And that links perfectly into the modelling paper, where they say look - we can resolve that. If you look at the models, the impactor and the Earth were similar, so we just solved your problem!"

http://www.eurekalert.org/pub_releases/2015-04/ru-ifh040615.php

In first human study, new antibody therapy shows promise in suppressing HIV infection

Fresh optimism to the field of HIV immunotherapy and new strategies for fighting or even preventing HIV infection

In the first results to emerge from HIV patient trials of a new generation of so-called broadly neutralizing antibodies, Rockefeller University researchers have found the experimental therapy can dramatically reduce the amount of virus present in a patient's blood. The work, reported this week in Nature, brings fresh optimism to the field of HIV immunotherapy and suggests new strategies for fighting or even preventing HIV infection.

In a person infected with HIV, there is an ongoing arms race between the virus and the body's immune system. Even as the body produces new antibodies that target the virus, the virus is constantly mutating to escape, managing to stay just a few steps ahead.

The new study, conducted in Michel Nussenzweig's Laboratory of Molecular Immunology, finds that administration of a potent antibody, called 3BNC117, can catch HIV off guard and reduce viral loads.

HIV antibodies previously tested in humans had shown disappointing results. 3BNC117 belongs to a new generation of broadly neutralizing antibodies that potently fight a wide range of HIV strains.

"What's special about these antibodies is that they have activity against over 80 percent of HIV strains and they are extremely potent," says Marina Caskey, assistant professor of clinical investigation in the Nussenzweig lab and co-first author of the study.

3BNC117, which was originally isolated by Johannes Scheid in the Nussenzweig laboratory, targets the CD4 binding site of the HIV envelope, and the CD4 receptor is the primary site of attachment of HIV to host cells, 3BNC117 shows activity against 195 out of 237 HIV strains.

Broadly neutralizing antibodies are produced naturally in some 10 to 30 percent of people with HIV, but only after several years of infection. By that time the virus in their bodies has typically evolved to escape even these powerful antibodies.

However, by isolating and then cloning these antibodies, researchers are able to harness them as therapeutic agents against HIV infections that have had less time to prepare. Earlier work in the Nussenzweig lab had demonstrated that these potent antibodies could prevent or suppress infection in mouse and non-human primate models of HIV. But these animal models are very rough approximations of human infections, explains Caskey. The mice must be genetically engineered to be susceptible to HIV and therefore lack an intact immune system, and the primates used in HIV studies can only be infected with a simian version of the virus. The proof of principle awaited human trials.

In the new study, uninfected and HIV-infected individuals were intravenously given a single dose of the antibody and monitored for 56 days. At the highest dosage level tested in the study, 30 milligrams per kilogram of weight, all eight infected individuals treated showed up to 300-fold decreases in the amount of virus measured in their blood, with most reaching their lowest viral load one week after treatment. The drop in viral load depended on the individual's starting viral load and also the sensitivity of their particular strains of HIV to the antibody.

This is the first time that the new generation of HIV antibodies has been tested in humans. Not only was a single dose of 3BN117 well tolerated and effective in temporarily reducing viral loads, in some individuals it remained active in the body for a long time. In half of the individuals receiving the highest dose, viral loads remained below starting levels even at the end of the 8-week study period and resistance to 3BNC117 did not occur. Researchers also believe that antibodies may be able to enhance the patient's immune responses against HIV, which can in turn lead to better control of the infection. In addition, antibodies like 3BNC117 may be able to kill viruses hidden in infected cells, which serve as viral reservoirs inaccessible to current antiretroviral drugs.

Most likely, 3BNC117, like other anti-retrovirals, will need to be used in combination with other antibodies or antiretroviral drugs to keep infections under control. "One antibody alone, like one drug alone, will not be sufficient to suppress viral load for a long time because resistance will arise," says Caskey. One important benefit is the dosing schedule: an antibody therapy for HIV might require treatment just once every few months, compared to daily regimens of antiretroviral drugs that are now the front-line treatment for HIV.

"In contrast to conventional antiretroviral therapy, antibody-mediated therapy can also engage the patient's immune cells, which can help to better neutralize the

virus," says co-first author Florian Klein, also assistant professor of clinical investigation in the Nussenzweig laboratory.

Besides the possibility of treatment, the study also raises hopes for an HIV vaccine. If researchers can induce an uninfected person's immune system to generate potent antibodies such as 3BNC117, it might be enough to block the HIV infection before it can be established.

Ongoing clinical research in Nussenzweig's lab and The Rockefeller University Hospital aims to address the impact of additional broadly neutralizing antibodies, alone or in combination, on viral load in HIV-infected patients.

Dr. Nussenzweig is Zanvil A. Cohn and Ralph M. Steinman Professor as well as a Howard Hughes Medical Institute investigator; the research received funding from the Robertson Fund at Rockefeller, a Clinical and Translational Science Award from the National Center for Research Resources of the National Institutes of Health, and the Bill and Melinda Gates Foundation.

http://www.eurekalert.org/pub_releases/2015-04/uot-bcr040815.php

Breast cancer research uncovers the fountain of youth

The Fountain of Youth has been discovered and it's not in Florida as Ponce de Leon claimed.

Instead, it was found in the mammary glands of genetically modified mice.

A research team led by Professor Rama Khokha has found that when two factors that control tissue development are removed, you can avoid the impact of aging.

Think of tissue as a building that is constantly under renovation. The contractors would be "metalloproteinases," which are constantly working to demolish and reconstruct the tissue. The architects in this case, who are trying to reign in and direct the contractors, are known as "tissue inhibitors of metalloproteinases" -- or TIMPs. When the architect and the contractors don't communicate well, a building can fall down. In the case of tissue, the result can be cancer.

To understand how metalloproteinases and TIMPs interact, medical researchers breed mice that have one or more of the four different types of TIMPs removed. Khokha's team examined the different combinations and found that when TIMP1 and TIMP3 were removed, breast tissue remained youthful in aged mice. The results are presented in Nature Cell Biology.

In the normal course of aging, your tissue loses its ability to develop and repair as fast as it did when you were young. That's because stem cells, which are abundant in your youth, decline with the passing of time. The U of T team found that with the TIMP1 and TIMP3 architects missing, the pool of stem cells expanded and remained functional throughout the lifetime of these mice.

"Normally you would see these pools of stem cells, which reach their peak at six months in the mice, start to decline. As a result, the mammary glands start to

degenerate, which increases the risk of breast cancer occurring," explains Khokha. "However, we found that in these particular mice, the stem cells remained consistently high when we measured them at every stage of life."

The team also found that despite large number of stem cells, there was no increased risk of cancer.

"It's generally assumed that the presence of a large number of stem cells can lead to an increased cancer risk," says Khokha. "However, we found these mice had no greater predisposition to cancer."

The next step in this research is to understand why this is happening. Khokha is also working with her colleagues at Princess Margaret to see how altered tissue remodeling might prevent cancer development or lead to a new therapeutic treatment for patients.

Khokha is a Professor in the departments of Medical Biophysics and Laboratory Medicine and Pathobiology, as well as a Senior Scientist at the Princess Margaret Cancer Centre. Her work is supported by the Canadian Breast Cancer Foundation and the Canadian Cancer Society Research Institute.

She was drawn to this research by the complexity of breast tissue.

"It's a fundamental tissue that is constantly reorganizing. It develops at puberty. It goes through cycles of change in the adult female. New structures appear and regress," she explains. "It is therefore a good system to explore in order to understand tissue maintenance and epithelial cell turnover - the cells that underlie carcinomas, the most frequent type of cancer."

