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Malaria drug protects fetuses from Zika infection

Treatment prevents virus from crossing placenta to infect fetus, mouse study shows

Devastating consequences of Zika virus infection are suffered in the womb, where the virus can cause brain damage and sometimes death.

Studying pregnant mice, researchers at Washington University School of Medicine in St. Louis have learned that the Zika virus infects the fetus by manipulating the body's normal barrier to infection. Moreover, they showed that a malaria drug that interferes with this process protects the fetus from viral infection. That drug already is approved for use in pregnant women for other medical purposes.

"We found that the malaria drug hydroxychloroquine effectively blocks viral transmission to the fetus," said senior author Indira Mysorekar, PhD, an associate professor of obstetrics and gynecology, and of pathology and immunology. "This drug already is used in pregnant women to treat malaria, and we suggest that it warrants evaluation in primates and women to diminish the risks of Zika infection and disease in developing fetuses." The findings are published July 10 in The Journal of Experimental Medicine.

In late 2015, doctors in Brazil began to notice a surge in the number of babies born with microcephaly, or unusually small heads, an indicator of neurological damage. The epidemic soon was linked to the mosquito-borne Zika virus, which was spreading through the tropical parts of the Americas. Doctors advised pregnant women to avoid mosquito bites by wearing bug spray and long-sleeved clothing, but had little other advice to offer. There were, and still are, no drugs or vaccines approved for use in pregnant women to protect them or their fetuses from Zika infection.

The developing fetus is uniquely vulnerable to damage from infection, so the body mobilizes robust defenses to keep microbes from ever reaching the fetus in the first place. The placenta is the last line of defense. Mysorekar and others have shown that a process known as autophagy -- the cellular waste-disposal pathway by which cells grind up debris, unwanted organelles and invading microbes - is an important part of the formidable placental barrier to infection. However, previous studies by Mysorekar and others have shown that Zika not only can invade the placenta, but multiply there.

To learn more about how Zika breaches the placenta, Mysorekar, postdoctoral fellow Bin Cao, PhD, and colleagues infected human placental cells with Zika virus. They found that exposure to the virus activated genes related to autophagy.

However, when the researchers treated the cells with drugs to ramp up the autophagy pathway, the number of cells infected with Zika virus increased. Drugs that suppressed autophagy resulted in fewer placental cells infected with Zika virus. In other words, the virus multiplied and spread more effectively when the researchers dialed up the barrier response, and performed more sluggishly when they dialed it down. The virus seemed to be doing a form of microbial martial arts, turning the body's weapons to its own advantage.

Mysorekar and colleagues verified these findings using mice whose autophagy response was hobbled by low levels of a key autophagy protein. They infected two groups of pregnant mice with Zika: one in which the autophagy process was disrupted and the other in which it worked normally.

Five days after infection, the mothers with a weak autophagy response had about the same amount of virus in their bloodstreams as the mice with a normal response. However, in mice with a weak autophagy response, the researchers found 10 times fewer viruses in the placenta and the heads of the fetuses and less damage to the placentas.

"It appears that Zika virus takes advantage of the autophagy process in the placenta to promote its survival and infection of placental cells," Cao said.

Since hydroxychloroquine suppresses the autophagy response, the researchers questioned whether it also could protect fetuses against Zika.

To find out, they repeated the mouse experiment using only mice with a normal autophagy response. Female mice at day nine of pregnancy were infected with Zika and then dosed with hydroxychloroquine or placebo every day for the next five days.

Following treatment, the researchers found significantly less virus in the fetuses and placentas from the mice that had received hydroxychloroquine. In addition, these placentas showed less damage and the fetuses regained normal growth. Both the untreated and the treated mothers had about the same amount of Zika virus in their bloodstreams, indicating that hydroxychloroquine was able to protect fetuses even when the virus was circulating through the mother.

Although hydroxychloroquine has been used safely in pregnant women for short periods of time, the researchers caution that further studies are needed before it can be used in pregnant women to fend off Zika. Pregnant women living in areas where Zika circulates may need to take the drug for the duration of their pregnancies, and the safety of hydroxychloroquine for long-term use is unknown.

"We would urge caution but nevertheless feel our study provides new avenues for feasible therapeutic interventions," said Mysorekar, who is also co-director of the university's Center for Reproductive Health Sciences. "Our study suggests that an autophagy-based therapeutic intervention against Zika may be warranted in pregnant women infected with Zika virus."

http://bit.ly/2vkAFon

Study clears way to growing replacement body organs

A discovery involving Monash University scientists promises to pave the way to producing replacement organs for damaged hearts, kidneys and bowels, using patients' own stem cells.

The research, pioneered by a team of scientists led by the Director of the Australian Regenerative Medicine Institute at Monash University, Professor Peter Currie, could overcome the severe shortage of donor organs for transplants.

The scientists focused on the zebrafish, a small, fast-growing tropical fish native to Southeast Asia, which is used widely as a model for human biology. They found that a protein called Meox1, active in stem cells, is central to directing muscle growth. The ground-breaking results have been published in the latest edition of the prestigious journal, Cell Stem Cell.

Scientists world-wide have long been growing miniature organs in petri dishes, using them to better understand disease and natural self-repair mechanisms in the body, and for drug testing. Monash University has been at the forefront of these fields.

"But, we have known almost nothing about how organs grow in the living animal – the cellular basis of how stem cells make all that tissue," Professor Currie said. "If we're ever going to grow complete organs in the laboratory or directly in a patient's body, we have to know how to grow them properly.

"My lab is exploring one of last frontiers of developmental biology – how organ growth is regulated by stem cells. "Prior to our work in this field, we didn't even know that these growth-specific stem cells existed or how they were used. Just knowing that they exist leads us to the possibility of orchestrating them, controlling them, or reactivating them to regrow damaged tissue."

Professor Currie said while the stem cell discovery represented a significant advance in knowledge, the timeline for producing replacement organs in the laboratory remained unknown, though closer now to science fact than fiction.

More information: Phong Dang Nguyen et al. Muscle Stem Cells Undergo Extensive Clonal Drift during Tissue Growth via Meox1-Mediated Induction of G2 Cell-Cycle Arrest, Cell Stem Cell (2017). DOI: 10.1016/j.stem.2017.06.003

http://bit.ly/2vkPVlu

Hidden herpes virus may play key role in MS, other brain disorders

The ubiquitous human herpesvirus 6 (HHV-6) may play a critical role in impeding the brain's ability to repair itself in diseases like multiple sclerosis.

The findings, which appear in the journal Scientific Reports, may help explain the differences in severity in symptoms that many people with the disease experience.

"While latent HHV-6 -- which can be found in cells throughout the brain -- has been associated with demyelinating disorders like multiple sclerosis it has not been clear what role, if any, it plays in these diseases," said Margot Mayer-Proschel, Ph.D., an associate professor at the University of Rochester Medical Center Department of Biomedical Genetics and co-author of the study. "These findings show that, while in the process of hiding from the immune system, the virus produces a protein that has the potential to impair the normal ability of cells in the brain to repair damaged myelin."

It is estimated that more than 80 percent of people have been exposed to HHV6 at some point during their early childhood. HHV-6 is the most common human herpesvirus and infections that occur during childhood often go unnoticed but the virus can cause roseola, which is characterized by a fever and rash in infants. A much smaller number -- one percent of people -have congenital HHV6 where a single copy of the virus is acquired through either the father's sperm or mother's egg and is passed on to the developing child.

While the immune system fights off the most active forms of the infection, the virus never truly leaves our bodies and can reactivate later in life. The herpesvirus 6 accomplishes this form of latency by integrating itself into our genetic code and thus hiding in cells and evading the immune system.

One of the first studies to show an association between latent HHV-6 infection and demyelinating disorders was conducted in 2003 by URMC researchers David Mock, M.D., who is a co-author of the current study, Andrew Goodman, M.D. and others. They noted that HHV6 genetic code could be found in the brain cells of individuals with severe forms of multiple sclerosis.

Viruses have long been suspected to contribute to multiple sclerosis, a disorder in which the body's own immune system attacks and destroys myelin -- the fatty tissue that insulates the connections between nerve cells. However, while the 2003 study indicated that the herpes virus played some role in multiple sclerosis, it has subsequently become clear that the virus is unlikely to trigger the disease.

The Rochester researchers in the current paper took a new approach and asked instead whether the virus could have an impact on a critical support cell found in the brain called oligodendrocyte progenitor cells (OPCs). These cells play an important role in maintaining the brain's supply of myelin. When myelin is lost to disease, age, or injury, OPCs are activated, migrate to where they are needed, and mature into myelin-producing cells which repair the damage.

The researchers examined the impact of the latent HHV-6 on the activity of human OPCs, which was possible through the work of Chris Proschel, a co-author of the manuscript with expertise in the generation of human OPCs. One of the ways the virus stays hidden in cells is by expressing a protein called U94 that helps it keep its place in the human DNA and remain undetected from the immune system. By studying human cells and transplanting human OPCs into animal models, the team discovered that when U94 was expressed in OPCs, the cells stopped migrating to where they were needed.

What is still not fully understood is the relationship between the extent of the viral infection in the brain and the severity of diseases like multiple sclerosis and other demyelinating diseases such as leukodystrophies and Vanishing White Matter disease. For example, do the number of infected cells need to reach a certain threshold before OPC function is impeded? Are individuals who have congenital HHV6 more vulnerable to severe forms of these diseases?

"More research is needed to understand by which mechanisms the virus impedes the function of OPCs and what impact this has on the progression of these diseases," said Mayer-Proschel. "But it is clear that HHV6, while not necessarily the cause of demyelinating diseases, is limiting the ability of the brain to repair damage to myelin thereby potentially accelerating the progression of these diseases."

Additional authors of the study include Andrew Campbell, Jessica Hogestyn and Brittany Lopez with URMC and Christopher Folts with Harvard Medical School. The study was supported with funding from National Multiple Sclerosis Society, the New York State Department of Health, and the Link Foundation.

http://bit.ly/2taFFzF

Sleep, Alzheimer's link explained

Poor sleep leads to increase in Alzheimer's proteins associated with cognitive decline

A good night's sleep refreshes body and mind, but a poor night's sleep can do just the opposite. A study from Washington University School of Medicine in St. Louis, Radboud University Medical Centre in the Netherlands, and Stanford University has shown that disrupting just one night of sleep in healthy, middle-aged adults causes an increase in amyloid beta, a brain protein associated with Alzheimer's disease. And a week of tossing and turning leads to an increase in another brain protein, tau, which has been linked to brain damage in Alzheimer's and other neurological diseases.

"We showed that poor sleep is associated with higher levels of two Alzheimer's-associated proteins," said David M. Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor, head of the Department of Neurology and the study's senior author. "We think that perhaps chronic poor sleep during middle age may increase the risk of Alzheimer's later in life." These findings, published July 10 in the journal Brain, may help explain why poor sleep has been associated with the development of dementias such as Alzheimer's.

More than 5 million Americans are living with Alzheimer's disease, which is characterized by gradual memory loss and cognitive decline. The brains of people with Alzheimer's are dotted with plaques of amyloid beta protein and tangles of tau protein, which together cause brain tissue to atrophy and die. There are no therapies that have been proven to prevent, slow or reverse the course of the disease.

Previous studies by Holtzman, co-first author Yo-El Ju, MD, an assistant professor of neurology, and others have shown that poor sleep increases the risk of cognitive problems. People with sleep apnea, for example, a condition in which people repeatedly stop breathing at night, are at risk for developing mild cognitive impairment an average of 10 years earlier than people without the sleep disorder. Mild cognitive impairment is an early warning sign for Alzheimer's disease.

But it wasn't clear how poor sleep damages the brain. To find out, the researchers -- Holtzman; Ju; co-first author and graduate student Sharon Ooms of Radboud; Jurgen Claassen, MD, PhD, of Radboud; Emmanuel Mignot, MD, PhD, of Stanford; and colleagues -- studied 17 healthy adults ages 35 to 65 with no sleep problems or cognitive impairments. Each participant wore an activity monitor on the wrist for up to two weeks that measured how much time they spent sleeping each night.

