http://bit.ly/2IYoowz

I never said that! High-tech deception of 'deepfake' videos

Hey, did my congressman really say that? Is that really President Donald Trump on that video, or am I being duped?

July 2, 2018 by Deb Riechmann

New technology on the internet lets anyone make videos of real people appearing to say things they've never said. Republicans and Democrats predict this high-tech way of putting words in someone's mouth will become the latest weapon in disinformation wars against the United States and other Western democracies.

This image made from video of a fake video featuring former President Barack Obama shows elements of facial mapping used in new technology that lets anyone make videos of real people appearing to say things they've never said. There is rising concern that U.S. adversaries will use new technology to make authentic-looking videos to influence political campaigns or jeopardize national security. **(AP Photo)**

We're not talking about lip-syncing videos. This technology uses facial mapping and artificial intelligence to produce videos that appear so genuine it's hard to spot the phonies. Lawmakers and intelligence officials worry that the bogus videos—called deepfakes—could be used to threaten national security or interfere in elections. So far, that hasn't happened, but experts say it's not a question of if, but when.

"I expect that here in the United States we will start to see this content in the upcoming midterms and national election two years from now," said Hany Farid, a digital forensics expert at Dartmouth College in Hanover, New Hampshire. "The technology, of course, knows no borders, so I expect the impact to ripple around the globe."

When an average person can create a realistic fake video of the president saying anything they want, Farid said, "we have entered a new world where it is going to be difficult to know how to believe what we see." The reverse is a concern, too. People may dismiss as fake genuine footage, say of a real atrocity, to score political points.

Realizing the implications of the technology, the U.S. Defense Advanced Research Projects Agency is already two years into a four-year program to develop technologies that can detect fake images and videos. Right now, it takes extensive analysis to identify phony videos. It's unclear if new ways to authenticate images or detect fakes will keep pace with deepfake technology.

Deepfakes are so named because they utilize deep learning, a form of artificial intelligence. They are made by feeding a computer an algorithm, or set of instructions, lots of images and audio of a certain person. The computer program learns how to mimic the person's facial expressions, mannerisms, voice and inflections. If you have enough video and audio of someone, you can combine a fake video of the person with a fake audio and get them to say anything you want.

So far, deepfakes have mostly been used to smear celebrities or as gags, but it's easy to foresee a nation state using them for nefarious activities against the U.S., said Sen. Marco Rubio, R-Fla., one of several members of the Senate intelligence committee who are expressing concern about deepfakes.

A foreign intelligence agency could use the technology to produce a fake video of an American politician using a racial epithet or taking a bribe, Rubio says. They could use a fake video of a U.S. soldier massacring civilians overseas, or one of a U.S. official supposedly admitting a secret plan to carry out a conspiracy. Imagine a fake

video of a U.S. leader—or an official from North Korea or Iran—warning the United States of an impending disaster.

"It's a weapon that could be used—timed appropriately and placed appropriately—in the same way fake news is used, except in a video form, which could create real chaos and instability on the eve of an election or a major decision of any sort," Rubio told The Associated Press.

Deepfake technology still has a few hitches. For instance, people's blinking in fake videos may appear unnatural. But the technology is improving.

"Within a year or two, it's going to be really hard for a person to distinguish between a real video and a fake video," said Andrew Grotto, an international security fellow at the Center for International Security and Cooperation at Stanford University in California.

"This technology, I think, will be irresistible for nation states to use in disinformation campaigns to manipulate public opinion, deceive populations and undermine confidence in our institutions," Grotto said. He called for government leaders and politicians to clearly say it has no place in civilized political debate. Crude videos have been used for malicious political purposes for years, so there's no reason to believe the higher-tech ones, which are more realistic, won't become tools in future disinformation campaigns.

Rubio noted that in 2009, the U.S. Embassy in Moscow complained to the Russian Foreign Ministry about a fake sex video it said was made to damage the reputation of a U.S. diplomat. The video showed the married diplomat, who was a liaison to Russian religious and human rights groups, making telephone calls on a dark street. The video then showed the diplomat in his hotel room, scenes that apparently were shot with a hidden camera. Later, the video appeared to show a man and a woman having sex in the same room with the lights off, although it was not at all clear that the man was the diplomat.

John Beyrle, who was the U.S. ambassador in Moscow at the time, blamed the Russian government for the video, which he said was clearly fabricated.