She worked closely with the paper's lead author, Dr. Hartland Jackson, who earned his PhD under her supervision. He is now completing a post-doctoral fellowship at the University of Zurich's Institute of Molecular Life Sciences.

"He's continuing his work in breast cancer and learning some really interesting techniques that, I hope, he'll bring back here," says Khokha, who beams with pride at her former student's success.

http://www.eurekalert.org/pub_releases/2015-04/acs-anp040815.php

A new piece in the 'French paradox' puzzle - cheese metabolism

Cheese metabolism may be a key to the French Paradox

Figuring out why the French have low cardiovascular disease rates despite a diet high in saturated fats has spurred research and many theories to account for this phenomenon known as the "French paradox." Most explanations focus on wine and lifestyle, but a key role could belong to another French staple: cheese. The evidence, say scientists in ACS' Journal of Agricultural and Food Chemistry, is in cheese metabolism.

Hanne Bertram and colleagues note that recent research on some dairy products' positive effects on health has cast doubt on the once-firm rule that saturated fats

are bad for our hearts. For example, one study found that cheese reduced "bad" cholesterol when compared to butter with the same fat content, suggesting that high cheese consumption could help explain the French paradox. To further investigate this possible explanation, Bertram's team looked into how cheese gets digested.

The researchers compared urine and fecal samples from 15 healthy men whose diets either contained cheese or milk, or who ate a control diet with butter but no other dairy products. They found that those who consumed cheese had higher fecal levels of butyrate, a compound produced by gut bacteria. Elevated butyrate levels were linked to a reduction in cholesterol. Their results, they say, suggest a role for gut microbes and further shore up the connection between cheese and the French paradox.

The authors acknowledge funding from the Danish Council for Strategic Research, Arla Foods and the Danish Dairy Research Foundation.

http://www.eurekalert.org/pub_releases/2015-04/uotm-urd040815.php

UTMB researchers develop Ebola vaccine effective in a single dose

Quick-acting Ebola vaccine that is both safe and effective with a single dose

An interdisciplinary team from The University of Texas Medical Branch at Galveston and Profectus BioSciences, Inc. has developed a quick-acting vaccine that is both safe and effective with a single dose against the Ebola strain that killed thousands of people in West Africa last year. These findings are detailed in the new edition of Nature.

During 2014, the outbreak of the West African Makona strain of Ebola Zaire virus killed nearly 10,000 and caused worldwide concern. With increasing population growth in West Africa, the frequency of contact between humans and natural Ebola virus hosts such as bats will likely rise, potentially leading to more catastrophic outbreaks.

Many vaccine approaches have shown promise in being able to protect nonhuman primates against Ebola Zaire. In response to the Ebola Zaire outbreak, several of these vaccines have been fast tracked for human use.

One of those vaccines, developed by UTMB and Profectus, has been undergoing testing in the Galveston National Laboratory, the only fully operational Biosafety Level 4 laboratory on an academic campus in the U.S.

"These findings may pave the way for the identification and manufacture of safer, single dose, high efficiency vaccines to combat current and future Ebola outbreaks," said Thomas Geisbert, UTMB professor of Microbiology and Immunology. "We are excited at the possibility of helping develop a way to stop

this deadly disease. We have a lot of more work to accomplish but it's important to note that this is a big step."

The research team developed a vaccine effective against Ebola Zaire with a single dose in a nonhuman primate model. This new vaccine employs a virus not harmful to humans called vesicular stomatitis virus that had a part of the Ebola virus inserted into it. This "Trojan horse" vaccine safely triggered an immune response against Ebola Zaire.

To address any possible safety concerns associated with this vaccine, the team developed two next generation candidate vaccines that contain further weakened forms of the vaccine. Both of these vaccines produced an approximately ten-fold lower level of virus in the blood compared to the first generation vaccine.

"It was not known whether any of these vaccines could provide protection against the new outbreak West African Makona strain of Ebola Zaire currently circulating in Guinea," said John Eldridge, Chief Scientific Officer-Vaccines at Profectus Biosciences, Inc. "Our findings show that our candidate vaccines provided complete, single dose protection from a lethal amount of the Makona strain of Ebola virus."

Both weakened vaccines have features of the Mayinga strain of Ebola virus, as do most other candidate Ebola Zaire vaccines currently under evaluation. The original 1976 Mayinga strain and the new West African Makona strain are quite similar. The researchers said it was important to test their candidate vaccines on the Makona strain to ensure that even small differences between the strains didn't impact the effectiveness of the vaccine.

Other authors include UTMB's Chad E. Mire, Joan B. Geisbert, Krystle N. Agans and Karla A. Fenton and Demetrius Matassov, Theresa E. Latham, Rong Xu, Ayuko Ota-Setlik, Michael A. Egan, David K. Clarke and John H. Eldridge from Profectus BioSciences, Inc.

This research was supported by the National Institutes of Health and the UTMB Department of Microbiology and Immunology.

<http://bit.ly/1FwZnzC>

Life below Antarctic ice survives on ancient forests

White on top, but what lies beneath? Antarctica's blanket of snow and ice sits atop a vast and rich landscape of volcanoes, rivers and lakes.

16:45 08 April 2015 by Catherine Brahic

Results from the first expedition to sample the sediment beneath the ice are revealing how the remnants of ancient forests are fuelling the communities that live there today. Lake Whillans sits beneath nearly 1 kilometre of ice in West Antarctica. Despite its heavy frozen lid, it is full of liquid water.

In January 2013, a US team drilled through the ice and sampled the lake's water and the sediment beneath. The sediment contained microfossils of marine

organisms and fossilised pollen from beech trees and conifers, Slawek Tulaczyk of the University of California at Santa Cruz told a meeting on subglacial Antarctic lakes held at Chicheley Hall near London last week.

The pollen dates back to before 34 million years ago, at a time when Antarctica was a collection of lush forested islands separated by salty fjords. Both are providing much-needed nutrients to a completely different community that now occupies the area; the water samples from the lake revealed a thriving microbial community that was living in the pitch dark and at huge pressures and low temperatures.

Fish in the dark

"I like to think that the long-dead life from a much happier time is now feeding the modern microbial ecosystem," says Tulaczyk.

The team have found bigger things too. In January they drilled down to a nearby subglacial beach and were stunned to find fish and crustaceans living in the dark. Ross Powell of Northern Illinois University says they have evidence the fish are stressed and struggling to survive, probably because they are starved of nutrients. They may have fled from an even worse environment, or could be early pioneers of a new subglacial world.

Nor is everything beneath the cap ice-cold. Previous expeditions have revealed seething volcanoes, and ones that erupted in the last couple millennia, punching large holes in the ice cap. Tulaczyk dropped thermometers into the lake bed at Whillans, and measured the geothermal activity.

"We found a huge heat flux, typical of places like Yellowstone," he says, adding that the region could be sitting on top of a geothermal hotspot. "That raises the possibility that there may be hydrothermal vents down there."

http://www.eurekalert.org/pub_releases/2015-04/p-nef040115.php

New evidence for combat and cannibalism in tyrannosaurs

Skull shows evidence of bites that healed, and also those inflicted after death by another tyrannosaur

A new study documents injuries inflicted in life and death to a large tyrannosaurine dinosaur. The paper shows that the skull of a genus of tyrannosaur called Daspletosaurus suffered numerous injuries during life, at least some of which were likely inflicted by another Daspletosaurus. It was also bitten after death in an apparent event of scavenging by another tyrannosaur. Thus there's evidence of combat between two large carnivores as well as one feeding on another after death.