After five or more successive nights of wearing the monitor, each participant came to the School of Medicine to spend a night in a specially designed sleep room. The room is dark, soundproof, climate-controlled and just big enough for one; a perfect place for sleeping, even as the participants wore headphones over the ears and electrodes on the scalp to monitor brain waves.

Half the participants were randomly assigned to have their sleep disrupted during the night they spent in the sleep room. Every time their brain signals settled into the slow-wave pattern characteristic of deep, dreamless sleep, the researchers sent a series of beeps through the headphones, gradually getting louder, until the participants' slow-wave patterns dissipated and they entered shallower sleep.

The next morning, the participants who had been beeped out of slow-wave sleep reported feeling tired and unrefreshed, even though they had slept just as long as usual and rarely recalled being awakened during the night. Each underwent a spinal tap so the researchers could measure the levels of amyloid beta and tau in the fluid surrounding the brain and spinal cord.

A month or more later, the process was repeated, except that those who had their sleep disrupted the first time were allowed to sleep

through the night undisturbed, and those who had slept uninterrupted the first time were disturbed by beeps when they began to enter slow-wave sleep.

The researchers compared each participant's amyloid beta and tau levels after the disrupted night to the levels after the uninterrupted night, and found a 10 percent increase in amyloid beta levels after a single night of interrupted sleep, but no corresponding increase in tau levels. However, participants whose activity monitors showed they had slept poorly at home for the week before the spinal tap showed a spike in levels of tau.

"We were not surprised to find that tau levels didn't budge after just one night of disrupted sleep while amyloid levels did, because amyloid levels normally change more quickly than tau levels," Ju said. "But we could see, when the participants had several bad nights in a row at home, that their tau levels had risen."

Slow-wave sleep is the deep sleep that people need to wake up feeling rested. Sleep apnea disrupts slow-wave sleep, so people with the disorder often wake up feeling unrefreshed, even after a full eight hours of shut-eye. Slow-wave sleep is also the time when neurons rest and the brain clears away the molecular byproducts of mental activity that accumulate during the day, when the brain is busily thinking and working.

Ju thinks it is unlikely that a single night or even a week of poor sleep, miserable though it may be, has much effect on overall risk of developing Alzheimer's disease. Amyloid beta and tau levels probably go back down the next time the person has a good night's sleep, she said.

"The main concern is people who have chronic sleep problems," Ju said. "I think that may lead to chronically elevated amyloid levels, which animal studies have shown lead to increased risk of amyloid plaques and Alzheimer's."

Ju emphasized that her study was not designed to determine whether sleeping more or sleeping better reduce risk of Alzheimer's but, she said, neither can hurt.

"Many, many Americans are chronically sleep-deprived, and it negatively affects their health in many ways," Ju said. "At this point, we can't say whether improving sleep will reduce your risk of developing Alzheimer's. All we can really say is that bad sleep increases levels of some proteins that are associated with Alzheimer's disease. But a good night's sleep is something you want to be striving for anyway."

http://bit.ly/2uZSdH2

Drinking coffee reduces risk of death from all causes, study finds

People who drink around three cups of coffee a day may live longer than non-coffee drinkers, a landmark study has found.

The findings come from the largest study of its kind, in which scientists analysed data from more than half a million people across 10 European countries, including the UK, to explore the effect of coffee consumption on risk of mortality.

Researchers from the International Agency for Research on Cancer (IARC) and Imperial College London found that higher levels of coffee consumption were associated with a reduced risk of death from all causes, particularly from circulatory diseases and diseases related to the digestive tract.

Coffee is one of the world's most commonly consumed beverages, with an estimated 2.25 billion cups drank around the world each day. It contains a number of compounds which can interact with the body, including caffeine, diterpenes and antioxidants, and the ratios of these compounds can be affected by the variety of methods used to prepare coffee.

Previous studies looking for a link between coffee consumption and health outcomes have revealed conflicting results, however, large

studies in both the US and Japan have since revealed a potential beneficial effect of drinking coffee on risk of death from all causes.

In the latest study, published in the journal Annals of Internal Medicine, researchers have carried out the largest analysis of the effects of coffee-drinking in a European population - where coffee consumption and preparation methods vary, from an espresso in Italy, to a cappuccino in the UK - finding a similar association between consumption and mortality.

"We found that higher coffee consumption was associated with a lower risk of death from any cause, and specifically for circulatory diseases, and digestive diseases," said lead author Dr Marc Gunter of the IARC and formerly at Imperial's School of Public Health. "Importantly, these results were similar across all of the 10 European countries, with variable coffee drinking habits and customs. Our study also offers important insights into the possible mechanisms for the beneficial health effects of coffee."

Using data from the EPIC study (European Prospective Investigation into Cancer and Nutrition), the group analysed data from 521,330 people from over the age of 35 from 10 EU countries, including the UK, France, Denmark and Italy. People's diets were assessed using questionnaires and interviews, with the highest level of coffee consumption (by volume) reported in Denmark (900 mL per day) and lowest in Italy (approximately 92 mL per day). Those who drank more coffee were also more likely to be younger, to be smokers, drinkers, eat more meat and less fruit and veg.

After 16 years of follow up, almost 42,000 people in the study had died from a range of conditions including cancer, circulatory diseases, heart failure and stroke.

Following careful statistical adjustments for lifestyle factors such as diet and smoking, the researchers found that the group with the highest consumption of coffee had a lower risk for all-causes of death, compared to those who did not drink coffee. They found that decaffeinated coffee had a similar effect. However, consumption of caffeinated and decaffeinated coffee is not simple to separate, as they could not exclude that decaffeinated coffee drinkers may have been consuming caffeinated coffee as well in different periods of their life.

In a subset of 14,000 people, they also analysed metabolic biomarkers, and found that coffee drinkers may have healthier livers overall and better glucose control than non-coffee drinkers.

"We found that drinking more coffee was associated with a more favourable liver function profile and immune response," explained Dr Gunter. "This, along with the consistency of the results with other studies in the U.S. and Japan gives us greater confidence that coffee may have beneficial health effects."

According to the group, more research is needed to find out which of the compounds in coffee may be giving a protective effect or potentially benefiting health. Other avenues of research to explore could include intervention studies, looking at the effect of coffee drinking on health outcomes.

Professor Elio Riboli, head of the School of Public Health at Imperial, who established the EPIC study, said: "These findings add to a growing body of evidence which indicates that drinking coffee not only is safe, but it may actually have a protective health effect for people. While further research is needed, we can be confident that the results from a large European study confirm previous findings seen around the world."

Dr Gunter added: "Due to the limitations of observational research, we are not at the stage of recommending people to drink more or less coffee. That said, our results suggest that moderate coffee drinking - up to around three cups per day - is not detrimental to your health, and that incorporating coffee into your diet could have health benefits."

The study was funded by the European Commission Directorate General for Health and Consumers and the IARC.

1. 'Coffee drinking and mortality in 10 European countries' by Gunter, M.J. et al, is published in the journal Annals of Internal Medicine.

2. Information specifically on caffeinated and decaffeinated coffee drinking was collected from participants in Germany, Greece, Italy, the Netherlands and the United Kingdom.

http://bit.ly/2uhKl6f

Stem cell-based therapy for targeting skin-to-brain cancer

Stem cells loaded with oncolytic viruses show promising results in preclinical models for targeting skin cancer metastases in the brain

Investigators from Brigham and Women's Hospital (BWH) and the Harvard Stem Cell Institute have a potential solution for how to kill tumor cells that have metastasized to the brain. The team has developed cancer-killing viruses that can deliver stem cells via the carotid artery, and applied them to metastatic tumors in the brain of clinically relevant mouse models. The investigators report the elimination of metastatic skin cancer cells from the brain of these preclinical models, resulting in prolonged survival. The study, published online this week in the journal PNAS, also describes a strategy of combining this therapy with immune check point inhibitors.

"Metastatic brain tumors - often from lung, breast or skin cancers - are the most commonly observed tumors within the brain and account for about 40 percent of advanced melanoma metastases. Current therapeutic options for such patients are limited, particularly when there are many metastases," says Khalid Shah, MS, PhD, director of the Center for Stem Cell Therapeutics and Imaging (CSTI) in the BWH Department of Neurosurgery, who led the study. "Our results are the first to provide insight into ways of targeting multiple brain metastatic deposits with stem-cell-loaded oncolytic viruses that specifically kill dividing tumor cells."

In their search for novel, tumor-specific therapies that could target multiple brain metastases without damaging adjacent tissues, the research team first developed different BRAF wild type and mutant mouse models that more closely mimic what is seen in patients. They found that injecting patient-derived, brain-seeking melanoma cells into the carotid artery of these preclinical models resulted in the formation of many metastatic tumors throughout the brain, mimicking what is seen in advanced melanoma cancer patients. The injected cells express markers that allow them to enter the brain and are labelled with bioluminescent and fluorescent markers to enable tracking by imaging technologies.

To devise a potential new therapy, the investigators engineered a population of bone marrow derived mesenchymal stem cells loaded with oncolytic herpes simplex virus (oHSV), which specifically kills dividing cancer cells while sparing normal cells. Previous research by Shah and his colleagues shows that different stem cell types are naturally attracted toward tumors in the brain. After first verifying that stem cells injected to the brain would travel to multiple metastatic sites and not to tumor-free areas in their model, the team injected stem cells loaded with oHSV into the carotid artery of metastasis-bearing mice.. Injecting the stem cells loaded with oHSV into the carotid artery, a likely strategy for clinical application, led to significantly slower tumor growth and increased survival, compared with the models that received unaltered stem cells or control injections. The oHSV loaded stem cells are ultimately killed by oHSV mediated oncolysis, preventing the engineered cells from persisting within the brain, which is an important safety component in the therapeutic use of these stem cells.

Due to an increasing body of evidence which suggests that the host immune response may be critical to the efficacy of oncolytic virotherapy, Shah and his colleagues also developed an immunocompetent melanoma mouse model and explored treating with both stem cell loaded oHSV and immune checkpoint blockers such as the ones that target the PD-1/PD-L1 pathway. They found that PD-L1 immune checkpoint blockade significantly improved the therapeutic efficacy of stem cell based oncolytic virotherapy in melanoma brain metastasis.

"We are currently developing similar animal models of brain metastasis from other cancer types as well as new oncolytic viruses that have the ability to specifically kill a wide variety of resistant tumor cells," said Shah, who is also a professor at Harvard Medical

School and a principal faculty member at the Harvard Stem Cell Institute. "We are hopeful that our findings will overcome problems associated with current clinical procedures. This work will have direct implications for designing clinical trials using oncolytic viruses for metastatic tumors in the brain."

The study was supported by grants from the Department of Defense Idea Award (CA138922) and National Institutes of Health (RO1 CA204720).

http://bbc.in/2umwqvk

Fossil sheds light on bird evolution after asteroid strike

The fossil of a tiny bird that lived 62 million years ago confirms that birds evolved very rapidly after the asteroid strike that wiped out the dinosaurs.

By Helen Briggs BBC News

The sparrow-sized tree-dweller lived "just a geological blink of an eye" after the mass extinction. Bird fossils from that time period are very rare.

Artist's impression of Tsidiiyazhi abini **Sean Murtha**

Analysis suggests the ancestors of most modern birds, from owls to woodpeckers, had taken to the wing within four million years of the asteroid strike. Like mammals, the birds that survived the extinction were able to expand and diversify to become one of the most successful animal groups on Earth.

Analysis of the fossil and its relationship to other members of the bird family tree suggests as many as 10 major bird groups had appeared within four million years of the extinction.

Dr Daniel Ksepka, curator of science at Bruce Museum in Greenwich, Connecticut, said Tsidiiyazhi abini was a very special little bird for several reasons. "It is very old, very small, and had zany little feet," he explained. "The age is between 62.2 and 62.5 million years, just a geological blink of the eye after the asteroid impact that wiped out the dinosaurs."

DNA evidence suggests birds recovered rapidly from the extinction event 66 million years ago that wiped out most animals on land, including flying reptiles, dinosaurs and primitive birds.