Michael McFaul, who was American ambassador in Russia between 2012 and 2014, said Russia has engaged in disinformation videos against various political actors for years and that he too had been a target. He has said that Russian state propaganda inserted his face into photographs and "spliced my speeches to make me say things I never uttered and even accused me of pedophilia."

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Could Aspirin Help Prevent Alzheimer's Disease? Mouse Study Says Maybe.

New research suggests there is some hope that aspirin may help to treat some aspects of Alzheimer's

By Christopher Wanjek, Live Science's Bad Medicine Columnist

Could an aspirin a day keep the Alzheimer's away? If only it were that simple. And yet, new research suggests that there does seem to be some hope that aspirin, one of the most widely used medications in the world, may help to treat some aspects of this devastating brain disease.

Scientists have discovered that aspirin works with certain subcellular machinery in the brain to prevent the buildup of amyloid plaque, sticky blobs of protein around brain cells that are thought to be the primary cause of Alzheimer's disease, according to the new study, which was done in mice.

In the study, mouse experiments revealed that aspirin enhanced the ability of lysosomes, which are sort of like the cells' waste processors and recyclers, to clear amyloid plaque or stop it from forming in the first place. Aspirin should have the same effect on the human form of Alzheimer's, too, said the researchers, who published their findings today (June 2) in *The Journal of Neuroscience*.

Alzheimer's disease, the most common type of dementia, is a progressive brain disease that affects nearly 6 million Americans and is the sixth-leading cause of death among all U.S. adults, according to the Centers for Disease Control and Prevention. There's no cure, and medications have had very limited success in slowing the progression of the disease.

Aspirin, also known as acetylsalicylic acid, is an inexpensive drug with a century-long history of being safe in low doses, aside from possible stomach irritation and a small risk of internal bleeding. Many adults take a low-dose aspirin daily as a mild blood thinner to help prevent heart attacks.

In fact, several population-wide studies on aspirin and heart health have found that aspirin may also lower the risk of Alzheimer's disease, albeit modestly. A meta-analysis that Chinese researchers published in March 2018 in the journal *Frontiers in Aging Neuroscience* reviewed 18 population-wide studies and found that the regular use of nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, was associated with a 20-percent lower risk, on average, of developing Alzheimer's disease.

Aspirin and Alzheimer's

Building on the possible connection between aspirin and Alzheimer's prevention, first observed more than a decade ago, researchers at Rush University Medical Center in Chicago crafted experiments that entailed giving aspirin to mice with a mouse version of Alzheimer's disease and also applying aspirin directly to mouse brain cells growing in the lab.

Both approaches — in vivo and in vitro — appeared to prevent or reverse the biological signs of Alzheimer's disease, said lead study author Kalipada Pahan, a professor of neurological sciences at Rush University.

Aspirin activates a cellular receptor called PPARα, which, in turn, regulates a protein called TFEB, a so-called master regulator of lysosomal activity, Pahan explained.

In short, aspirin helps cells clear cellular debris, including proteins that form amyloid plaque. "We expect to see similar results in human brain cells," Pahan told Live Science.

Indeed, other drugs, such as the triglyceride-lowering drug gemfibrozil (sold as Lopid), also target TFEB, Pahan said, but aspirin is safe enough to be available without a prescription and has fewer side effects.

Rajini Rao, a professor of physiology at Johns Hopkins University School of Medicine in Baltimore who was not involved with this research, said the new study "offers an elegant mechanistic explanation for protective effects of aspirin seen at the cellular and model animal level." However, she noted that it was unclear from the study whether the degree of improvement in amyloid removal would translate into better brain function.

"Results from epidemiological studies on aspirin use and dementia are mixed," Rao told Live Science. "While there have been some indications of protection, other studies have failed to replicate this. Unfortunately, this is the case for virtually every drug used in Alzheimer's trials — over 99 percent have failed in the clinic — which is why Alzheimer's research is especially challenging."

Pahan said that, although aspirin is relatively safe, it does carry some risks when used daily and shouldn't be used casually as an unproven way to treat or prevent Alzheimer's disease. He added that for aspirin to stimulate lysosomal activity, the cellular receptor PPARα needs to be present, and thus any person with Alzheimer's who lacks a sufficient number of PPARα receptors wouldn't benefit from aspirin. That may explain the mixed results of population-wide studies, Pahan said.