Daspletosaurus was a large carnivore that lived in Canada and was only a little smaller than its more famous cousin Tyrannosaurus. Like other tyrannosaurs it was most likely both an active predator and scavenger. The individual in question,

from Alberta Canada, was not fully grown and would be considered a 'sub-adult' in dinosaur terms (approximately equivalent to an older teenager in human terms). It would have been just under 6 m long and around 500 kg when it died.

Researchers found numerous injuries on the skull that occurred during life. Although not all of them can be attributed to bites, several are close in shape to the teeth of tyrannosaurs. In particular one bite to the back of the head had broken off part of the skull and left a circular tooth-shaped puncture through the bone. The fact that alterations to the bone's surface indicate healing means that these injuries were not fatal and the animal lived for some time after they were inflicted.



Artists reconstruction of combat between two Daspletosaurus. Luis Rey

Lead author Dr David Hone from Queen Mary, University of London said "This animal clearly had a tough life suffering numerous injuries across the head including some that must have been quite nasty.

The most likely candidate to have done this is another member of the same species, suggesting some serious fights between these animals during their lives". There is no evidence that the animal died at the hands (or mouth) of another tyrannosaur.

However, the preservation of the skull and other bones, and damage to the jaw bones show that after the specimen began to decay, a large tyrannosaur (possibly of the same species) bit into the animal and presumably ate at least part of it.

Combat between large carnivorous dinosaurs is already known and there is already evidence for cannibalism in various groups, including tyrannosaurs. This is however an apparently unique record with evidence of both pre- and post-mortem injuries to a single individual.

Unusually, this project was made possible via crowd-funded fundraising through the website Experiment.com.

Numerous donors contributed to the project allowing the work to be carried out and as a result, publication of the paper in the Open Access journal PeerJ, means that these exciting new results are now fully open to the public, who can read them without restriction.

http://www.eurekalert.org/pub_releases/2015-04/uom-nes040915.php

New evidence supports success of fecal transplants in treatment of Clostridium difficile infection

Research demonstrates dynamic nature of fecal microbiota

MINNEAPOLIS/ST.PAUL - Research published in the open access journal Microbiome offers new evidence for the success of fecal microbial transplantation (FMT) in treating severe Clostridium difficile infection (CDI), a growing problem worldwide that leads to thousands of fatalities every year.

Research led by Michael Sadowsky, Alex Khoruts, and colleagues at the University of Minnesota in collaboration with the Rob Knight Lab at the University of Colorado, Boulder, reveals that healthy changes to a patient's microbiome are sustained for up to 21 weeks after transplant, and has implications for the regulation of the treatment. Findings also demonstrate the dynamic nature of fecal microbiota in FMT donors and recipients.

In FMT, fecal matter is collected from a donor, purified, mixed with a saline solution and placed in a patient, usually by colonoscopy. In contrast to standard antibiotic therapies, which further disrupt intestinal microflora and may contribute to the recurrence of CDI, FMT restores the intestinal microbiome and healthy gut function.

Using DNA samples of healthy individuals from the Human Microbiome Project (HMP) as a baseline, Sadowsky and his team compared changes in fecal microbial communities of recipients over time to the changes observed within samples from the donor. Significantly, the composition of gut microbes in the both donor and recipient groups varied over the course of the study, but remained within the normal range when compared to hundreds of samples collected by the HMP.

According to Sadowsky, the findings have important implications for a range of diseases associated with microbial imbalance, or dysbiosis, and could influence the regulatory regime surrounding FMT, currently treated as a drug by the U.S. Food and Drug Administration (USFDA).

"The dynamic nature of fecal microbiota in both the donor and recipients suggests that the current framework of regulation, requiring consistent composition, may need to be reexamined for fecal transplantations," says Michael Sadowsky. "Change in fecal microbial composition is consistent with normal responsiveness to shifts in the diet and other environment factors. Variability should be taken into account when comparing microbial composition in normal individuals to those with dysbiosis characteristic of disease states, especially when assessing clinical interventions and outcomes.

Also discovered in the research, the performance of frozen and fresh preparations of fecal material was indistinguishable. Though the sample was limited and warrants further study with a larger cohort, it has several implications for the widespread adoption of FMT. The frozen preparation greatly simplifies the standardization and distribution of the fecal material. It also facilitates long-term storage of donor material for future study and makes FMT accessible to a greater number of physicians and patients. Finally, it offers advantages over fresh material in the testing of fecal samples for pathogens, which in some cases can take several weeks to complete.

While FMT is particularly successful in patients who suffer from recurrent CDI, University of Minnesota researchers led by Sadowsky and Dr. Alex Khoruts are currently preparing for a clinical trial using FMT to improve insulin sensitivity in pre-diabetic patients and to treat metabolic syndrome.

http://www.eurekalert.org/pub_releases/2015-04/tl-tld040815.php

The Lancet Diabetes & Endocrinology: Being underweight in middle age associated with increased dementia risk

Underweight middle-aged people are a third more likely to develop dementia Than those with healthy BMI

Middle-aged people who are underweight (with a Body Mass Index [BMI] less than 20 kg/m² ^[1]) are a third more likely to develop dementia than people of similar age with a healthy BMI, according to new research published in The Lancet Diabetes & Endocrinology journal.

The findings, which come from the largest ever study to examine the statistical association between BMI and dementia risk, also show that middle-aged obese people (BMI greater than 30 kg/m²) are nearly 30% less likely to develop dementia than people of a healthy weight, contradicting findings from some previous research, which suggested that obesity leads to an increased risk of dementia.

Researchers based at the London School of Hygiene & Tropical Medicine, and OXON Epidemiology, both in London, UK, analysed data from the Clinical Practice Research Datalink (CPRD), a large database of patient information recorded during routine general practice over nearly 20 years, representing around 9% of the UK population.

The researchers analysed the medical records of nearly two million (1,958,191) people with an average (median) age of 55 years at the start of the study period, and an average (median) BMI of 26.5 kg/m², just within the range usually classed as overweight. During an average (median) of nine years follow-up, nearly fifty thousand (45,507) people were diagnosed with dementia.

People who were underweight in middle age were a third (34%) more likely to be diagnosed with dementia than those of a healthy weight, and this increased risk of dementia persisted even 15 years after the underweight was recorded.

As participants' BMI at middle age increased, the risk of dementia reduced, with very obese people (BMI greater than 40 kg/m²) 29% less likely to get dementia than people in the normal weight range. An increase in BMI was associated with a substantial steadily decreasing risk of dementia for BMI of up to 25 kg/m² (classed as a healthy weight). Above a BMI of 25 kg/m² (classed as overweight or obese), dementia risk decreased more gradually, and this trend continued up to a BMI of 35 kg/m² or higher.

The association between BMI and dementia risk wasn't affected by the decade in which the participants were born, nor by their age at diagnosis. Adjusting for confounding factors known to increase the risk of dementia, such as alcohol use or smoking, made little difference to the results.