The origins of modern birds can be traced back to this time. However, bird fossils from this era in geological history are very rare because their bones are so small and delicate.

This has made it difficult to resolve how modern birds arose and diversified, leading to some controversy. The discovery of Tsidiiyazhi abini, an ancient species of mousebird, is a new source of evidence.

"When we place the bird in the evolutionary tree, it reveals that other closely related groups must have also split off by then because they occupy lower branches," Dr Ksepka told the BBC.

"So this discovery shows not only mousebirds but things like owls, raptors, the Coraciimorphae (a group that includes birds like kingfishers and woodpeckers) and many other groups were all showing up just a short time after the asteroid impact that wiped out the dinosaurs." Tsidiiyazhi abini, or "little morning bird" was found in 62.5-million-year-old rocks in the Nacimiento Formation of New Mexico.

Dr Thomas Williamson was on a fossil hunting trip with his twin sons, when the birds' bones came to light. "They discovered an unusually rich site that had some skeletons of small mammals," the curator of Palaeontology at the New Mexico Museum of Natural History and Science explained. "Over the next several months, I collected some bulk samples from the site and within these I discovered the bones of a small bird."

He said the new birds were close to modern mousebirds (Coliiformes), a group now found only in Africa, but which was geographically more widespread in the Palaeogene [from 66 million years ago to 23 million years ago]. The bird was able to flip the fourth toe on its foot to face backwards - something that is useful for climbing and grasping. This feature is also seen in other birds, such as modern owls.

Tsidiiyazhi lived at a time when the planet was undergoing great change, with placental mammals and flowering plants also diversifying rapidly. The bird lived in forests and dined on fruits and seeds from flowering plants. Today, there are more than 10,000 living species of bird. The research is published in the journal PNAS.

http://bbc.in/2sYlBw8

First vaccine shows gonorrhoea protection

A vaccine has for the first time been shown to protect against the sexually transmitted infection gonorrhoea, scientists in New Zealand say.

By James Gallagher Health and science reporter, BBC News website

There are fears gonorrhoea is becoming untreatable as antibiotics fail.

The World Health Organization sees developing a vaccine as vital in stopping the global spread of "super-gonorrhoea".

The study of 15,000 young people, published in the Lancet, showed infections were cut by about a third.

About 78 million people pick up the sexually transmitted infection each year, and it can cause infertility. But the body does not build up resistance no matter how many times someone is infected.

Unusual start

The vaccine, originally developed to stop an outbreak of meningitis B, was given to about a million adolescents in New Zealand between 2004 and 2006.

Researchers at the University of Auckland analysed data from sexual health clinics and found gonorrhoea cases had fallen 31% in those vaccinated.

The bacterium that causes meningitis, *Neisseria meningitidis*, is a very close relative of the species that causes gonorrhoea - *Neisseria gonorrhoeae*. It appears the Men B jab was giving "cross-protection" against gonorrhoea.

Dr Helen Petousis-Harris, one of the researchers, said: "This is the first time a vaccine has shown any protection against gonorrhoea.

"At the moment, the mechanism behind this immune response is unknown, but our findings could inform future vaccine development."

Protection seemed to last about two years.

What is gonorrhoea?

The disease is caused by the bacterium Neisseria gonorrhoeae and spread by unprotected sex.

Symptoms can include a thick green or yellow discharge from sexual organs, pain when urinating and bleeding between periods.

However, of those infected, about one in 10 heterosexual men and more than three-quarters of women and gay men have no easily recognisable symptoms.

Untreated infection can lead to infertility, pelvic inflammatory disease and be passed on to a child during pregnancy.

However, the vaccine in question - known as MeNZB - is no longer available. Many of its components are also in a new Men B jab - called 4CMenB. The UK is the only country in the world to be rolling 4CMenB out as a routine childhood immunisation.

Fellow researcher Prof Steven Black, from Cincinnati Children's Hospital in the US, said: "The potential ability of a group B meningococcal vaccine to provide even moderate protection against gonorrhoea would have substantial public health benefits."

The importance of preventing people developing a gonorrhoea infection is of mounting importance as the infection is getting much harder to treat.

Last week, the World Health Organization warned about the global spread of gonorrhoea that could not be treated with antibiotics.

Dr Teodora Wi, from the WHO, said there had even been three cases - in Japan, France and Spain - where the infection was completely untreatable.

She said: "There are high hopes that now there's going to be some cross-protection. "We are still a long way before we develop a vaccine for gonorrhoea, but we have now some evidence that it is possible."

http://bit.ly/2vnSLGk

Immune system may keep body from neutralizing HIV-1 virus

Findings could help develop a vaccine for the virus that causes AIDS

AURORA, Colo. - Researchers at the University of Colorado Anschutz Medical Campus have discovered that a process protecting the body from autoimmune disease appears to prevent it from creating antibodies that can neutralize the HIV-1 virus, a finding that could possibly help lead to a vaccine that stimulates production of these antibodies.

The study, led by Raul M. Torres, PhD, professor of immunology and microbiology at the University of Colorado School of Medicine, was published Tuesday in The Journal of Experimental Medicine.

Torres and his team sought to better understand how the body's own immune system might be getting in the way of neutralizing the HIV-1 virus.

They knew that some patients infected with HIV-1 developed what are known as 'broadly neutralizing antibodies,' or bnAbs, that can protect against a wide variety of HIV-1 strains by recognizing a protein on the surface of the virus called Env. But the patients only develop these antibodies after many years of infection.

Because of shared features found in a number of HIV-1 bnAbs, researchers suspected the inability or delayed ability to make these type of protective antibodies against HIV was due to the immune system suppressing production of the antibodies to prevent the body from creating self-reactive antibodies that could cause autoimmune diseases like systemic lupus erythematosus.

At the same time, patients with lupus showed slower rates of HIV-1 infection. Scientists believe that's because these autoimmune patients produce self-reactive antibodies that recognize and neutralize HIV-1.

The process by which the body prevents the creation of antibodies that can cause autoimmune disease is known as immunological tolerance. Torres wanted to break through that tolerance and stimulate the production of antibodies that could neutralize HIV-1.

"We wanted to see if people could make a protective response to HIV-1 without the normal restraint imposed by the immune system to prevent autoimmunity," Torres said.

The researchers first tested mice with genetic defects that caused lupus-like symptoms. They found that many of them produced antibodies that could neutralize HIV-1 after being injected with alum, a chemical that promotes antibody secretion and is often used in vaccinations.

Next, they treated normal mice with a drug that impairs immunological tolerance and found that they began producing antibodies capable of neutralizing HIV-1. The production of these antibodies was increased by alum injections. And if the mice were also injected with the HIV-1 protein Env, they produced potent broadly neutralizing antibodies capable of neutralizing a range of HIV-1 strains.

In every case, the production of these HIV-neutralizing antibodies correlated with the levels of a self-reactive antibody that recognizes a chromosomal protein called Histone H2A. The researchers confirmed these antibodies could neutralize HIV-1.

"We think this may reflect an example of molecular mimicry where the virus has evolved to mimic or look like a self protein," Torres said.

Torres suggested that the difficulty in developing a vaccine against HIV-1 may be because of the ability of the virus to camouflage itself as a normal part of the body.

"But breaching peripheral immunological tolerance permits the production of cross-reactive antibodies able to neutralize HIV-1," Torres said.

Since the research was done on animals, scientists must still determine its relevance for HIV-1 immunity in humans.

"The primary consideration will be determining whether immunological tolerance can be temporarily relaxed without leading

to detrimental autoimmune manifestations and as a means to possibly elicit HIV-1 bnAbs with vaccination," he said.

http://bit.ly/2un2rE9

Meningitis Vaccine May Protect Against Gonorrhea

Individuals who received a meningitis B vaccine were less likely to have contracted the sexually transmitted infection than their unvaccinated counterparts.

By Diana Kwon | July 11, 2017

As rates of antibiotic resistant gonorrhea rise around the world, scientists are scrambling for solutions. A study, published yesterday (July 10) in *The Lancet*, reveals a potential new strategy to prevent the disease: vaccination.

In the mid-2000s, researchers in New Zealand developed a vaccine, MeNZB, to fight an outbreak of meningitis type B. This vaccine was "more broadly effective than expected," study coauthor Helen Petousis-Harris, a vaccinology researcher at the University of Auckland, writes in *The Conversation*. "One of the observations was that gonorrhea rates appeared to decline immediately following the use of both the MeNZB vaccine and similar vaccines in Cuba, and to a lesser extent in Norway."

To further investigate the link between MeNZB and gonorrhea, Petousis-Harris and colleagues assessed 14,730 cases of 15- to 30-year olds in New Zealand diagnosed with gonorrhea, chlamydia, or both. The researchers found that individuals vaccinated with MeNZB were significantly less likely to have contracted gonorrhea that those who were not.

The link is "quite probably real," Petousis-Harris tells *STAT News*. This association is also biologically plausible, because the bacterium that causes meningitis B, *Neisseria meningitides*, is related to *N. gonorrhoeae*, which causes gonorrhea.

"We are in desperate need for new therapies," Christine Johnston, an infectious disease specialist at the University of Washington in Seattle who was not involved in the study, told *Science News*. The new results are "the first to show that vaccination against gonorrhea could be possible," she adds.

http://bbc.in/2uw0Igl

Do you live in the world's laziest country?

US scientists have amassed "planetary-scale" data from people's smartphones to see how active we really are.

By James Gallagher Health and science reporter, BBC News website

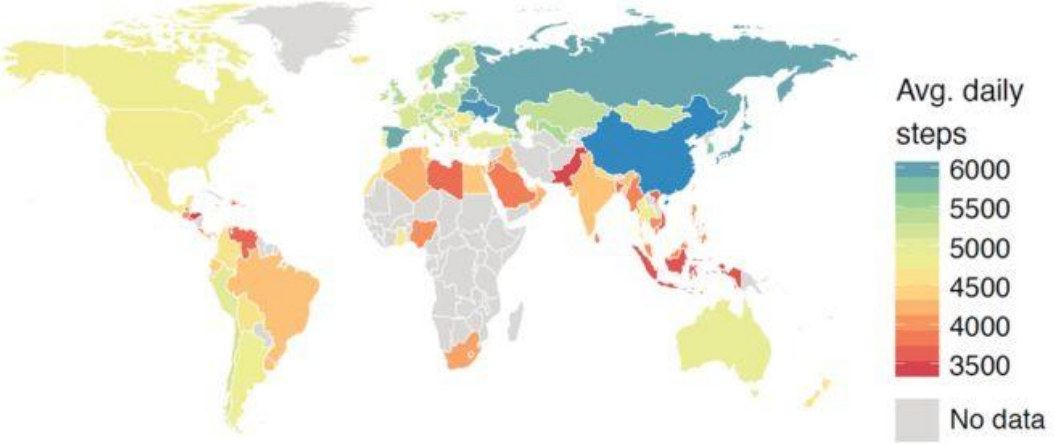
The Stanford University analysis of 68 million days' worth of minute-by-minute data showed the average number of daily steps was 4,961.

Hong Kong was top averaging 6,880 a day, while Indonesia was bottom of the rankings with just 3,513. But the findings also uncovered intriguing details that could help tackle obesity.

Most smartphones have a built-in accelerometer that can record steps and the researchers used anonymous data from more than 700,000 people who used the Argus activity monitoring app.

Scott Delp, a professor of bioengineering and one of the researchers, said: "The study is 1,000 times larger than any previous study on human movement. "There have been wonderful health surveys done, but our new study provides data from more countries, many more subjects, and tracks people's activity on an ongoing basis.

"This opens the door to new ways of doing science at a much larger scale than we have been able to do before."



Activity inequality

The findings have been published in the journal Nature and the study authors say the results give important insights for improving people's health. The average number of steps in a country appears to be less important for obesity levels, for example.