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Another Cup? More Coffee Could Be Linked to Longer Life Span

Coffee lovers may not have to feel that familiar pang of guilt when pouring themselves yet another cup of joe for the day.

By Yasemin Saplakoglu, Staff Writer | July 2, 2018 02:29pm ET

A new study found that drinking coffee, even more than 8 cups a day, was linked with a lower risk of death within a 10-year follow-up period. However, the researchers stressed that the study only found an association with coffee and longevity and didn't prove that coffee leads to a longer life.

"Although these findings may reassure coffee drinkers, these results are from an observational study and should be interpreted cautiously," said lead study author Erikka Loftfield, a research fellow at the National Cancer Institute (NCI).

In the study, published today (July 2) in the journal JAMA Internal Medicine, Loftfield and her team at the NCI analyzed data from nearly 500,000 people who took part in the U.K. Biobank study. That project gathered health information from more than 9 million people. As a part of the Biobank study, people were asked how many cups of coffee they drank daily, including decaf. The participants also answered questions about their general health, education, and smoking and drinking habits. Researchers additionally sampled the subjects' DNA.

In a 10-year follow-up period, around 14,000 people in the study died (the leading causes of death were cancer, cardiovascular disease and respiratory diseases). The researchers found that the more cups of coffee people drank, the less likely they were to die during the study period. Though there were slight differences among the types of coffee people drank, the results generally held true for instant, ground and decaf coffee.

That decaf coffee was associated with longevity "suggest[s] that the many other compounds in coffee, besides caffeine, may be responsible," Loftfield told Live Science.

When the researchers looked at the participants' genetic data, they identified four gene variations that were known to be associated with caffeine metabolism, or how the body breaks down caffeine. Some prior studies had suggested that people with these gene variations could be at higher risk for cardiovascular disease, Loftfield said.

But in the new study, the researchers found no link between having these variations and a person's risk of death over the study period.

Just enough coffee or too much?

It's not necessarily news that coffee can be healthy; the 2015 U.S. Dietary Guidelines Advisory Committee, for example, reported that drinking coffee moderately could be part of a healthy diet. But the new study suggests even higher amounts of coffee could be beneficial.

That doesn't mean people should dramatically up their coffee intake, though: There isn't enough data to change the guidelines to include more cups of coffee, Loftfield said. Indeed, only a fraction of the people in the study reported drinking 8 or more cups of coffee a day, she added — about 10,000 of the 500,000 participants.

Edward Giovannucci, a professor of nutrition and epidemiology at the Harvard T.H. Chan School of Public Health, who was not part of the study, agreed. "This new study is consistent with the previous studies but show[s] that the potential benefit extends to higher intakes of coffee, "he said. "But [it] doesn't mean that everyone should drink 8 cups of coffee a day."

The study didn't have enough data from people who drink that much coffee, Giovannucci said. And the risk of death during the follow-up period was only slightly higher for people drinking around 4 cups of coffee a day compared with those who drank more than 8, he told

Live Science. So, the benefit of drinking more than 8 cups of coffee over around 4 may be small.

There are so many studies that come out about coffee, yet it's still difficult for researchers to come to a consensus about whether the drink is good for our health. It's hard to conclude causality, because "the best data we have are [from] observational studies, where people self-[report] how much coffee they consume," Giovannucci said. "Nonetheless, the very large body of consistent evidence [for] lower risk for many outcomes, including overall mortality, is reassuring.

"While the evidence may not be strong enough to suggest that [a person start] drinking coffee for health benefits, people drinking coffee should feel reassured of no harm and probably even benefits of coffee," Giovannucci added. But don't overdo the sugar and cream, he said.

http://bit.ly/2KOY1OG

Horses Have Had Dental Appointments in Mongolia for Over 3,000 Years

Oldest known evidence of veterinary dentists on record

By Laura Geggel, Senior Writer | July 2, 2018 05:11pm ET

Imagine extracting a wayward tooth from a young horse more than two millennia before the discovery of laughing gas. It may sound like a Herculean task, but the ancient people of Mongolia figured it out, making them the oldest veterinary dentists on record.

Researchers made the discovery by examining 85 ancient horse remains, dating from about 1200 B.C. to 700 B.C., that had been buried in equine graves by the nomadic Deer Stone-Khirigsuur culture in Mongolia. The researchers found that one of these teeth was sticking out at an odd angle and had been cut, possibly with a stone, in about 1150 B.C., making it the oldest known evidence of horse dentistry in the world.