According to study author Professor Stuart Pocock from the London School of Hygiene & Tropical Medicine, "Our results suggest that doctors, public health scientists, and policy makers need to re-think how to best identify who is at high risk of dementia. We also need to pay attention to the causes and public health consequences of the link between underweight and increased dementia risk which our research has established. However, our results also open up an intriguing new avenue in the search for protective factors for dementia - if we can understand why people with a high BMI have a reduced risk of dementia, it's possible that further down the line, researchers might be able to use these insights to develop new treatments for dementia." ^[2]

"The reasons why a high BMI might be associated with a reduced risk of dementia aren't clear, and further work is needed to understand why this might be the case," adds Dr Nawab Qizilbash from OXON Epidemiology in London, UK and Madrid, Spain, the study's lead author. "If increased weight in mid-life is protective against dementia, the reasons for this inverse association are unclear at present. Many different issues related to diet, exercise, frailty, genetic factors, and weight change could play a part." ^[2]

Writing in a linked Comment, Professor Deborah Gustafson from SUNY Downstate Medical Center in New York, USA, says, "The published literature about BMI and dementia is equivocal. Some studies report a positive association between high mid-life BMI and dementia, whereas others do not... Many considerations are needed in the assessment of the epidemiology of the association between BMI and late-onset dementia, as is the case for many recorded associations involving late-life disorders. To understand the association between BMI and late-onset dementia should sober us as to the complexity of

identifying risk and protective factors for dementia. The report by Qizilbash and colleagues is not the final word on this controversial topic."

NOTES TO EDITORS:

^[1] Although a BMI less than 18.5 kg/m² is usually classed as underweight, a slightly higher threshold (20 kg/m²) was used in this study to enable comparison with earlier studies, which had taken BMI lower than 20 kg/m² as the threshold.

^[2] Quotes direct from authors and cannot be found in text of Article

http://www.eurekalert.org/pub_releases/2015-04/uosc-urp040115.php

USC researcher plucks hair to grow hair

If there's a cure for male pattern baldness, it might hurt a little.

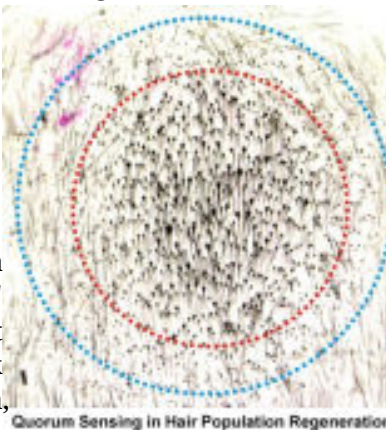
A team led by USC Stem Cell Principal Investigator Cheng-Ming Chuong has demonstrated that by plucking 200 hairs in a specific pattern and density, they can induce up to 1,200 replacement hairs to grow in a mouse. These results are published in the April 9 edition of the journal *Cell*.

"It is a good example of how basic research can lead to a work with potential translational value," said Chuong, who is a professor of pathology at the Keck School of Medicine of USC. "The work leads to potential new targets for treating alopecia, a form of hair loss."

Quorum sensing in hair population regeneration is shown. Courtesy of Cheng-Ming Chuong

The study began a couple of years ago when first author and visiting scholar Chih-Chiang Chen arrived at USC from National Yang-Ming University and Veterans General Hospital, Taiwan. As a dermatologist, Chen knew that hair follicle injury affects its adjacent environment, and the Chuong lab had already established that this environment in turn can influence hair regeneration. Based on this combined knowledge, they reasoned that they might be able to use the environment to activate more follicles.

To test this concept, Chen devised an elegant strategy to pluck 200 hair follicles, one by one, in different configurations on the back of a mouse. When plucking the hairs in a low-density pattern from an area exceeding six millimeters in diameter, no hairs regenerated. However, higher-density plucking from circular areas with diameters between three and five millimeters triggered the regeneration of between 450 and 1,300 hairs, including ones outside of the plucked region.



Working with Arthur D. Lander from the University of California, Irvine, the team showed that this regenerative process relies on the principle of "quorum sensing," which defines how a system responds to stimuli that affect some, but not all members. In this case, quorum sensing underlies how the hair follicle system responds to the plucking of some, but not all hairs.

Through molecular analyses, the team showed that these plucked follicles signal distress by releasing inflammatory proteins, which recruit immune cells to rush to the site of the injury. These immune cells then secrete signaling molecules such as tumor necrosis factor alpha (TNF- α), which, at a certain concentration, communicate to both plucked and unplucked follicles that it's time to grow hair.

"The implication of the work is that parallel processes may also exist in the physiological or pathogenic processes of other organs, although they are not as easily observed as hair regeneration," said Chuong.

In addition to these latest findings, *Science* recently selected Chuong's work on how the regulation of feather follicle stem cells contributed to the evolution of feathered dinosaurs into modern birds as one of the top 10 breakthroughs of 2014. Chuong was also inducted as a fellow of the American Association for the Advancement of Science (AAAS) in February 2015.

Additional coauthors on the *Cell* paper are Ting Xin Jiang and Randall B. Widetz from USC; Lei Wang from The Fourth Military Medical University, China; Maksim V. Plikus, Raul Ramos, Christian F. Guerrero-Juarez from University of California, Irvine; Philip J. Murray from University of Dundee, Scotland; Michael W. Hughes from National Cheng Kong University, Taiwan; Oscar K. Lee from National Yang-Ming University and Veterans General Hospital, Taiwan; and Songtao Shi from the University of Pennsylvania.

Research funding came from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (R01-AR42177, R01-AR067273, AR47364 and AR60306); NSC (100-2314-B-075-044 and 101-2314-B-075-008-MY3); the Taipei Veterans General Hospital (VN103-12, V103C-010, V102B-009 and R-1100403); the National Institutes for Health (R01DE17449); an Edward Mallinckrodt Jr. Foundation grant; a California Institute for Regenerative Medicine training grant (TG2-01152); the National Science Foundation Graduate Research Fellowship Program (DGE-1321846); and the Top Notch University plan of Cheng Kong University, Taiwan.

http://www.eurekalert.org/pub_releases/2015-04/cp-its040215.php

In the sea, a deadly form of leukemia is catching

Outbreaks of leukemia that have devastated some populations of soft-shell clams along the east coast of North America for decades can be explained by the spread of cancerous tumor cells from one clam to another.

Researchers call the discovery, reported in the *Cell Press* journal *Cell* on April 9, 2015, "beyond surprising." "The evidence indicates that the tumor cells themselves are contagious--that the cells can spread from one animal to another in

the ocean," said Stephen Goff of the Howard Hughes Medical Institute and Columbia University. "We know this must be true because the genotypes of the tumor cells do not match those of the host animals that acquire the disease, but instead all derive from a single lineage of tumor cells."

In other words, the cancer that has killed so many clams all trace to one incidence of disease. The cancer originated in some unfortunate clam somewhere and has persisted ever since as those cancerous cells divide, break free, and make their way to other clams.

Only two other examples of transmissible cancer are known in the wild. These cancers include the canine transmissible venereal tumor, transmitted by sexual contact, and the Tasmanian devil facial tumor disease, transmitted through biting. In early studies of the cancer in clams, Goff and his colleagues found that a particular sequence of DNA (which they named Steamer) was found at incredibly high levels in leukemic versus normal clam cells. While normal cells contain only two to five copies of Steamer, cancerous cells can have 150 copies. The researchers at first thought that this difference was the result of a genetic amplification process occurring within each individual clam.

But when first author of the study Michael Metzger analyzed the genomes of cancer cells collected in New York, Maine, and Prince Edward Island, he discovered something else entirely. The cancerous cells they'd collected from clams living at different locations were nearly identical to one another at the genetic level. They were clones. "We were astonished to realize that the tumors did not arise from the cells of their diseased host animals, but rather from a rogue clonal cell line spreading over huge geographical distances," Goff said.