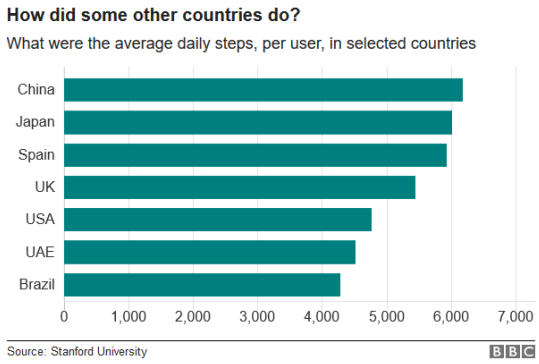
The key ingredient was "activity inequality" - it's like wealth inequality, except instead of the difference between rich and poor, it's the difference between the fittest and laziest. The bigger the activity inequality, the higher the rates of obesity.

Tim Althoff, one of the researchers, said: "For instance, Sweden had one of the smallest gaps between activity rich and activity poor... it also had one of the lowest rates of obesity."

The United States and Mexico both have similar average steps, but the US has higher activity inequality and obesity levels.

The researchers were surprised that activity inequality was largely driven by differences between men and women. In countries like Japan - with low obesity and low inequality - men and women exercised to similar degrees. But in countries with high inequality, like the US and Saudi Arabia, it was women spending less time being active.

Jure Leskovec, also part of the research team, said: "When activity inequality is greatest, women's activity is reduced much more dramatically than men's activity, and thus the negative connections to obesity can affect women more greatly."



The Stanford team say the findings help explain global patterns of obesity and give new ideas for tackling it. For example, they rated 69 US cities for how easy they were to get about on foot. The smartphone data showed that cities like New York and San Francisco were pedestrian friendly and had "high walkability". Whereas you really need a car to get around "low walkability" cities including Houston and Memphis.

Unsurprisingly, people walked more in places where it was easier to walk. The researchers say this could help design town and cities that promote greater physical activity.

Follow James on Twitter. **Reporter conflict of interest:** ***I made 10,590 steps yesterday but clocked up only 129 on Sunday, I left my phone on the kitchen table all day - that's my excuse and I'm sticking to it.***

http://bbc.in/2tfwttz

Lark or night owl? Blame your ancestors

Our ancestors could be to blame for the wide variety of human sleeping habits, from larks to night owls.

By Helen Briggs BBC News

Staggered sleeping patterns would have been an advantage in the distant past, when we lived in groups and needed someone to look out for wild beasts, say researchers.

Anthropologists monitored sleep in the Hadza people of Tanzania who still live a hunter-gatherer existence.

Over 20 days and nights, someone was awake for almost all of the time.

"Out of some 200 hours for the entire study, for only 18 minutes were they actually all sleeping synchronously," said lead researcher Dr David Samson of the University of Toronto, Canada.

"The median was eight individual adults who were alert at any given time throughout the night - so that's 40% of the entire adult population of these camps.

"So, it was pretty astounding how asynchronous the sleep was in this group."

Past research has shown that about 40% -70% of a person's circadian rhythm, or body clock, is genetic. The rest is influenced by environment and, interestingly, age.

When factors such as nursing status, temperature, wind, humidity and other factors that affect sleep were taken into account, age was one of

the drivers of the variation in sleep types, said Dr Samson, the lead researcher on the study.

"When you are younger, you're much more owlish, so you're much more inclined to have your peak activity later in the day than to be up earlier in the morning," he explained. "When you're older, you're much more larkish."

Grandmother hypothesis

The research adds a new dimension to the "grandmother hypothesis", he added. According to this idea, having older people living in a group had some sort of evolutionary advantage.

The researchers have come up with "the poorly sleeping grandparent hypothesis", which builds on this idea, he said.

Older people waking in the night or getting up early because they could not sleep may have helped all members of the group survive hundreds of thousands of years ago.

Animals living in social groups such as meerkats always have someone on guard during rest periods, a theory known as the sentinel hypothesis.

Anthropologists decided to test this theory in humans by studying the Hadza people in Tanzania, whose lifestyle has changed little in thousands of years.

The Hadza population live in camps of around 30 people and are hunter gatherers, eating game animals, birds, honey, berries and seeds. Anthropologists say their environment is similar to that in which all humans evolved.

Hadza volunteers were given "super fit bits" that plotted their sleep patterns. The scientists found that over 20 days and nights, there were only 18 minutes when no-one was awake in the group of about 20 adults.

Most sleep studies take place in sleep labs, making the research, published in Proceedings of the Royal Society of London B, somewhat novel.

http://bit.ly/2urrbKT

Anti-CRISPR proteins decrease off-target side effects of CRISPR-Cas9

Proteins adapted from viruses could be standard kill switch for CRISPR therapies

CRISPR-Cas9 gene editing is based on a tactic bacteria developed to protect themselves from viruses.

Research now shows that the countermeasure viruses came up with -- inhibitory proteins referred to as anti-CRISPRs -- can be used to improve CRISPR-Cas9 as a gene-therapy tool, decreasing off-target gene editing that could cause unwanted side effects.

In a study reported online this week in the journal Science Advances, researchers from UC Berkeley and UC San Francisco show that recently discovered anti-CRISPR proteins decrease off-target effects by as much as a factor of four, acting like a kill switch to disable CRISPR-Cas9 after it's done its job.

The study demonstrated that one particular anti-CRISPR protein called AcrIIA4 reduced by four-fold the off-target effects of a CRISPR-Cas9 molecule that uses a guide RNA to find, snip and replace the mutated hemoglobin gene responsible for sickle cell disease. It does this without significantly reducing the desired on-target gene-editing.

"Unexpected mutations can arise as a result of off-target gene editing, but our paper -- like many others -- shows that off-target effects can be modulated and it is not as serious as people might think," said UC Berkeley postdoctoral fellow Jiyung Jenny Shin, from the lab of Jacob Corn at the Innovative Genomics Institute and one of three first authors of the paper.

In her experiments on human cells in culture, Shin found that delivering CRISPR-Cas9 and then, several hours later, the anti-CRISPR protein, was the most effective way to reduce off-target effects. The protein mimics DNA, glomming onto Cas9, the enzyme

that actually cuts the double-stranded DNA, and preventing further cutting.

"Even after six hours of effective CRISPR, inserting anti-CRISPR decreases off-target effects by more than two-fold compared to on-target effects," Shin said. "Therapeutically, you could treat a patient with CRISPR first, and then treat with anti-CRISPR at a later time and decrease off-target effects."

The researcher who discovered AcrIIA4, Joseph Bondy-Denomy of UC San Francisco, foresees these anti-CRISPR proteins becoming a standard part of CRISPR gene therapy, given along with CRISPR-Cas9 to disable gene editing after a fixed period of time to prevent random off-target cutting.

"This Cas9 inhibitor could be encoded on the same piece of DNA as Cas9, for example, precisely timed to turn Cas9 off after the gene editing is done, instead of letting Cas9 linger in the cell and risk off-target effects," said Bondy-Denomy, who is also a co-author of the paper.

Anti-CRISPR binding

The team included researchers in the lab of Jennifer Doudna, one of the inventors of CRISPR-Cas9 gene editing, who determined how the anti-CRISPR protein binds to the CRISPR-Cas9 complex. Using cryo-electron microscopy, they found that anti-CRISPR essentially mimics DNA, tricking CRISPR-Cas9 into binding with it, and then never letting go.

The CRISPR inhibitor targets a spot on the Cas9 protein that is so essential for Cas9's function that it cannot operate to cut DNA when it's bound by the anti-CRISPR.

Last year, Bondy-Denomy reported finding four anti-CRISPR proteins used by attacking viruses to inactivate the version of the Cas9 protein found in the bacterium Listeria monocytogenes. Two of these also inhibited the Cas9 protein most commonly used by researchers, which is adapted from the bacterium Streptococcus pyogenes and is referred to as SpyCas9. Another team found three other anti-CRISPR proteins that work against a different but promising Cas9 protein adapted from the bacterium Neisseria meningitidis.

The current study looked at the effect of one of the proteins from Listeria, AcrIIA4, on SpyCas9 loaded with a guide RNA that homes in on complementary DNA to bind and cut.

Research at UC Berkeley and elsewhere suggests that CRISPR-Cas9 constantly feints with the cell's DNA repair system: as the enzyme cuts at its target site, the cell repairs the DNA, and CRISPR-Cas9 cuts again, repeating this vicious cycle until a mutation arises in the DNA that prevents enzyme binding, at which point the CRISPR-Cas9 molecule moves on to find another binding site.

The current work from the Corn and Doudna labs now suggests that adding an anti-CRISPR after Cas9 has successfully edited a target gene would prevent unintended damage to other portions of a genome.

"The ability to turn Cas9 gene editing off is just as important as the ability to turn it on," said Corn, scientific director for biomedicine of the IGI and a UC Berkeley assistant adjunct professor of molecular and cell biology. "Imagine if you had an electric razor with no off-switch! For eventual therapeutic applications, it is critical to be able to precisely control when and where gene editing is active. The anti-CRISPR proteins offer opportunities to completely turn off Cas9 as well as fine-tune its activity."

"Jenny's data suggests that there is an ideal time window for letting Cas9 do its job and then turning it off after that amount of time has passed," Bondy-Denomy said. "We can actually use the anti-CRISPR proteins as tools to figure out what that time window is, that is, for any one cell type with any one guide RNA sequence, how long we want Cas9 to be active in the cell."

Shin and postdoctoral fellows Fuguo Jiang and Jun-Jie Liu are the three first authors of the paper, which was also co-authored by Benjamin Rauch of UCSF and postdoc Nicolas Bray, researcher Seung Hyun Baik and professor Eva Nogales, in addition to Corn and Doudna, of IGI and UC Berkeley's Department of Molecular and Cell Biology. Doudna and Nogales are Howard Hughes Medical Institute investigators.

The work was supported in part by HHMI, the Li Ka Shing Foundation, the Heritage Medical Research Institute and the National Institute on Aging (T32 AG000266).

http://bit.ly/2tsHMd5

Spread of breast cancer reduced by targeting acid metabolite

Inhibiting 20-HETE, reduces size of breast cancer and its ability to spread to the lungs

AUGUSTA, Ga. - It's a metabolite found in essentially all our cells that, like so many things, cancer overexpresses. Now scientists have shown that when they inhibit 20-HETE, it reduces both the size of a breast cancer tumor and its ability to spread to the lungs.

"The drug is reducing the ability of cancer cells to create a distant microenvironment where they can thrive," said Dr. Ali S. Arbab, leader of the Tumor Angiogenesis Initiative at the Georgia Cancer Center and a professor in the Department of Biochemistry and Molecular Biology at the Medical College of Georgia at Augusta University.

Arbab notes that cancer cells are constantly doing test runs, sending cells out into the bloodstream to see if they will take hold. About 30 percent of patients with breast cancer experience spread, or metastasis, of the disease. The most common sites are the lymph nodes, liver, bones and brain, as well as the lungs.

For the preclinical studies by postdoctoral fellow, Dr. Thaiz F. Borin, published in the journal PLOS ONE, the scientists used the drug HET0016, a 20-HETE inhibitor developed to learn more about the metabolite's many functions.

While not ready to say that the drug has potential use in humans, Arbab says the work points toward a new and logical target for reducing tumor spread. He notes that there are already drugs out there, including some over-the-counter anti-inflammatory drugs, which may also inhibit this overexpressed and now destructive pathway.

20-HETE - 20-Hydroxyeicosatetraenoic acid - is a metabolite of arachidonic acid, a fatty acid we make and constantly use for a wide variety of functions like helping make lipids for our cell membranes. 20-HETE also has a wide range of normal functions, including helping regulate blood pressure and blood flow. It's also a known mediator of inflammation, which under healthy conditions can help us fight infection and protect us from cancer and other invaders.

"There is normal function and there is tumor-associated function," says Dr. B.R. Achyut, cancer biologist, assistant professor in the MCG Department of Biochemistry and Molecular Biology and a study coauthor. "Tumors highjack our system and use that molecule against us."

In fact, Arbab's research team has shown that the high production of 20-HETE that occurs in cancer becomes an unwitting provider of almost everything cancer needs to prepare a place to comfortably spread.