Later, in teeth dated to 750 B.C. and afterward, the researchers found evidence that people from the Deer Stone-Khirigsuur culture were pulling the so-called wolf tooth, a vestigial (functionless) premolar that erupts during a horse's first year of life. The wolf tooth typically falls out before the horse's third birthday, but if it doesn't, its presence can be painful for horses wearing a metal bit, the researchers said.

Perhaps the introduction of metal bits explains why the people of the Deer Stone-Khirigsuur culture (about 1300 B.C. to 700 B.C.) began pulling out horses' wolf teeth, although the finding is correlational, so it's hard to say so for sure, said study lead researcher William Taylor, a postdoctoral research fellow of archaeology at the Max Planck Institute for the Science of Human History, in Germany.

Before the use of metal bits, people of the Deer Stone-Khirigsuur culture used organic bits — possibly made out of leather, rope, bone or wood — to guide the horses they were riding. There's no evidence that these organic bits damaged the horses' mouths, even when horses still had wolf teeth.

Once metal bits first appeared in Mongolia in about 800 B.C., the people of the Deer Stone-Khirigsuur culture likely saw the new bits' advantages, Taylor said. For instance, metal bits allowed riders to control horses with more precision, which may have helped people use horses as vehicles for warfare and long-distance travel, Taylor said.

But the metal bits would have damaged the mouths of horses with wolf teeth, and this painful chafing likely led to health and behavioral problems in the horses, he said. So, it may not be a coincidence that wolf-tooth extraction and the introduction of metal bits happened at the same time, Taylor added.

"It's really shocking and cool that that [wolf-tooth removal] directly accompanied the introduction of metal bits," Taylor told Live Science. "It speaks to not just this passive tradition of health care, but instead one that was actively responding to the new challenges of the day."

Taylor noted that the discovery was made during a collaboration with Mongolian archaeologists, some of whom grew up in the countryside as herders. These colleagues provided valuable knowledge about the "rich tradition of animal health care" in the region, which, even today, includes removing wayward wolf teeth from horses, Taylor said.

A Mongolian herder uses a screwdriver to remove the first premolar — also known as a "wolf tooth" — of a young horse during the spring roundup
Credit: Photo: Dimitri Staszewski; Taylor et al. 2018. Origins of Equine Dentistry. PNAS.

The Deer Stone-Khirigsuur culture no longer exists, but its myriad burials have helped archaeologists learn the ways of its people. These burials are accompanied by tall stones adorned with carvings of deer. Over the past 10 to 20 years, archaeologists have learned that these graves have a few to hundreds, and even thousands, of sacrificed horses buried around them, Taylor said.

"In many ways, the movements of horses and horse-mounted peoples during the first millennium B.C. reshaped the cultural and biological landscapes of Eurasia," study senior researcher Nicole Boivin, director of the Department of Archaeology at the Max Planck Institute for the Science of Human History, said in a statement. The new study suggests that veterinary dentistry "may have been a key factor that helped to stimulate the spread of people, ideas and organisms between East and West," Boivin said.

The study was published online today (July 2) in the journal Proceedings of the National Academy of Sciences.

http://bit.ly/2IZDty1

This virus actually may boost -- not weaken -- our immune system

Our immune system is at its peak when we're young, but after a certain age, it declines and it becomes more difficult for our bodies to fight off new infections.

"That's why older people are more susceptible to infections than younger people," explains Janko Nikolich-Žugich, MD, PhD, co-director or the University of Arizona Center on Aging and chairman of the Department of Immunobiology at the University of Arizona College of Medicine - Tucson.

In search of a way to rejuvenate the immune system of older adults, Dr. Nikolich-Žugich and Megan Smithey, PhD, have found that one particular virus may not weaken, but actually enhance our immune system. Their findings are published this week in the *Proceedings of the National Academy of Sciences*.

For the study, the researchers infected mice with the cytomegalovirus (CMV). The virus affects more than half of all individuals and is contracted, for most part, at a young age. Because there is no cure, the virus is carried for life, and is particularly prevalent in older adults.

"CMV doesn't usually cause outward symptoms, but we still have to live with it every day since there's no cure," Dr. Smithey says. "Our immune system always will be busy in the background dealing with this virus."