The result shows that the cells can survive in seawater long enough to reach and sicken a new host. It is not yet known whether the soft-shell tumor can spread to other molluscs, or whether there are mechanisms that recognize the malignant cells as foreign invaders and attack them.

Goff says there is plenty they don't know about this cancer, including when it first arose and how it spreads from one clam to another. They don't know what role Steamer played in the cancer's origin, if any. And they don't know how often these sorts of cancers might arise in molluscs or other marine animals. But, the researchers say, the findings do suggest that transmissible cancers are more common than anyone suspected.

"Natural horizontal transmission of cancer between individuals has been considered a rare phenomenon, restricted to two exceptional cases in mammals," the researchers wrote. "Our finding of the horizontal transmission of a clonal clam leukemia extends the phenomenon to the marine environment, and demonstrates that this mechanism is more widespread in nature than previously supposed."

This work was supported by the Howard Hughes Medical Institute and the National Institutes of Health.

Cell, Metzger et al.: "Horizontal Transmission of Clonal Cancer Cells Causes Leukemia in Soft-Shell Clams"

http://www.eurekalert.org/pub_releases/2015-04/fhcr-sph040915.php

Selenide protects heart muscle in the wake of cardiac arrest Tissue damage is diminished by nearly 90 percent, finds preclinical study

SEATTLE - Damage to heart muscle from insufficient blood supply during cardiac arrest and reperfusion injury after blood flow is restored can be reduced by nearly 90 percent if selenide, a form of the essential nutrient selenium, is administered intravenously in the wake of the attack, according to a new preclinical study by researchers at Fred Hutchinson Cancer Research Center. Mark Roth, Ph.D., and colleagues in the Fred Hutch Basic Sciences Division have published their findings online ahead of the July print edition of *Critical Care Medicine*.

"We found that administration of selenide after the heart has been deprived of blood flow and before blood flow is restored significantly protects the heart tissue in a mouse model of acute myocardial infarction and reperfusion injury," Roth said.

Ischemia, or insufficient blood supply, as occurs during a heart attack or stroke, causes tissues to become starved of oxygen. In the highly oxygenated tissues of the heart and brain, ischemia can cause irreversible damage in as little as three to four minutes at normal body temperature.

Reperfusion injury is the tissue damage caused when blood supply returns to the tissue after a period of ischemia or lack of oxygen. The absence of oxygen and nutrients from blood during the ischemic period creates a condition in which the restoration of circulation results in inflammation and oxidative damage through the induction of oxidative stress rather than restoration of normal function.

Using two different mouse models of ischemia reperfusion injury, Roth and colleagues found that selenium is specifically taken up by injured tissues following temporary loss of blood flow while blood selenium levels simultaneously decrease. "These results suggest there is a natural mechanism that targets selenide to recently reperfused tissue and protects it from injury," Roth said. To assess the role of the body's naturally occurring selenide in tissue repair, the researchers conducted a series of experiments in a mouse model.

First, they induced ischemia by temporarily blocking the left anterior descending coronary artery for 60 minutes. Blood flow was then restored and selenium levels in the blood and heart were measured two hours later. "We observed that the greater the injury, the greater the loss of selenium in the blood and the greater amount of selenium was found in the heart," Roth said.

To determine whether the buildup of selenium in injured tissues could happen elsewhere in the body and not just in the heart, Roth and colleagues repeated the experiment in a mouse model in which blood flow was temporarily stopped in one of two hind limbs. In the first five minutes after blood flow was restored, they observed a five-fold increase in the amount of selenide in the injured limb as compared to the untreated limb.

"These results, along with prior understanding of selenium biology, show that endogenous, or naturally occurring, selenium is rapidly mobilized from the blood to help protect injured tissue after blood flow is restored," Roth said. "This led us to wonder whether supplementing the body's naturally occurring selenide with an infusion of selenide might further protect tissues after a heart attack once blood flow is restored."

To test this, using a mouse model of heart attack, Roth and colleagues administered selenide just prior to restoring blood flow and found that it reduced heart damage by 88 percent. To determine the extent of heart-cell damage, the researchers tracked the levels of a heart-specific protein called cardiac troponin two hours after blood flow was restored. To assess the degree of inflammation, they measured neutrophil accumulation in heart tissue 24 hours after reperfusion.

"Both biomarkers were decreased in selenide-treated mice as compared to control mice, which provides compelling evidence that selenide improves tissue viability after heart attack," Roth said.

As a final step, the researchers used echocardiography to measure heart function two days after inducing cardiac ischemia. The mice that received a dose of selenide after ischemia and prior to reperfusion had a statistically significant improvement in heart function.

The nutrient selenium is regarded as an essential element required for sustaining the health of bodily tissues such as heart muscle, and selenium deficiency is associated with heart disease. For example, in the 1970s it was discovered that a large region of China produced food grown in selenium-deficient soil. As a result, tens of thousands of residents, including many children, suffered from selenium deficiency and heart disease. Dietary supplementation with selenium throughout the region cured the epidemic.

In the clinical setting, decreased selenium levels are correlated with tissue injury. For example, in a study of intensive-care patients, blood selenium levels were reduced by as much as 50 percent compared to a healthy comparison group. Additional studies have found that selenium levels increase as patients heal from burns or systemic infection, which suggests that the body's naturally occurring selenium may be redistributed during critical illness to target the injured tissue and enhance recovery.

<http://bit.ly/1yfPokU>

Only Three Countries Left With Polio

Sixty years ago on April 12, Dr. Jonas Salk's polio vaccine was declared safe and effective. In just three years, the entire world could be polio free.

Polio is a life-changing disease that mostly affects young children. It's been around for thousands of years. In fact, ancient Egyptian carvings show young men with withered legs, but it wasn't until the 1900s that the number of cases began to increase in the U.S.

Oddly enough, it had to do with improved sanitation. Until then, children were repeatedly exposed to the polio virus, and that exposure gave them immunity. With better hygiene, children had less contact with the virus as infants, and polio began to spread. By the 1940s, polio epidemics became common in the warm, summer months in the U.S. Each year, thousands of children and adults contracted this highly contagious virus. Most survived, about 1 percent were permanently crippled, others died.

An American president, Franklin D. Roosevelt, caught the virus before entering the White House. Under his leadership, the National Foundation for Infantile Paralysis, as polio was then known, asked Americans to donate a dime to fight polio. The foundation later became known as The March of Dimes.

With an infusion of money, researchers started working on a vaccine to prevent polio. Salk wanted to produce a vaccine containing a killed polio virus. Because the virus was dead, it could not cause disease, but it could trick the body into thinking it had been attacked and then produce antibodies against the disease. Its disadvantage was it might not provide long-term immunity. At the same time, Dr. Albert Sabin tried making a vaccine with a live but much weaker polio virus.

On April 12, 1955, Salk announced that he had developed a polio vaccine that was ready for use. A few years later, Sabin's oral vaccine was ready.

Before a vaccine was widely available, the U.S. Centers for Disease Control and Prevention reported that the virus crippled more than 35,000 people in the U.S. each year. By 1979, polio had been eradicated in the U.S., but unless it was wiped out worldwide, it could come back.

Rotary launched a polio eradication program in 1985, and three years later (1988) the Global Polio Eradication Initiative was formed, led by the World Health Organization, UNICEF, Rotary and the U.S. Centers for Disease Control and prevention. More recently, the Bill and Melinda Gates Foundation has joined the effort.

Since then, the WHO reports the number of polio cases has decreased by more than 99 percent, from an estimated 350,000 cases in 1988, to 416 reported cases in 2013.