Scientists call it the "seed and soil" hypothesis. To spread, cancer cells must detach from the primary site, in this case breast tissue, get aggressive enough to survive travel, gather supporting tissue and blood vessels where they land, take seed and eventually colonize the distant site, in this case, the lungs.

Arbab and his team have shown 20-HETE appears to help prepare this distant site by activating things like protein kinases that can change the function of proteins, their location and what cells they associate with, as well as growth factors that can make cells grow in size, proliferate and differentiate.

It can even help make blood vessels, which a tumor will need once it reaches a certain size. 20-HETE also activates signaling kinases that enable cell division. It encourages inflammation-promoting factors like tumor necrosis factor alpha and several of the interleukins, another class of proteins that help regulate the immune response. In this scenario, they are turning up inflammation, which is a hallmark of cancer and other diseases.

"We are going after that tumor microenvironment," says Arbab.

For their studies, they put human breast cancer cells and mouse mammary tumor cells in the mammary fat pad of mice, waited for the

cancer to take hold and begin to spread, then intravenously gave mice HET0016 five days per week for three weeks.

They found HET0016 reduced the migration and invasion of tumor cells: 48 hours after the drug was given, cancer cells were less able to move about in small test tubes. The drug also reduced levels of metalloproteinases in the lungs, enzymes that can destroy existing protein structures, so that, in this case, cancer cells can penetrate the area and new blood vessels can grow.

It also reduced levels of other key inhabitants of a tumor microenvironment like growth factors as well as myeloid-derived suppressor cells that can help shield cancer from the immune system.

"It gets rid of one of the natural protections tumors use, and tumor growth in the lung goes down," Arbab notes.

He, Achyut and their colleague Dr. Meenu Jain, assistant research scientist, reported earlier this year in the journal Scientific Reports that the drug also reduced tumor growth and prolonged survival in an animal model of the highly lethal, rapidly growing and vascular brain tumor, glioblastoma.

That finding and related work got the scientists wondering if the research drug - or something similar - could one day help control the typically deadly spread of cancer.

Now they are looking at exosomes, traveling packages all cells send out as a way to communicate and swap substances. In the case of cancer cells, exosomes appear to be packed with items needed to build the supportive environment for their new distant location in the lungs or elsewhere. Once exosomes establish a niche, they send back a signal to the primary site for cancer cells to join them. The scientists want to further pursue the ability of HET0016 to block these cancer-derived packages.

20-HETE's co-opting by cancer has it emerging as a focal point for cancer treatment, says Arbab who has published more than half of the 20-HETE-related studies on the rapidly emerging topic.

The research was supported by the National Institutes of Health.

http://bit.ly/2v5FrqE

Tumor-targeting drug shows potential for treating bone cancer patients

Preclinical study shows BMTP-11 targets high-risk osteosarcoma

The treatment of osteosarcoma, the most common tumor of bone, is challenging. A study led by The University of Texas MD Anderson Cancer Center found a drug known as bone metastasis-targeting peptidomimetic (BMTP-11) has potential as a new therapeutic strategy for this devastating illness.

Results from the preclinical study, which looked at BMTP-11 alone and in combination with the chemotherapy agent gemcitabine, were published in the July 11, 2017, online issue of Proceedings of the National Academy of Sciences.

Although osteosarcoma is a relatively rare cancer, it is a leading disease-related cause of death in children and young adults ages 10 to 20. However, over the last 25 years, the five-year survival rate has remained unchanged, and the treatment options for these patients are few. In addition, the side effects of available treatment options often are significant and cumulative, and may cause other health problems and damage to major organs.

"What's novel about this treatment is that BMTP -11 targets the tumor and spares other organs," said Valerae O. Lewis, M.D., chair of Orthopaedic Oncology at MD Anderson. "We believe this study lays the groundwork for a clinical trial for the treatment of osteosarcoma without the cumulative and mortal side effects seen with the current treatment options."

The study results identified IL-11Rα as an osteosarcoma cell surface receptor that correlated with tumor progression and poor prognosis in osteosarcoma patients. The team, which included co-authors Renata Pasqualini, Ph.D., and Wadih Arap, M.D., Ph.D., both of whom worked on the study while at MD Anderson and are now professors at the University of New Mexico Health Sciences Center (UNMSC) School of Medicine, also illustrated that IL-11Rα and IL-11 are up-

regulated in human metastatic osteosarcoma cell lines, and this correlated with the development of lung metastases in mouse models of the disease. The metastatic potential of the osteosarcoma cell lines could be modulated by targeting IL-11Rα expression. Death from respiratory failure linked to metastasis to the lungs remains a significant problem among osteosarcoma patients.

"We were able to document anti-tumor activity against osteosarcoma models," said Pasqualini. "Given that a first-in-human trial of BMTP-11 has recently been reported, one would hope that this proof-of-concept study might lead to early translational clinical trials in human osteosarcoma as a logical next step in the context of an unmet medical oncology need."

Arap added that "this work provides a preclinical foundation for the potential design and development of a second line combination therapy regimen composed of conventional chemotherapeutics plus the targeted candidate drug BMTP-11 for application in unfortunate patients with recalcitrant osteosarcoma."

MD Anderson team participants included Eugenie Kleinerman, M.D., Pediatrics Research and Eswaran Devarajan, Ph.D., Orthopaedic Oncology Research. Other authors on the study include Marina Cardò-Vila, Ph.D., UNMSC; Dafydd G. Thomas, M.D., Ph.D., University of Michigan; Richard L. Sidman, M.D., Harvard Medical School; and Serena Marchiò, Ph.D., University of Torino.

BMTP-11 and associated intellectual property has been licensed by MD Anderson to Arrowhead Research Corporation (Pasadena, California). The study was funded by the Triumph Over Kid Cancer Foundation, the National Institutes of Health (P30CA016672 and P30CA118100) the Gillson-Longenbaugh Foundation and the Marcus Foundation.

http://bit.ly/2t4oOds

Mountain gorillas have herpes virus similar to that found in humans

Epstein Barr-like virus in gorillas may hold clues for conservation and human disease

Scientists from the University of California, Davis, have detected a herpes virus in wild mountain gorillas that is very similar to the Epstein-Barr virus in humans, according to a study published today in the journal Scientific Reports.

Epstein Barr virus, or EBV, infects more than 90 percent of the human population, typically without major health consequences or symptoms. It can be challenging, however, for people with HIV/AIDS and suppressed immune systems, leading to certain forms of cancer. The Epstein-Barr virus is also one of the major causes of mononucleosis, commonly called the "kissing disease."

The study found that the mountain gorillas, a critically endangered species, have their own version of this herpes virus - a specific strain of lymphocryptovirus 1, or GbbLCV-1.

Virus Widespread, But Few Symptoms

For the study, UC Davis researchers from Gorilla Doctors collected plants chewed by wild mountain gorillas in Rwanda and Uganda and analyzed the saliva left on the plants. This non-invasive, oral sampling technique showed that the virus is widespread, infecting 52 percent of infant gorillas studied. That is a similar rate to what is found in human infants in less developed countries.

The researchers say that the virus carries little health risk for otherwise healthy mountain gorillas and, like EBV, is typically dormant in their bodies. None of the live gorillas studied showed symptoms of having it.

However, the research team found that some infant gorillas who died of natural causes and were necropsied had "pulmonary reactive lymphoid hyperplasia," a condition seen in human infants and young children with HIV/AIDS who become infected with EBV.

The findings could provide valuable information for human disease and have conservation implications for the gorillas.

"Viruses can behave similarly in different species," said lead author Tierra Smiley Evans, a post-doctoral researcher with the UC Davis One Health Institute in the School of Veterinary Medicine. "Learning about how gorillas react to this virus in their natural setting may help us have a better understanding of how Epstein-Barr virus affects human infants."

Mountain gorillas are one of humans' closest genetic relatives. Among the great apes, they are among the most studied. Veterinarians from the Gorilla Doctors, a partnership between the UC Davis Wildlife Health Institute and the nonprofit Mountain Gorilla Veterinary Project, treat injured wild mountain gorillas and can continue to study this condition in the future.

Additional co-authoring institutions include the UC Davis Center for Comparative Medicine, One Health Approach for Conservation - Gorilla Health Rwanda, and the Rwanda Development Board in Kigali, Rwanda.

The study was funded by a William J. Fulbright Fellowship and the USAID Emerging Pandemic Threats PREDICT project.

http://bit.ly/2urYCgj

Nickel is crucial for the Earth's magnetic field

Scientists at TU Wien and Würzburg University are changing our idea of the earth's magnetic field: iron alone cannot explain the concept of the geodynamo. The crucial ingredient is nickel.

It only takes a simple compass to demonstrate that the earth has a magnetic field - but it is quite difficult to explain how exactly it is created. Without any doubt, our planet's hot core, consisting mainly of iron, plays an important part. In combination with the earth's rotation, it builds up a powerful "dynamo effect", which creates a magnetic field.

But with iron alone, this effect cannot be explained. A team of researchers, led by Prof. Alessandro Toschi and Prof. Karsten Held (TU Wien) and Prof. Giorgio Sangiovanni (Würzburg University) has now published calculations in the journal "Nature Communications", which show that the theory of the geodynamo has to be revised. As it turns out, it is crucial for the dynamo effect that the earth's core contains up to 20% nickel - a metal, which under extreme conditions behaves quite differently from iron.

Extreme Heat and Pressure

The earth's core is about as big as the moon and as hot as the surface of the sun. There is a pressure of hundreds of gigapascals - that is comparable to the pressure which several railway locomotives would exert if they could be balanced on one square millimetre. "Under these extreme conditions, materials behave in a way which may be quite different from what we are used to", says Karsten Held. "It is hardly possible to recreate these conditions in a lab, but with sophisticated computer simulations, we are able to calculate the behaviour of metals in the earth's core on a quantum mechanical level."

The heat of the earth's core has to find a way to escape. Hot material rises up to the outer layers of the globe, creating convection currents. At the same time, the earth's rotation leads to strong Coriolis forces. In combination these effects produce a complicated spiralling flow of hot material. "When electrical currents are created in such a system of flows, they can cause a magnetic field which in turn increases the electrical current and so forth - and finally the magnetic field becomes so strong that we can measure it on the surface of the earth", says Alessandro Toschi.

Conducting Heat

Up until now, however, nobody could really explain how these convection currents emerge in the first place: iron is a very good heat conductor and at high pressure its thermal conductivity increases even more. "If the earth's core consisted only of iron, the free electrons in the iron could handle the heat transport by themselves, without the need for any convection currents", says Karsten Held. "Then, earth would not have a magnetic field at all."

However, our planet's core also contains almost 20% nickel. For a long time, this fact was not considered to be particularly important. But as it turns out, nickel plays a crucial role: "Under pressure, nickel behaves differently from iron", says Alessandro Toschi. "At high pressure, the electrons in nickel tend to scatter much more than the electrons in iron. As a consequence, the thermal conductivity of nickel and, thus, the thermal conductivity of the earth's core is much lower than it would be in a core consisting only of iron." Due to the significant proportion of nickel, the heat of the high-temperature earth core cannot flow towards the planet's surface by means of the motion

of the electrons alone. As a result, convection currents have to emerge, which eventually build up the earth's magnetic field.

To obtain these results, different metallic structures had to be analysed in large-scale computer simulations, and the behaviour of their electrons had to be calculated. The many-particle-calculations were performed by Andreas Hausoel (University of Würzburg), some of them on the Vienna Scientific Cluster (VSC). "Together with our colleagues from Würzburg, we did not only have a look at iron and nickel, but also at alloys of these two materials. We also had to take imperfections and irregularities into account, which made the computer simulations even more challenging", says Karsten Held.

These advanced simulation methods are not only important to obtain a better understanding of the earth's magnetic field, they also provide new insights into the electronic scattering processes in different materials. Alessandro Toschi is convinced: "Soon, these improvements of computational material algorithms will also lead to exciting forefront applications in chemistry, biology, industry and technology."

http://bit.ly/2tq5iyN

Ravens can plan ahead, similar to humans and great apes

Ravens can plan ahead for different types of events, and are willing to forgo an immediate reward for a later, better one

Despite previous research that indicates such behaviors are unique to humans and great apes, a new study shows that ravens, too, can plan ahead for different types of events, and further, that they are willing to forgo an immediate reward in order to gain a better one in the future.