Drs. Smithey and Nikolich-Žugich wondered how this lifelong virus ultimately affects the immune system. "We assumed it would make mice more vulnerable to other infections because it was using up resources and keeping the immune system busy," Dr. Smithey said.

But that's not what happens.

When infected with listeria, old mice carrying CMV proved to be tougher than old mice without CMV. "We were completely

surprised; we expected these mice to be worse off," Dr. Smithey says. "But they had a more robust, effective response to the infection."

The researchers are not certain how CMV strengthens the immune system -- they are investigating that in a separate study -- but they do believe they have gained new insight into the aging immune system. "This study shows us that there is more capacity in the immune system at an older age than we thought," Dr. Smithey says.

When the researchers examined the mice's T-cells -- the army of defenders that fights off infection -- they found that both groups of older mice had a decent supply of diverse T-cells.

"Diversity is good," Dr. Nikolich-Žugich says. "Different types of T-cells respond to different types of infections; the more diverse T-cells you have, the more likely you'll be able to fight off infections."

For years, immunobiologists assumed that T-cell diversity decreased as we age. This was one of the reasons why older adults succumbed to disease more easily.

But Drs. Smithey and Nikolich-Žugich's study shows that T-cells are almost as diverse in old mice as they are in young mice. The problem is that diverse T-cells are not recruited to the battlefield in older mice -- unless they are infected with CMV.

Dr. Nikolich-Žugich explains, "It's as if CMV is issuing a signal that gets the best defenses out onto the field." "This shows that the ability to generate a good immune response exists in old age -- and CMV, or the body's response to CMV, can help harness that ability," Dr. Smithey adds.

The UA College of Medicine - Tucson team plans to continue to study CMV. It hopes to see similar results in human studies. The team's ultimate goal is to create a vaccine that can improve the immune system of older adults and protect against infection.

This work was supported by U.S. Public Health Service Grant U54 AI081680 (Pacific Northwest Research Center of Excellence in Biodefense and Emerging Diseases), National Institute of Allergy and Infectious Diseases Grant HHSN27220110017C and National Institute on Aging Grant R01 AG048021 from the National Institutes of Health.

Dr. Nikolich-Žugich also is a member of the UA BIO5 Institute. Dr. Smithey is a research assistant professor who specializes in immunobiology and a member of the Arizona Center on Aging.

Other members of the research team included Vanessa Venturi and Miles P. Davenport, Infection Analytics Program, Kirby Institute for Infection and Immunity, University of New South Wales Australia; Adam S. Buntzman, UA BIO5 Institute; Benjamin G. Vincent, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill; and Jeffrey A. Frelinger, UA Department of Immunobiology.

http://bit.ly/2KVcK7p

A pretty plant of summer produces a promising anti-diabetes compound

Roughly half of the western medicines used today were derived from naturally occurring plant metabolites.

Montbretia (ヒメトウショウブ属), a popular summer garden plant.
Seohyun (Jenny) Jo, University of British Columbia.

Plants produce over 200,000 of these specialized metabolites, but identifying medicinally useful ones is challenging, and obtaining sufficient quantities for human use poses an even greater challenge.

Type-2 diabetes, a disease characterized by elevated blood glucose levels due to the body's inefficient use of insulin, affects over 320 million people worldwide. Drugs that are commonly used to treat type-2 diabetes reduce blood glucose levels by inhibiting the activities of two enzymes: HPA (pancreatic alpha-amylase), which cleaves complex starches into strings of sugar molecules called oligosaccharides and alpha-glucosidases, which convert oligosaccharides into glucose in the gut. Unfortunately, the inhibition of alpha-glucosidases causes some undigested oligosaccharides to move into the lower bowel, leading to flatulence and diarrhea.

Ten years ago, in an effort to produce a diabetes drug that specifically inhibits HPA activity without having nasty side effects, scientists screened 30,000 extracts derived from plants and other organisms

and found a single compound that fit the bill: montbretin A (MbA) from the bulb-like underground corms of the ornamental plant montbretia (*Crocosmia* x *crocosmiiflora*) (see figure). Unfortunately, MbA can't be produced in large quantities without understanding the biochemical pathway and genes involved in its biosynthesis, a difficult task considering the diversity and complexity of plant metabolic pathways.