Dr. John Sever has worked to eradicate polio through the Rotary Foundation since 1979. He told VOA, "We narrowed it down from being an infection and disease throughout the world to one that's now only in three countries."

Those three countries are Nigeria, Afghanistan and Pakistan. Oyewale Tomori said Nigeria has made a lot of progress. Tomori is president of the Nigerian Academy of Science. "Last year alone, we had only six cases," he said. "The year before, it was 53."

Nigeria has had no cases of polio for at least eight months. But Tomori noted that it is not easy to get children vaccinated in parts of the country experiencing conflict. That's largely why polio still exists in Afghanistan and Pakistan as well. Conflicts in these countries present a real challenge to the international goal of eradicating polio by 2018. As Sever said, "The idea is that you have to eradicate it everywhere, or it can continue to live in people and be transmitted to nonimmunized people."

http://www.eurekalert.org/pub_releases/2015-04/cwru-bef041015.php

Basis established for nitric oxide joining oxygen and carbon dioxide in respiratory cycle

Discovery could lead to treatment focus on red blood cell dysfunction in cardiovascular diseases and blood disorders

Professor Jonathan Stamler's latest findings regarding nitric oxide have the potential to reshape fundamentally the way we think about the respiratory system - and offer new avenues to save lives. It may be time to rewrite the textbooks.

Scientific dogma has the respiration process involving only two elements -- oxygen and carbon dioxide. Specifically, the delivery of oxygen from lungs to tissues, and the removal of the waste product, carbon dioxide, through exhaling.

Recently published online in the journal Proceedings of the National Academy of Sciences (PNAS), Stamler and colleagues demonstrate that nitric oxide is essential for the delivery of oxygen to the cells and tissues that need it.

Stamler, MD, a Professor of Medicine at Case Western Reserve University School of Medicine and Cardiologist at University Hospitals Case Medical Center, led a team that showed that nitric oxide must accompany hemoglobin to enable blood vessels to open and then supply oxygen to tissues.

Doctors have long known that a major disconnect exists between the amount of oxygen carried in the blood and the amount of oxygen delivered to the tissues. Until now, they had no way to explain the discrepancy. The new findings show that nitric oxide within the red blood cell itself is the gatekeeper to the respiratory cycle - nitric oxide makes the cycle run.

"The bottom line is that we have discovered the molecular basis of blood flow control in the respiratory cycle loop," Stamler said. "It's in the hemoglobin protein itself, which has the ability to deliver the nitric oxide together with oxygen. The simplified textbook view of two gases carried by hemoglobin is missing an essential element - nitric oxide - because blood flow to tissues is actually more important in most circumstances than how much oxygen is carried by hemoglobin. So the respiratory cycle is actually a three-gas system."

Stamler's previous research had revealed that the respiratory cycle was more than an oxygen and carbon dioxide exchange proposition. Stamler and colleagues also had shown that red blood cells carry and release nitric oxide, but had not yet explained the exact physiologic ramifications of nitric oxide release.

In this most recent research, investigators uncovered the key role of nitric oxide in controlling the blood flow in small vessels within tissues responsible for delivering oxygen (known as "blood flow autoregulation") - a process whose molecular basis had been a longstanding mystery in medicine. Investigators specifically examined the respiratory cycle in mice lacking the one amino acid site that carries nitric oxide in their red blood cells. Low and behold, blood flow autoregulation was eliminated entirely - the animals could not oxygenate tissues. Initially, investigators found low oxygen levels in the animals' muscles at baseline, despite the animals' red blood cells carrying a full load of oxygen. When the mice were then stressed to bring on slight oxygen deprivation (hypoxia), the blood flow to their organs dropped precipitously. The lack of oxygen should have prompted a spike in blood flow to send more oxygenated blood to tissues and cells. Instead, the reduced blood flow and ensuing oxygen shortfall triggered heart attacks and heart failure in these nitric oxide-deficient animals.

The experiment demonstrated that the nitric oxide-release mechanism regulates oxygen delivery. When nitric oxide flows from the cysteine-binding site in hemoglobin, blood vessels dilate (stretch) and allow oxygen-carrying red blood cells access to tissues.

"These mice had red blood cells that by all traditional measures are completely normal in carrying oxygen and releasing it and then in picking up carbon dioxide, yet these animals cannot oxygenate their tissues," said Stamler, director of Case Western Reserve's Institute for Transformative Molecular Medicine. "Lacking nitric oxide in red cells, oxygen deficiency could not induce vasodilation, which is essential for sustaining life as we know it."

Historically, the control of blood flow has been thought to be the purview of blood vessels and their endothelial linings, while the role of the red blood cell went unappreciated. Blood flow deficits that cause heart attacks and strokes were thought not to be linked to red blood cells.

Historically, the control of blood flow has been thought to be the purview of blood vessels and their endothelial linings, while the role of the red blood cell went unappreciated. Blood flow deficits that cause heart attacks and strokes were thought not to be linked to red blood cells.

"Within the tissues, the tiny vessels and the red blood cells together make up the critical entity controlling blood flow," Stamler said. "Red blood cell dysfunction is likely a hidden contributor to diseases of the heart, lung and blood such as heart attack, heart failure, stroke and ischemic injury to kidneys."

Low nitric oxide levels in red blood cells make blood disorders, such as sickle cell anemia, particularly dangerous. Laboratory research has shown that the red blood cells in individuals with these conditions do not trigger the hypoxic vasodilation required for blood flow autoregulation to work well.

In addition, blood transfusions, which have recently been shown to be deficient in nitric oxide, are associated with increased morbidity and mortality, including heart attacks. The effects of blood transfusions are suspiciously similar to effects seen in the mice, Stamler said. They both lack nitric oxide.

"It's not enough to increase to oxygen content of blood by transfusion; if the nitric oxide mechanism is shot, oxygen cannot make it to its destination," he said. "We know that blood in a blood bank is deficient in nitric oxide, so infusing that blood may cause plugging of blood vessels in tissues, making things worse. Essentially, blood flow cannot autoregulate (increase) without nitric oxide. In terms of developing future therapies, the goal must be restoring red blood cell function, complete with nitric oxide delivery capability. As for the nation's blood supply, the blood should be replenished with nitric oxide."

Stamler also serves as the Director of the Harrington Discovery Institute at University Hospitals Case Medical Center. Joining him in this research were lead author Rongli Zhang and contributing authors Douglas T. Hess, Zhaoxia Qian, Alfred Hausladen, Fabio Fonseca and Ruchi Chaube, all of the department of medicine, and the Institute for Transformative Molecular Medicine, Case Western Reserve University School of Medicine, and James D. Reynolds, the department of anesthesiology, University Hospitals Case Medical Center, and the Institute for Transformative Molecular Medicine, Case Western Reserve University School of Medicine. This research was funded by National Institutes of Health, Defense Advanced Research Projects Agency, Case Western Reserve University School of Medicine and UH Case Medical Center.

<http://bit.ly/1GYq9Ma>

Ocean Acidification Could Have Driven Earth's Biggest Mass Extinction

Study shows the world's oceans were dangerously acidic during the Permian Extinction Event

Samantha Larson smithsonian.com

The Permian Extinction Event was the biggest die-off in Earth's history, in which over 90 percent of species were wiped out. But what, exactly, caused the calamity is still uncertain. Now, in a study published in Science this week, geochemists offer evidence to support the theory that ocean acidification was a key culprit.

Reuters reports:

Scientists said on Thursday that huge amounts of carbon dioxide spewed from colossal volcanic eruptions in Siberia may have turned the world's oceans dangerously acidic 252 million years ago, helping to drive a global environmental calamity that killed most land and sea creatures.