As ravens and great apes have not shared a common ancestor for over 300 million years, these results suggest that the cognitive "planning" abilities they share in common re-appeared, on a separate evolutionary path, in the birds. The complex cognitive task of planning ahead has almost exclusively been observed in humans and great apes.

Some corvids, a family of birds that includes ravens, have also demonstrated the ability to plan beyond the current moment - but such findings have been confined to caching food.

Here, Can Kabadayi and colleagues sought to further explore the ability of ravens to plan ahead through a series of experiments. First, ravens were trained to use a tool to open a puzzle box in order to access a reward. The ravens were then presented with the box, but not the tool.

The box was removed and one hour later the ravens were given the opening tool, as well as several "distractors." Nearly every raven chose the correct, apparatus-opening tool; upon being presented with the box 15 minutes later, they used the tool to open it, with a success rate of 86%. A high success rate (78%) was also seen in similar experiments where ravens used a token to later barter for a reward.

The ravens planned for bartering more accurately than apes, the researchers report, and they were on par with them in the tool-using tasks, despite lacking predispositions for tool handling.

Next, the ravens were presented with the correct, apparatus-opening tool, distractor tools, and an immediate reward, but were only permitted to select one item. The immediate reward was less appealing than the reward in the box, the researchers report, demonstrating a level of self-control in the birds similar to that seen in apes. Markus Boeckle and Nicola S. Clayton discuss these finding in a related Perspective.

http://bit.ly/2urYD4e

Bacterium actively drives colorectal cancer tumor cell growth

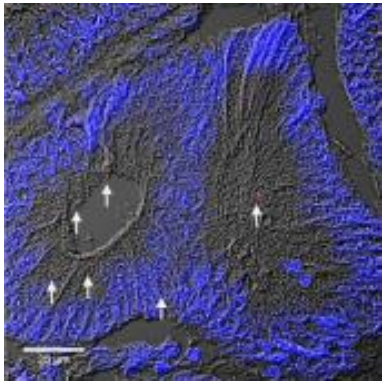
A subspecies of the bacterium Streptococcus gallolyticus appears to actively promote the development of colorectal cancer, according to new research published in PLOS Pathogens.

Scientists have known for some time that people infected with the S. gallolyticus subspecies gallolyticus (Sg) are more likely to have colorectal cancer (CRC), a leading cause of cancer death. However, it

was unknown whether Sg actively promotes CRC or whether it simply grows comfortably in the environment provided by CRC tumor cells.

To investigate the precise role of Sg in CRC, Ritesh Kumar of Texas A&M Health Science Center and colleagues performed several experiments using cultured human colorectal cells, mice with CRC, and tissue from human tumors.

Experiments in which CRC cells and Sg were grown together showed that Sg promotes proliferation of CRC cells, and that this effect depends on what phase of growth the Sg bacteria are in. Sg¬-driven proliferation of CRC cells only occurred when the bacteria and CRC cells were in direct contact with each other; substances secreted by bacterial cells did not drive proliferation on their own.



***Detection of Sg (shown as individual red dots)in a human colon tumor. Immunofluorescence detection of Sg in tumor tissues from CRC patients. Formalin-fixed and paraffin embedded human tumor (stage II) (A and B) and normal tissues (C and D) were deparaffinized rehydrated, and stained with anti-Sg antibodies as described in the Methods and Materials section. Nuclei were stained with DAPI. Arrows point towards Sg-positive staining. The scale bar represents 25μm.* Kumar R, et al. (2017)**

The researchers also explored the effects of Sg on a human protein known as β-catenin, which plays a key role in the development of CRC. They found that Sg did not promote proliferation of CRC cells in which β-catenin production or activity were deliberately reduced, suggesting that Sg drives proliferation through the β-catenin cell signaling pathway.

In mice with CRC, those injected with Sg developed more tumors and had greater β-catenin production (as well as other signs of cancer severity) than did mice injected with a different type of bacteria as a control. The researchers also analyzed normal and tumor tissue samples from more than 100 human CRC patients and found that most were infected with Sg, which was previously unknown.

Overall, these findings strongly suggest that Sg plays an active role in CRC development in humans. In the future, the precise mechanisms of its tumor-promoting activity could potentially be exploited to develop new strategies to diagnose, prevent, and treat CRC. "A bacterium that has been well documented to have a strong clinical association with CRC is now found to also functionally promote the development of CRC."

Citation: Kumar R, Herold JL, Schady D, Davis J, Kopetz S, Martinez-Moczygemba M, et al. (2017) Streptococcus gallolyticus subsp. gallolyticus promotes colorectal tumor development. PLoS Pathog 13(7): e1006440. https://doi.org/10.1371/journal.ppat.1006440

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http://bit.ly/2urN39c

Could calcium hold the key to fighting a dangerous hospital infection?

U-M and FDA scientists show key role of excess gut calcium in 'awakening' of Clostridium difficile spores

ANN ARBOR, MI - It lurks in hospitals and nursing homes, surviving the cleaning crew's attempt to kill it by holing up in a tiny hard shell. It preys upon patients already weak from disease or advanced age.

And when it reaches their guts, it breaks open its shell and unleashes infections that kill nearly 30,000 Americans a year, and sicken half a million more.

But, new research shows, it can't make this last, crucial move without enough of a humble nutrient: calcium. And that new knowledge about Clostridium difficile (a bacterium also known as "C. diff") may lead to better treatment for the most vulnerable patients.

The discovery, made in research laboratories at the University of Michigan Medical School and the U.S. Food and Drug Administration, is published in the online journal PLoS Pathogens. It helps solve a key mystery about C. diff: What triggers it to germinate, or break its dormancy, from its hard spore form when it reaches the gut.

Though the findings were made in mice, not humans, the researchers say the crucial role of calcium may help explain another mystery: Why some hospital patients and nursing home residents have a much higher risk of contracting C. diff infections and the resulting diarrhea that carries its spores out of the body.

That group includes people whose guts are flooded with extra calcium because they're taking certain medications or supplements, have low levels of Vitamin D in their blood or have gut diseases that keep them from absorbing calcium.

The new discovery shows that C. diff can recognize this extra calcium, along with a substance called bile salt produced in the liver, to trigger its awakening and the breaking of its shell.

Previous research had suggested it couldn't do this without another key component, an amino acid called glycine. But the new findings show calcium and the bile salt called taurochlorate alone are enough. Mouse gut contents that were depleted of gut calcium had a 90 percent lower rate of C. diff spore germination.

"These spores are like armored seeds, and they can pass through the gut's acidic environment intact," says Philip Hanna, Ph.D., senior author of the new paper and a professor of microbiology and immunology at U-M. "Much of the spore's own weight is made of calcium, but we've shown that calcium from the gut can work with bile salts to trigger the enzyme needed to activate the spore and start the germination process."

Ironically, the researchers say, one way to use this new knowledge in human patients might be to add even more calcium to the system.

That could awaken all the dormant C. diff spores in a patient's gut at once, and make them vulnerable to antibiotics that can only kill the germinated form. That could also prevent the transmission of more spores through diarrhea to the patient's room. That could slow or stop the cycle of transmission that could threaten them or other patients in the future.

Hanna's graduate student, Travis Kochan, made a key observation that led to the discovery. He noted that the fluid "growth medium" that the researchers typically grow C. diff in for their studies had calcium in it. He realized this could artificially alter the results of their experiments about what caused C. diff spores to germinate.

So, he used a chemical to remove the calcium while leaving all the other nutrients that keep C. diff growing. The result: no new spore germination happened in the calcium-free growth medium.

FDA's Center for Biologics Evaluation and Research conducted further research in laboratory dishes and in the guts of mice. FDA's Paul Carlson, Ph.D., a former U-M research fellow, and his laboratory found that C. diff spores that were mutated so that glycine couldn't act on them could still germinate and colonize mice. This suggested that calcium, and not glycine, was critical for this process.

Both mutant and regular forms of the bacteria could still activate an enzyme inside the C. diff spore that led the bacteria to start dissolving their hard shell. This released the store of calcium that the spore had been harboring inside itself, and increases the local level of the nutrient even further.

"These spores don't want to germinate in the wrong place," says Kochan, whose grandfather suffered from a severe C. diff infection which ultimately led to his death. "C. diff spores have specialized to germinate in the gut environment, especially in the environment of the small intestine, where calcium and the bile salt injection from the liver comes in."

Hanna notes that the bile salt connection to C. diff spore germination was first discovered at U-M in 1982 by a team led by Ken Wilson, M.D.

Calcium and the gut

Certain ailments and treatments cause defects in calcium absorption, but are also risk factors for C. diff infections. For example, patients with vitamin D deficiency are five times more likely to get C. diff.

Medications aimed at calming acid reflux - such as proton pump inhibitors - and steroids can increase the amount of calcium in the gut. A Vitamin D deficiency can keep the body from reabsorbing calcium through the gut wall, allowing it to build up. And people with inflammatory bowel diseases such as Crohn's and colitis also have a harder time absorbing calcium from food through their gut walls. Older adults are also often counseled to take calcium supplements to compensate for lower calcium levels and protect their bones from fracturing.

Hanna cautions that the new findings should not cause any patients to stop taking their medications or doctor-recommended supplements, or to start taking new ones. But he hopes to work with clinicians at U-M and beyond to test the new knowledge in a clinical setting. Meanwhile, he and Kochan and their FDA and U-M colleagues will continue to study C. diff germination in mice and look for ways to block the enzymes crucial to spore germination.

Many of the world's Clostridia researchers will travel to U-M next month for a major meeting, the 10th such gathering. More information is at http://www.clostpath2017.org/.

In addition to Kochan, Carlson and Hanna, the study's authors are Madeline Somers, Alyssa Kaiser, Michelle Shoshiev, Ada Hagan of U-M Microbiology & Immunology, and Jessica Hastie, Nicole Giordano, Ashley Smith, and Alyxandria Schubert of FDA's Center for Biologics Evaluation and Research.

Reference: PLoS Pathogens, DOI 10.1371/journal.ppat.1006443,
http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006443

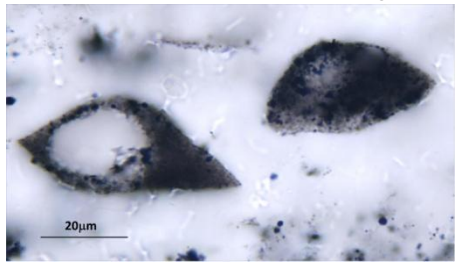
http://bit.ly/2v6znOI

Ancient plankton-like microfossils span 2 continents

South African microfossils are not only among the oldest known microorganisms, are related to other microfossils found in Australia

Large, robust, lens-shaped microfossils from the approximately 3.4 billion-year-old Kromberg Formation of the Kaapvaal Craton in eastern South Africa are not only among the oldest elaborate microorganisms known, but are also related to other intricate microfossils of the same age found in the Pilbara Craton of Australia, according to an international team of scientists.

The researchers report that the "Kromberg Formation (KF) forms are bona fide, organic Archean microfossils and represent some of the oldest morphologically preserved organisms on Earth," in the July issue of Precambrian Research. They also state that the combination of morphology, occurrence and carbon isotope values argues that the lenticular forms represent microbes that had planktonic stages to their life cycles.



Lenticular organic microfossils in the Kromberg Formation, Onverwacht Group, Barberton Mountain Land of South Africa. Image shown is an optical photomicrograph of a polished thin section, taken in transmitted light. **Dorothy Oehler on a sample provided by Maud Walsh (Louisiana State University**

"We hoped to determine if, in fact, the South African examples could be linked with the Australian examples, as it would give us additional insight into the evolutionary history and significance of these unusual forms," said Dorothy Z. Oehler, senior scientist, Planetary Science Institute, Tuscon Arizona. "Maud (M. Walsh, professor of plant, environmental and soil sciences, Louisiana State University) first discovered the lenticular forms in the Kromberg formation and sent us some samples and we all collaborated on the interpretation. We did isotopic analysis along with comparison of the South African and Australian examples in terms of their morphologies and the types of rocks and geologic settings in which the fossils occurred."