Scientists from the University of British Columbia and the Canadian Glycomics Network analyzed this crucial pathway, as discussed in this month's issue of *The Plant Cell*. The scientists discovered the first three intermediate metabolites in the MbA biosynthesis pathway, including a product called mini-MbA, which also strongly inhibits HPA activity, as well as the four enzymes involved in mini-MbA production. Importantly, when they cloned the genes for these enzymes and used them to genetically transform wild tobacco, they successfully obtained mini-MbA. According to lead scientist Dr. Joerg Bohlmann of the University of British Columbia, Vancouver BC, "This is a fascinating example of the largely undiscovered potential of plant specialized metabolism that may lead to new treatments for the improvement of human health".

The Plant Cell, *DOI: 10.1105/tpc.18.00406*

http://bit.ly/2zcjk89

People Ration Where They Roam

Analysis of 40,000 people' movements suggests most of us frequent only 25 places

By Christopher Intagliata on July 2, 2018

An analysis of the movement of some 40,000 people suggests most of us frequent only 25 places—and as we sub in new favorites, we drop old ones. Christopher Intagliata reports.

Tally up all your "regular spots"—places you visit on a weekly basis like restaurants, markets, parks. And what do you get? A new study says that most of us limit our hangouts to some 25 places.

"So every time we adopt a new place, we abandon another one. This is how we reshape our routines." Andrea Baronchelli, a physicist at City, University of London. "So we are actually boring at any point in time. But over the course of time we change the places we are boring in."

Baronchelli and his team analyzed the movements of nearly 40,000 people worldwide, using mostly anonymized location data from the Sony Lifelog app. And they found that—regardless of age, gender, geographic location—as users explored new places, they maintained a steady roster of about 25 regular haunts.

"I think this is really a universal, a deep property of us as humans, of the way we balance this tension between exploration and exploitation."

The researchers did see a link between how active study subjects were socially and the number of spots they frequented. People who were more active had a slightly higher number of regular spots. The scientists estimated social activity by phone calls, texts and Facebook interactions. That finding suggests that our friends could ramp up our exploratory behavior. The results are in the journal *Nature Human Behavior*. [Laura Alessandretti et al., Evidence for a conserved quantity in human mobility]

The researchers themselves admit that their lunch routine is in keeping with their discovery. "Every day we say we should try something else, and then we say, 'maybe tomorrow.'"

https://go.nature.com/2zqPr6r

Europe's biggest research fund cracks down on 'ethics dumping'

The practice of conducting ethically dubious research in foreign countries is under fresh scrutiny.

Linda Nordling

Ethics dumping — doing research deemed unethical in a scientist's home country in a foreign setting with laxer ethical rules — will be

rooted out in research funded by the European Union, officials announced last week.

Applications to the EU's €80-billion (US$93-billion) Horizon 2020 research fund will face fresh levels of scrutiny to make sure that research practices deemed unethical in Europe are not exported to other parts of the world. Wolfgang Burtscher, the European Commission's deputy director-general for research, made the announcement at the European Parliament in Brussels on 29 June.

Burtscher said that a new code of conduct developed to curb ethics dumping will soon be applied to all EU-funded research projects. That means applicants will be referred to the code when they submit their proposals, and ethics committees will use the document when considering grant applications.

Isidoros Karatzas, whose office is in charge of ethics review in the European Commission, calls ethics dumping "a real threat to the quality of science" and compares it to research misconduct. "What is important is that it does not take place, and that our researchers have the knowledge and awareness not to allow it to happen," he adds.

The rules will apply to all research funded under Horizon 2020, and to all future EU funding programmes. The EU had banned ethics dumping in Horizon 2020 grants since 2013. But no clear guidelines existed to help ethics reviewers and researchers identify potential digressions in grant applications. The code, which was drafted as part of a Horizon 2020-funded project called TRUST, was published in May; the latest announcement gives it teeth.

The code provides clear guidance for doing research in resource-poor settings. Animal research, for example, must not be conducted outside the EU if it would not be allowed in the scientists' home country. Another provision states that "lower educational standards, illiteracy or language barriers" among research participants can never be an excuse to hide information from them or provide it incompletely. The code also addresses situations that might not arise in Europe-based studies. For instance, sex work is legal in many countries in Europe but not in Kenya. And homosexuality is illegal in many countries worldwide. So studies involving sex workers or gay people, for example, must take measures to ensure the safety of participants.