The researchers came to this conclusion after collecting rocks on the seafloor that had been there for hundreds of millions of years and then using the rocks' boron isotopes to unfold the story of the ocean's ancient acidity. "This is one of the few cases where we have been able to show that an ocean acidification event happened in deep time," University of Edinburgh geoscientist Rachel Wood says.

The findings have implications for our oceans today, too. "We are concerned about modern ocean acidification," Wood tells Motherboard.

Wood continues:

Although the amount of carbon added to the atmosphere that triggered the mass extinction was probably greater than today's fossil fuel reserves, the rate at which the carbon was released was at a rate similar to modern emissions. The rate of release is critical because the oceans absorb a lot of the carbon dioxide (CO2) from the atmosphere, around 30 percent of the carbon dioxide released by humans. To achieve chemical equilibrium, some of this CO2 reacts with the water to form carbonic acid. Some of these molecules react with a water molecule to give a bicarbonate ion and a hydronium ion, thus increasing "acidity" (H+ ion concentration).

Current ocean acidification is already taking its toll on animals like sea snails, oysters and coral. In fact, some argue that we are already in the midst of an extinction event, affecting land and sea animals alike.

<http://bit.ly/1D99nAx>

Plague hits prairie dogs and changes US ecosystems

PLAGUE is creeping through the grasslands of the US.

The same bacterium that caused the Black Death seems to be quietly and irrevocably changing the landscape.

Though the plague bacteria, *Yersinia pestis*, now rarely infects people in North America, it's been responsible for the deaths of many black-tailed prairie dogs. This is a problem for the grasslands, where many other species rely on prairie dogs to survive. Predators eat them, animals make homes in their burrows and grass growth is shaped by them (Conservation Biology, doi.org/3cj).

The ecosystem will be affected by their disappearance, says David Eads at Colorado State University in Fort Collins. "The connection between these animals and plants will be distorted and even broken."

To stem the problem, Eads and colleagues are searching for new ways to control the spread of the plague. They are experimenting with an insecticide called delta dust to see if that reduces the numbers of fleas. "If we can't control the problem,

the grasslands are probably going to be far different within the next 100 years," says Eads.

<http://bit.ly/1CKyHtt>

Wine and glue tape ideal for post-surgery patch-ups

IT DOESN'T come unstuck when things get sticky. An adhesive with remarkable strength could be ideal for patching people up after surgery.

Most glues are not suited to medical applications: they may be toxic, or fail when exposed to moisture. Others, like fibrin, are costly and not particularly sticky. But a simple mixture of two cheap, safe chemicals seems to solve these problems, creating an adhesive that sticks to tissues covered in blood or mucus. It is even reusable like a Post-It Note.

Haeshin Lee from the Korea Advanced Institute of Science and Technology and colleagues mixed tannic acid –an antibacterial compound found in plants that also gives wine its edge – with polyethylene glycol or PEG, which can help rejoin broken nerves. He called the resulting substance TAPE (Advanced Functional Materials, doi.org/f26jp5).

They tested its ability to stop bleeding by poking a hole in a mouse's liver and patching it up. After 30 seconds, TAPE-treated mice had bled one-sixth as much as those treated with fibrin. Within 2 minutes, the TAPE mice had stopped bleeding altogether.

<http://nyti.ms/1DaSO7B>

Pattern of Safety Lapses Where Group Worked to Battle Ebola Outbreak

Partners in Health, a Boston-based charity dedicated to improving health care for people in poor countries, signed on to the Ebola fight last fall with high ambitions.

By SHERI FINK APRIL 12, 2015

Unlike Doctors Without Borders and other relief agencies that specialize in acute response to crises, Partners in Health pledged to support the deeply inadequate health systems in Sierra Leone and Liberia for the long haul. Its leaders also publicly criticized the low level of care provided to Ebola patients and promised that its treatment units would do better. "Let's have a medical moon shot," the group's co-founder, Dr. Paul Farmer, said last October.

But the medical group, which had never responded to an Ebola outbreak before and had rarely worked in emergencies, encountered serious challenges.

Now, a previously undisclosed inquiry by international health officials and interviews with employees and managers of the aid group describe a pattern of safety lapses at a government-run treatment center in Port Loko, Sierra Leone,

where Partners in Health worked. Staff members at the charity also cited a confusing leadership structure at the site.

The safety deficiencies, which included inadequate protective clothing, inconsistent protocols in using it and inappropriate disposal of contaminated waste products, led to the closing of the center in mid-March after an American and a Sierra Leonean clinician developed Ebola, and many of the aid group's staff members were evacuated.

Some staff members argued that the site should have closed last winter. Patient numbers had declined, and two newly built Ebola facilities run by other nonprofits had opened nearby, while Partners in Health worked at a converted vocational training center that was run by the Sierra Leone health ministry and was never ideal for patient treatment.

But the medical group kept its American staff at the site despite the risks, deferring to government officials who wanted it to remain open and with whom the aid group needed to maintain good relations in order to work in coming years on strengthening health care there.

"We knew there were gaps and places to improve," said Sheila Davis, the head of Ebola response for Partners in Health. "Because it was a ministry facility, it really wasn't our say whether it opened or closed." She added, "We don't tell the ministry what to do."

The group's leaders say they remain committed to working in tandem with governments, despite the risks and the difficulties that come with not having control. "We signed up for those challenges," Dr. Farmer said in an interview. Achieving lasting change of the type that would prevent Ebola outbreaks in the future, he said, requires working with local ministries through thick and thin.

However, after the two clinicians developed Ebola, Partners in Health pulled its staff out of the treatment unit and a nearby government hospital, workers said, and temporarily forbade them to speak with their Sierra Leonean colleagues with whom they had worked side by side. "This was unacceptable," said Nick Sarchet, an American volunteer at the site, who said he had become a nurse because the philosophy of Partners in Health inspired him.

Ms. Davis said the group intends to increase monitoring and adherence to safety protocols at other sites where it is still working to triage patients, train health workers and care for survivors.

"We saved many, many lives," Ms. Davis said in an interview.

Responding to desperate calls for help last summer as people with Ebola died in the streets without care, a group of senior Partners in Health staff members, who jokingly referred to themselves as "the junta," prevailed on the organization's board of trustees to let the group go into Sierra Leone and Liberia.

The nonprofit organization raised millions of dollars and advertised for medical professionals, not realizing at first that it would also need to recruit officers with expertise in logistics and running facilities to make the medical work possible and safe.

Within weeks, the group was asked to support the overwhelmed Maforki treatment unit in the Port Loko district of Sierra Leone at the epidemic's peak. "It was a complete mess," Dr. Farmer said in an interview. "That's why they sent us there. There were dead people in the courtyard."

Mr. Sarchet, who arrived in mid-November, said there were about 100 patients there. "It was crazy insane," he said. A holding center for suspected Ebola patients at the nearby government hospital, where he also assisted, was even worse. "It was totally not safe to go in," he said. Sharp needles were all over, the incinerator did not work and used gowns were piled up in the dirt, he said.

Two government workers at the treatment unit developed Ebola in the early months, and one of them died, according to interviews with several staff members. "The conditions had been investigated several times," Mr. Sarchet said. "The W.H.O. and C.D.C. always had a laundry list of things that were unsafe."