These fossils all occur in sedimentary rocks -- chert -- in what was once shallow water. And, according to the researchers, it appears that the samples from two sites in Australia and one in South Africa are related.

"Many people believe that the Kaapvaal Craton of Southern Africa and the Pilbara Craton of Australia formed a single continent at that time," said Christopher H. House, professor of geosciences and

director, Penn State Astrobiology Research Center. "But we really don't know."

These microfossils are unusual not only because they are so old, appearing in the geologic record about a billion years after the Earth formed 4.6 billion years ago, but because they are large, complex, plankton-like and autotrophs -- organisms that can turn inorganic elements into organic material.

Familiar fossils such as trilobites were alive just 200 million years ago and first appeared 500 million years ago. The lenticular organisms appeared 3,450 million years ago, spread at least from where Australia was then to South Africa and then disappeared from the fossil record. They are larger and more elaborate than any other organism existing around at that time.

"These fossils don't appear to relate to anything on the Earth that we know of," said House. "They seem to be an experiment in adaptation that does not leave a lineage."

The researchers analyzed the fossils to determine the isotopic relationship between carbon 12 and carbon 13, two isotopes of carbon that exist in everything but whose ratios can indicate organic material. They used Secondary Ion Mass Spectroscopy, a process where an ion beam kicks ions off the surface of a substance so that those ions can be identified.

"When the carbon isotope data came back we were excited," said Oehler. "It helped to confirm the biogenicity of the South African forms and told us that the organic microfossils from the three deposits were likely to represent organisms that were biologically related."

The researchers also note that the isotopic make up and morphology of these fossils set them apart from other microfossils found from the Precambrian -- 4,600 million years ago to 541 million years ago. These robust microorganisms existed for 400 million years and were abundant and widespread. Because they have thick robust walls and behave like plankton -- floating in the ocean surface waters -- they may have had an advantage for survival in the early Earth's higher ultraviolet radiation and sometimes chaotic environment, which was still being bombarded by large impacts.

Also working on this project were Kenichiro Sugitani, professor, Graduate School of Environmental Studies, Nagoya University, Japan and Australian Centre for Astrobiology, University of New South Wales discoverer of the Australian examples; and Ming-Chang Liu, academic specialist, Department of Earth, Planetary and Space Sciences, University of California at Los Angeles.

The NASA Astrobiology Program, the Planetary Space Institute, Louisiana State University Council for Research, Louisiana Space Consortium, Japanese Society for the Promotion of Science and the National Science Foundation supported this work.

http://bit.ly/2v9mIKY

France looks to curb its growing anti-vaccination movement with a new law

Proposal would make 11 vaccines mandatory for children, but details on how it will be enforced remain unclear

by Amar Toor@amartoo Jul 13, 2017, 12:32pm EDT

France, the birthplace of vaccine pioneer Louis Pasteur, has a major problem with vaccines. Skepticism around the safety of vaccines has soared in the country, fueled by growing distrust in public health institutions and the pharmaceutical industry. French authorities hope that a new law will change that.

Last week, the French Health Ministry announced plans to make 11 vaccines mandatory for young children by 2018. French law currently mandates three vaccines — diphtheria, tetanus, and polio — for children under the age of two. The government's proposal would expand that list to include eight other vaccines — including those against Hepatitis B, whooping cough, and measles — that were previously only recommended.

The proposal, which is to be presented to lawmakers by the end of this year, comes amid an ongoing measles outbreak across Europe, which the World Health Organization (WHO) attributed to low immunization rates. Italy passed a similar decree in May, requiring children to receive 10 vaccines as a condition for school enrollment. Germany, while stopping short of a mandate, has moved to tighten its laws on child immunization.

But some experts question whether a vaccination mandate will sway public opinion in France, where distrust in vaccines has risen alarmingly in recent years. In a survey published last year, 41 percent of respondents in France disagreed with the statement that vaccines are safe — the highest rate of distrust among the 67 countries that were surveyed, and more than three times higher than the global average.

"It's one of these decisions that, if it's well managed, could be helpful," says Heidi Larson, director of the Vaccine Confidence Project and lead author of the survey. "If it's very top-down, [it] could totally backfire."

Larson says the measure will "undoubtedly" rile up hard-line anti-vaccine activists; the home of a government spokesperson was spray-painted with anti-vaccine slogans this week, and far-right politician Marine Le Pen has already voiced her opposition to the proposal. But Larson says it's important for the government to engage with more moderate skeptics, and to convince them "that this is not just a control effort, in terms of controlling people's actions," but a public health initiative.

France's vaccination rates for diphtheria and tetanus are among the highest in the world, according to the OECD, but it lags behind in measles immunization, below the 95 percent threshold considered necessary to prevent outbreaks. More than 24,000 measles cases were reported between 2008 and 2016, according to government figures, and 10 people died from the disease during that period.

Vaccination policies vary widely from country to country, though Western European nations have generally preferred voluntary approaches to mandates. States in the US require vaccines for children to attend school, though all offer medical exemptions, and some offer exemptions for religious or philosophical reasons.

France stopped mandating vaccinations in the 1950s, classifying many newly developed immunizations as "recommended," and vaccination rates remained high through the early 2000s. But experts say high-profile legal cases over alleged vaccine side effects undermined confidence in both the government and pharmaceutical companies, while anti-vaccine activists have effectively used social media to spread conspiracy theories.

Conspiracy theories concerning vaccines have circulated for decades in France, but as with the "anti-vax" movement in the US, the rise of social media has allowed them to reach wider audiences. Sites such as the pro-homeopathy *Sante Nature Innovation* (Health Nature Innovation) and *AlterInfo* routinely publish articles about unfounded links between vaccines and various conditions, such as autism or sudden infant death syndrome, supported by prominent "experts" like the discredited physician Henri Joyeux. Such conspiracies appear to have resonated with the French public; fourteen of the first 16 results on an Amazon France search for "vaccines" are books that either explicitly condemn or raise doubts about vaccination.

"The difference between France and the Anglo-Saxon world is that there are very few citizen groups or associations that mobilize in favor of vaccinations," says Jocelyn Raude, a sociologist at the EHESP French School of Public Health, who describes the call for mandatory vaccines as "courageous." Raude says that over time, a "constellation" of anti-vaccine groups has emerged online, uniting both far-left ecologists and far-right nationalists, like Le Pen.

Recent controversies have helped fuel vaccine skepticism in France. A nationwide Hepatitis B vaccination campaign was suspended in 1998 amid concerns over possible secondary effects, and subsequent lawsuits were filed over deaths that were allegedly caused by the vaccine. Legal cases have also been filed over alleged links between the Hepatitis B vaccine and multiple sclerosis (there is no evidence of such a link), and French media outlets seized on allegations that the WHO was unduly influenced by pharmaceutical companies in launching a H1N1 flu vaccination campaign in 2009.

Conspiracies have even filtered into the French medical community, converting French doctors and fueling calls among some for more

intensive vaccine education in medical schools. “At the beginning, only a few [doctors] were critical or skeptical, but now the rates are much higher,” Raude says. “Even in recent surveys we even see that a lot of them have misbeliefs about vaccinations.”

Whether the proposed mandate will help curb such skepticism depends largely on its enforcement mechanisms, experts say. Raude says it’s unlikely that those who fail to vaccinate their children will face fines, as Italy’s law calls for, but both he and Larson agree that the law should include an exemption clause — both to appease critics, and to accommodate those who may not be able to receive vaccinations due to immune deficiencies. Such an exemption would help the government balance public health with individual liberties, Larson says, though she believes it shouldn’t be too easy to obtain.

“When they do put in these exemptions, it should be more than checking a box,” says Larson. “You need people to consciously exempt, knowing fully the risks that they’re taking.”

Experts acknowledge that an exemption risks opening the floodgates to an increasingly skeptical public, pointing to what they see as a need for greater awareness. Anne-Marie Moulin, research director at France’s National Center for Scientific Research, was part of a government committee convened last year to develop proposals to boost public confidence in vaccines. In a phone interview, she said she was in favor of expanding the mandate to include measles and whooping cough, but feared that expanding it to 11 vaccines “that people don’t know well” would be misguided without proper explanation of their importance.

The success of the proposal, in Moulin’s view, will ultimately hinge on confidence in public institutions, and she says it’s unclear whether a single piece of legislation can do much to bolster that.

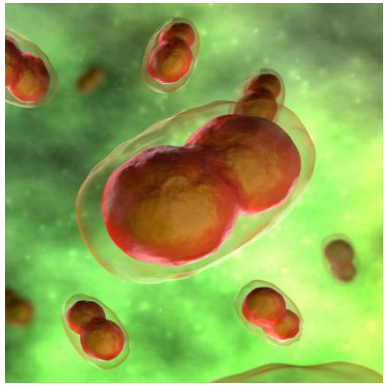
“In order to reestablish confidence in vaccines, one must reestablish confidence in politics — in politicians, in the government, and in public health authorities,” Moulin says. “And for the moment, that’s a challenge, and it’s not at all certain that it will happen.”

http://bit.ly/2uutjl9

People Could Make Smallpox from Scratch in a Lab, Scientists Warn

Scientists have re-created a relative of the smallpox virus in a lab, from scratch.

By Rachael Rettner, Senior Writer



***An illustration of the smallpox virus*decade3d - anatomy online/Shutterstock**

This virus, called the horsepox virus, is not harmful to humans, but the new findings suggest that it's possible for people to make the deadly smallpox virus in a lab. That virus was eradicated from the world in 1980, according to the journal Science. Re-creating the horsepox virus wasn't a trivial feat, but it did not require extensive resources, either.

The researchers ordered the DNA fragments they used to make the virus from a company that makes DNA pieces for researchers, with made-to-order sequences, and sends them through the mail. In total, the project cost $100,000 and took six months, Science reported.

The researchers, from the University of Alberta in Canada, hope their effort could one day lead to a better smallpox vaccine.

Although most people no longer receive smallpox vaccination, the shot is sometimes given to people who may be at risk for contracting the disease, such as those who work with smallpox or similar viruses in a lab.

A small percentage of those vaccinated with the current vaccine may experience serious, life-threatening side effects, according to the Centers for Disease Control and Prevention.

The Canadian researchers are working with the pharmaceutical company Tonix to develop a smallpox vaccine.

In March, Tonix issued a statement announcing that it had used the horsepox virus to develop a potential smallpox vaccine, which showed protective effects in an early study in mice.

Although many researchers assumed it would one day be possible to re-create poxviruses — the family of viruses to which smallpox and horsepox belong — there was still some debate about the issue.

David Evans, the lead researcher of the horsepox virus work, told Science that he performed the feat in part to put an end to the debate. "The world just needs to accept the fact that you can do this, and now we have to figure out what is the best strategy for dealing with that," Evans told Science.

Some experts praised the work. "I think he did a terrific service," Peter Jahrling, chief of the Emerging Viral Pathogens Section at the National Institute of Allergy and Infectious Disease, told The Washington Post.

"You had a lot of people saying this can't be done. And he said yes it can."

Evans' findings have not yet been published, but he presented the work in November 2016 at a World Health Organization meeting.

In a summary report of that presentation, the committee said it acknowledged that "given the advent of synthetic biology, it was no longer possible for society to entirely rid itself of the threat of smallpox or, indeed, other dangerous pathogens."

However, there are already measures in place to prevent people from re-creating smallpox.

The World Health Organization recommends that no institution should be allowed to possess more than 20 percent of the smallpox genome, according to The Washington Post.

And companies that synthesize DNA for research purposes are required to check the orders they receive for matches against certain human pathogens, the Post reported.

http://bit.ly/2u113Vd

Diesel is now better than gas, study says

Diesel is now better than gas

July 14, 2017 by Jeff Heinrich

Modern diesel cars emit less pollution generally than cars that run on gasoline, says a new six-nation study published today in Scientific Reports whose groundwork was laid in part by an American chemist now working at Université de Montréal.