Investigators from the World Health Organization and other experts who conducted the recent inquiry cited a lack of standardized procedures for donning protective equipment and no posters to remind workers of the proper sequence in which to remove pieces of their gear, according to an excerpt from the findings. The masks that workers wore over their noses and mouths were not tested to ensure they fit properly, the inquiry found.

Unlike Doctors Without Borders, which runs self-contained Ebola units supplied by its own warehouses, Partners in Health relied on the government's supply chain for protective gear worn at Maforki. As a result, the equipment was ever-changing, said Tim Cunningham, an American nurse who worked at Maforki last winter.

The type of masks available frequently varied, as did other materials, he said. One batch of gowns ripped apart during doffing and were quickly set aside. Others were too restrictive. The head clinician kept a log of breaches, Mr. Cunningham said.

The lack of consistency stemmed in part from the lack of unified leadership, given that both the health ministry and Partners in Health leaders were running operations. "From Day 1 there wasn't somebody in charge of the whole scene," said Mr. Sarchet. "You were constantly trying to work within two different systems. That was a huge hardship."

The investigators noted in the report that gowns and other materials were not regularly checked for holes or other problems before being worn. They found contaminated waste strewn in the open in an area used for burning garbage.

"When somebody was tired, sometimes they did not put it right inside the pit," said Usman Mohamed Koroma, a ministry employee who helped oversee infection prevention and control at the site. He contracted Ebola in March, the same week as the American. After being critically ill, the American patient, who the charity said has not been identified because he requested privacy, was released last week from the National Institutes of Health in Bethesda, Md.

Mr. Koroma said he briefly wondered whether he, too, would be evacuated to the United States. "I gave that idea just a casual thought. I said, 'because I'm not a white folk, I'm not from America. I'm an indigenous Sierra Leonean. I'm an African Sierra Leonean. They are not going to move me.' "

It took two days, and daily calls from a Partners in Health staff member for him to be admitted to a British-run treatment unit set up for sick health workers in Freetown, Sierra Leone's capital. The Maforki treatment unit never reopened. More than 350 confirmed Ebola patients were treated at the site, according to the district's medical officer, Dr. Adikali Kamara.

"They were doing their best to make sure to protect the health care workers," he said of Partners in Health. Maforki was not the only treatment unit with infection problems, and even Doctors Without Borders, with long experience treating Ebola, had health workers who became infected.

Leaders of Partners in Health have reiterated their commitment to staying in Sierra Leone and Liberia. "We're there to build the system. We're not going anywhere," Dr. Farmer said. "Let's have the highest aspirations we can, and if we fail then just say we fail and keep on trying."

http://www.eurekalert.org/pub_releases/2015-04/uops-oto041015.php

One type of airway cell can regenerate another lung cell type
Findings from animal study have implications for disorders such as chronic obstructive pulmonary disease

PHILADELPHIA - A new collaborative study describes a way that lung tissue can regenerate after injury. The team found that lung tissue has more dexterity in repairing tissue than once thought. Researchers from the Perelman School of Medicine at the University of Pennsylvania and Duke University, including co-senior authors Jon Epstein, MD, chair of the department of Cell and Developmental Biology, and Brigid L.M Hogan, Duke Medicine, along with co-first authors Rajan Jain, MD, a cardiologist and instructor in the Department of Medicine and Christina E. Barkauskas, also from Duke, report their findings in *Nature Communications*

"It's as if the lung cells can regenerate from one another as needed to repair missing tissue, suggesting that there is much more flexibility in the system than we have previously appreciated," says Epstein. "These aren't classic stem cells that we see regenerating the lung. They are mature lung cells that awaken in response to injury. We want to learn how the lung regenerates so that we can stimulate the process in situations where it is insufficient, such as in patients with COPD [chronic obstructive pulmonary disease]."

The two types of airway cells in the alveoli, the gas-exchanging part of the lung, have very different functions, but can morph into each other under the right circumstances, the investigators found. Long, thin Type 1 cells are where gases (oxygen and carbon dioxide) are exchanged - the actual breath. Type 2 cells secrete surfactant, a soapy substance that helps keep airways open. In fact, premature babies need to be treated with surfactant to help them breathe.

The team showed in mouse models that these two types of cells originate from a common precursor stem cell in the embryo. Next, the team used other mouse models in which part of the lung was removed and single cell culture to study the plasticity of cell types during lung regrowth. The team showed that Type 1 cells can give rise to Type 2 cells, and vice-versa.

The Duke team had previously established that Type 2 cells produce surfactant and function as progenitors in adult mice, demonstrating differentiation into gas-exchanging Type 1 cells. The ability of Type I cells to give rise to alternate lineages had not been previously reported.

"We decided to test that hypothesis about Type 1 cells," says Jain. "We found that Type 1 cells give rise to the Type 2 cells over about three weeks in various models of regeneration. We saw new cells growing back into these new areas of the lung. It's as if the lung knows it has to grow back and can call into action some Type 1 cells to help in that process."

This is one of the first studies to show that a specialized cell type that was thought to be at the end of its ability to differentiate can revert to an earlier state under the right conditions. In this case, it was not by using a special formula of transcription factors, but by inducing damage to tell the body to repair itself and that it needs new cells of a certain type to do that.

The team is also applying the approaches outlined in this paper to cells in the intestine and skin to study basic ideas of stem cell maintenance and differentiation to relate back to similar mechanisms in the heart. They also hope to apply this knowledge to such other lung conditions as acute respiratory distress syndrome and idiopathic pulmonary fibrosis, where the alveoli cannot get enough oxygen into the blood. "We want to know if we can, and how, to make new lung cells as work-arounds for diseased alveoli cells," says Jain.

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http://www.eurekalert.org/pub_releases/2015-04/w-hvo040815.php

HPV vaccination of adolescent boys may be cost-effective for preventing oropharyngeal cancer

A new study indicates that vaccinating 12-year-old boys against the humanpapilloma virus (HPV) may be a cost-effective strategy for preventing oropharyngeal squamous cell cancer, a cancer that starts at the back of the throat and mouth, and involves the tonsils and base of the tongue. Published early online in *CANCER*, a peer-reviewed journal of the American Cancer Society, the study provides important information about HPV vaccination, which has proven effective against HPV-related disease in both sexes but remains controversial, especially in males.

Many western countries have established female HPV vaccination programs for preventing cervical cancer. Little is known about the cost-effectiveness of male-HPV vaccination, however. Donna Graham, MB, BCh, MRCPUK and Lillian Siu, MD, FRCPC, of the Princess Margaret Cancer Centre, University Health Network, in Toronto, led a team that compared the potential costs and effectiveness of vaccinating adolescent boys in Canada against HPV for preventing HPV-related oropharyngeal cancer. When the investigators applied a statistical model to a population of 192,940 Canadian boys who were 12 years old in 2012, they found that HPV vaccination could save from \$8 million to \$28 million Canadian dollars over the boys' lifetimes. Factors that could impact the cost savings of HPV vaccination in boys include, among others, vaccine cost, vaccine effectiveness, costs of cancer treatment, and survival of patients with HPV-related oropharyngeal cancers.

"We believe this study is important because HPV-related oropharyngeal cancer has increased significantly in incidence, especially in developed countries," said Dr. Graham. "It is projected that by 2020, HPV-related oropharyngeal cancer will become the most common HPV-related cancer in the US, surpassing cervical cancer."

Policy makers in many countries such as the United States, Canada, Austria, and Australia have recommended HPV vaccination in boys, but it is unfunded and is excluded from national immunization programs in many countries worldwide, notes Dr. Siu. "We hope that results from this study would raise awareness and lead to further assessment of this important public health issue," she said.