And since diesel is so much cleaner than before, environmental regulators should increasingly shift their focus to dirtier gasoline-powered cars and other sources of air pollution, says the UdeM scientist, Patrick Hayes.

"Diesel has a bad reputation because you can see the pollution, but it's actually the invisible pollution that comes from gasoline in cars that's worse," said Hayes, 36, an assistant professor at UdeM.

"The next step should be to focus on gasoline or removing old diesel vehicles from the road.

Modern diesel vehicles have adopted new standards and are now very clean, so attention needs to now turn to regulating on-road and off-road gasoline engines more. That's really the next target."

The study, led by researchers in Switzerland and Norway with help from Hayes and colleagues in Italy, France and the U.S., looked at carbonaceous particulate matter (PM) emitted from the tailpipes of cars.

Carbonaceous PM is made up of black carbon, primary organic aerosol (POA) and, especially, secondary organic aerosol (SOA), which is known to contain harmful reactive oxygen species and can damage lung tissue.

Particle filters required on diesel engines

In recent years, newer diesel cars in Europe and North America have been required to be equipped with diesel particle filters (DPFs), which significantly cut down on the pollution they emit.

In the lab (at the Paul Scherrer Institute, near Zurich in Switzerland), "gasoline cars emitted on average 10 times more carbonaceous PM at 22°C and 62 times more at -7°C compared to diesel cars," the researchers noted in their study.

"The increase in emissions at lower temperatures is related to a more pronounced cold-start effect," when a gasoline engine is less efficient because it's not yet warned up and its catalytic converter is not yet on, the study noted.

It added: "These results challenge the existing paradigm that diesel cars are associated, in general, with far higher PM emission rates, reflecting the effectiveness" of engine add-ons like DPFs to stem pollution.

That said, it is true that older diesel cars do pollute more than gasoline cars, because they don't have DPFs, and diesel cars in general emit far more nitrogen oxides, which cause smog and acid rain, the study also noted.

The air in traffic-heavy LA ... and in the Arctic

For their investigation, the researchers utilized field work on air pollution that Hayes carried out in California in 2010 and published in 2013 when he was a researcher at the University of Colorado working with Jose-Luis Jimenez (also a co-author of the new study).

Over four weeks in a parking lot of the California Institute of Technology, in Pasadena, Hayes analyzed air coming from nearby traffic-heavy Los Angeles, drawn through a tube in the roof of a modified construction trailer.

Now he's doing something similar up in Canada's Far North, "the final resting place of atmospheric pollution," said Hayes, a New Yorker from Albany who has lived in Montreal since 2013.

He's interested in whether the carbonaceous PM up North exacerbates climate change.

Soot that settles on snow makes the snow darker and, warmed by the sun, the snow melts faster, for example. To better understand the origins of PM in the Arctic, for the past two years Hayes has been taking measurements at Eureka, Nunavut on Ellesmere Island.

He plans to publish his findings next year.

More information: S. M. Platt et al. Gasoline cars produce more carbonaceous particulate matter than modern filter-equipped diesel cars, Scientific Reports (2017). DOI: 10.1038/s41598-017-03714-9

http://bit.ly/2twEPbu

Asteroids may have been giant mudballs in the early solar system

Before there were asteroids, there were giant mudballs hurtling around the solar system.

By Sam Wong

The most common type of asteroid, called carbonaceous asteroids, may have delivered water and organic molecules to Earth, and could even be the precursors of rocky planets.

They are thought to have formed from ice, dust and mineral grains called chondrules in the disc of dense gas and dust that birthed our solar system.

But not much is known about their history, and they have some unexplained characteristics. These rocks appear to have been altered at relatively low and uniform temperatures, so they must have had some way to lose heat from within.

Some have proposed that water flowing inside the early asteroids cooled them down, but soluble elements don’t appear to have been moved around, as would be expected if water had been present.

Modelling early asteroids as mud makes more sense, says Philip Bland at Curtin University in Perth, Australia, and his collaborator Bryan Travis at the Planetary Science Institute in Tucson, Arizona.

Muddy mixture

When the ice, dust and chondrules came together, they wouldn’t have been compacted under pressure into rock straight away, says Bland. Instead, the ice would have been melted by decaying radioactive atoms present among the dust and gas, turning the mixture into a sludgy mud.

Their model shows that these mudball asteroids likely formed from dusty material left over after the sun's formation, and that convection would take place, allowing the interior to lose heat easily.

Soluble and insoluble elements would be mixed together, preserving the primitive chemistry of the asteroid. "It turns out that that explains many more features of interest than if it's a rock," says Bland.

The mud would have turned to rock later on, perhaps aided by gravitational pressure once the asteroid got big enough, or by impacts with other objects.

"I think it's a very exciting idea," says Tom Davison at Imperial College London. "From the way they've presented it, it's almost inevitable that this would happen in at least some bodies."

Matching our meteorites

Sara Russell at the Natural History Museum in London says the mudball model aligns well with what is found in meteorites.

"We see from our meteorite collection that chondrules within a single sample are the same size as each other," she says. That's difficult to explain without this model, she says.

Two space missions are currently en route to asteroids formed in the early universe that could be former mudballs: NASA's Osiris-Rex and Japan's Hayabusa 2 (depicted above). Both of these will map the asteroids in detail and return a sample to Earth, potentially allowing us to test this idea.

Understanding how asteroids formed will help us explain how organic chemistry evolved in the solar system, and could even help in the search for life elsewhere, says Bland. "It will help us make more sophisticated models of where we can look for habitable worlds around other stars," he says.

Journal reference: Science Advances, DOI: 10.1126/sciadv.1602514

http://bit.ly/2vtpOZF

Concerns over side effects of statins stopping stroke survivors taking medication

Stroke survivors and carers stop using potentially life-saving drugs due to reports of side effects and personal experiences

Negative media coverage of the side effects associated with taking statins, and patients' own experiences of taking the drugs, are among the reasons cited by stroke survivors and their carers for stopping taking potentially life-saving drugs, according to research published today.

Individuals who have had a stroke are at risk of a second stroke, which carries a greater risk of disability and death than first time strokes. In fact, one third of all strokes occur in individuals who have previously had a stroke. To prevent this recurrence, patients are offered secondary preventative medications; however, adherence is a problem with 30% of stroke patients failing to take their medications as prescribed.

To examine the barriers to taking these medications, researchers at the University of Cambridge and Queen Mary University, London (QMUL), analysed posts to TalkStroke, a UK-based online forum hosted by the Stroke Association, across a seven year period (2004-2011). The forum was used by stroke survivors and their carers.

The team, led by Dr Anna De Simoni, a lecturer in Primary Care Research at QMUL and visiting researcher at the Department of Public Health and Primary Care, University of Cambridge, has previously used the forum to explore issues such as the impairment that can make it difficult for stroke survivors to maintain a job.

The findings of the study, which looked at posts by 84 participants, including 49 stroke survivors and 33 caregivers, are published today in the journal BMJ Open. The Stroke Association gave the researchers permission to analyse the results, and to prevent identification of individuals, the team did not use verbatim comments.

Among the reasons cited by the forum users, side effects were a major factor in decisions to stop taking medication. Several contributors had experienced negative side effects and as a result had stopped taking the medication, sometimes in consultation with their GP and other times unilaterally. Others reported that they, or the person they were caring for, had stopped taking the medication after reading negative stories in the press about side effects.

Other users expressed concerns over the medication they were offered. There were conflicting views about the efficacy of the medications - some contributors believed they were very important, while others believed that their risk could be managed by lifestyle changes alone.

Contributors also reported mixed views of healthcare professionals -- some felt confident in their doctor's decision, while others questioned their decisions, some even questioning their motivation for prescribing particular drugs.

"These findings have highlighted the need for an open, honest dialogue between patients and/or their carers, and healthcare professionals," says Dr De Simoni. "Doctors need to listen to these concerns, discuss the benefits and drawbacks of taking the medication, and be willing to support a patient's informed decision to refuse medications."

However, perceptions did not present the only barriers to adherence: there were often practical considerations. Drugs were sometimes too large and difficult to swallow, or a drug regime was too burdensome. The complexities of the drug regimes sometimes meant having to develop routines and strategies to ensure patients kept to them. One survivor described having to pay for the medications by credit card as she was unable to work and had no money or benefits coming in.

"By analysing people's views as expressed in online forums, where they are more open and less guarded, we've seen some valuable insights into why some stroke survivors have difficulty adhering to their medication," says PhD candidate and first author James Jamison from the Department of Public Health and Primary Care at Cambridge.

"Challenging negative beliefs about medication and adopting practices that make routines for taking medication simpler, particularly for those patients who have suffered disability as a result of stroke, should increase adherence and ultimately improve health outcomes."

The research was supported by the National Institute of Health Research, the Stroke Association and the British Heart Foundation.

Jamison, J et al. Barriers and facilitators to adherence to secondary stroke prevention medications after stroke: Analysis of survivors' and caregivers' views from an online stroke forum. BMJ Open; 19 July 2017; DOI: 10.17863/CAM.10458

http://bit.ly/2twBvqO

Let's twist again: the secrets of kissing angles revealed

Humans hard-wired to favour leaning to the right while locking lips with romantic partners, an international study has found

Humans are hard-wired to favour leaning to the right while kissing romantic partners, an international study by psychologists and neuroscientists has found.

The research, by the universities of Dhaka, Bath and Bath Spa, found that kiss recipients have a tendency to match their partners' head-leaning direction.

Experts built on work from Western countries to investigate kissing behaviours in a non-Western context, including a bias for turning the head to one side.

Their work, published in the journal Scientific Reports, studied 48 married couples in Bangladesh, where romantic kissing is not typically observed in public. Couples were asked to kiss privately in their own homes, then go into different rooms and independently report back on various aspects of the kiss.

Men were about 15 times more likely to initiate kissing than women, and both partners showed a bias for turning their heads to the right.

Dr Rezaul Karim, from the department of psychology at the University of Dhaka, said: "This is the first study to show sex differences in the initiation of kissing, with males more likely to be the initiator, and also that the kiss initiators' head-turning direction tends to modulate the head-turning direction in the kiss recipients.

"Based on our prior theoretical work, we are also able to make new hypotheses about the underlying neural basis for these behaviours."

The study found that more than two-thirds of kiss initiators and kiss recipients turned their heads to the right. Men accounted for 79% of the kiss initiations.

A person being left- or right-handed predicted their head-leaning direction, but this was only the case if they initiated the kiss. The head-leaning direction of the kiss initiator also strongly predicted the head-leaning direction of the kiss recipient.

This suggests that the kiss recipients have a tendency to match their partners' direction in order to avoid the discomfort of mirroring heads. People who were requested to mirror each other's head movements for a kiss reported that they felt discomfort.

"This further suggests the underlying cognitive mechanisms of the act of kissing and head-turning," the authors said. "Though this action tends to be performed intuitively, a decision must be made about the direction to which the partners should lean to kiss each other."

The setting for the study was significant, as kissing in Bangladesh is very private and censored from television or film, they added. Results from Western countries could be attributed to cultural factors or learning to kiss through influences on TV or film, but this cannot be said for countries like Bangladesh. Previous studies have involved couples kissing in public places such as airports, railways stations, beaches or parks.

Dr Michael Proulx, from the department of psychology at the University of Bath, said: "This study is unique in giving us a look into a private behaviour in a private culture, with implications for all people.

"Prior works could not rule out cultural learning due to having Western samples. It turns out we as humans are similar, even if our social values differ."

The research suggests that the act of kissing is determined by the brain splitting up tasks to its different hemispheres, similar to being either right- or left-handed. This is specific to the functions in the left cerebral hemisphere, located in the emotion- and decision-related areas of the brain. Levels of hormones such as testosterone might be unevenly distributed in each hemisphere, causing a bias to turn right.

It is hoped the findings will feed in to further studies of the neurophysiological mechanisms of such behaviours.