The ethics-dumping guidelines were produced with representatives from such vulnerable populations. Joyce Adhiambo, a Kenyan former sex worker who promotes sex worker rights in research and in HIV-prevention services, sees the code as a matter of mutual respect. "When [researchers] want something from sex workers, we deal with it respectfully. We ask the same in return," she said at the Brussels event.

Adhiambo told *Nature* that researchers must use their privileged position to encourage communities to become actively involved in studies. Members could be hired as research assistants, for example, or to help translate and explain consent forms to participants. "We come from a poor setting but we have a voice. We have a culture and a way of living. We have our traditional knowledge, and when we walk in the path together we are going to make a brighter future for all these research projects."

Ethics dumping — coined by the European Commission in 2013 — is a contentious term and few researchers admit to the practice. In a book published recently, researchers with the TRUST project cited research carried out on wild-caught monkeys in Africa, and clinical trials in India in which people living in poverty were denied life-saving screening in the control arm, as examples of ethics dumping.

None of those projects was funded by the EU, says Doris Schroeder, a lead investigator on the TRUST project. But in her 15 years chairing ethics review panels for EU funding programmes, Schroeder has seen many applications that would violate the new code.

These ranged from researchers wanting to interview workers about their rights in dictatorial states (potentially placing these people at

risk) to art installations portraying vulnerable populations without their involvement. Those projects were changed before getting funding approval, Schroeder says. But without a clear code of conduct it's possible that other ethics committees might have let them through.

Ron Iphofen, an adviser on research ethics to the European Commission, believes the code will have a profound impact on how funding proposals to the EU are designed and reviewed. "I could envisage reviewers now looking suspiciously at any application for funds that entailed research by wealthy nations on the less wealthy that did not mention the code," he says.

Opportunities for ethics dumping have grown with the globalization of research, says Philip Brey, a research ethics specialist at the University of Twente in the Netherlands. Increasingly, researchers from high-income countries carry out projects in low- and middle-income ones.

But Brey says that the decision to export research is often driven by scientific opportunities or economic realities, rather than a desire to skirt ethics. Moreover, some scientists in poorer countries find the term 'ethics dumping' offensive. "They tend to see themselves not as having lower ethical standards, but different ethical standards," says Brey.

Reinhard Hiller, managing director of the Centre for Proteomic and Genomic Research in Cape Town, South Africa, worries that in some cases developed nations' ethical standards could stifle research in developing nations. For example, to speed up and improve the quality of their diagnoses, doctors in Africa might want to use WhatsApp to share patient information such as X-rays, says Hiller. Yet this could fall foul of Europe's strict data privacy rules, for example. "It's not black or white, but needs to be assessed on a case-by-case basis."

Nature ***559***, *17-18 (2018) doi: 10.1038/d41586-018-05616-w*

https://bbc.in/2MWuBLT

Drug gets body cells to 'eat and destroy' cancer

Scientists have designed a special type of drug that helps the body eat and destroy cancerous cells.

The treatment boosts the action of white blood cells, called macrophages, that the immune system uses to gobble up unwanted invaders. Tests in mice showed the therapy worked for aggressive breast and skin tumours, Nature Biomedical Engineering journal reports. The US team behind the study hope to begin human trials within a few years.

The drug that they designed already has a licence, which they say should hasten the approval process. It is a "supramolecule" - a drug built from component molecules that fit together like building blocks.

Treatments that target the immune system to fight cancer are a growing area of research that lots of scientists around the world are investigating. This latest work involves a devouring or "phagocytic" immune cell called the macrophage.

Eating cancer

Macrophages are already good at fighting bacterial and viral infections because they can recognise and attack these "foreign" invaders. But they are not so effective at tackling cancer, since tumours grow from our own cells and have clever mechanisms to hide from immune attack. The drug Dr Ashish Kulkarni and colleagues at Harvard Medical School's Brigham and Women's Hospital used in their study works in two ways.

Firstly, it stops cancer cells from hiding and sending out "eat me not" signals to macrophages. Secondly, it prevents the tumour from telling macrophages to turn docile. The supramolecular therapy appeared to stop cancer from growing and spreading in the test mice.

The researchers envisage that it could be used alongside other cancer treatments such as checkpoint inhibitors.

Carl Alexander, from Cancer Research UK, said: "It's promising to see yet another new approach. More work is now needed to show that this approach could be used to treat cancer patients."

http://bit.ly/2KBQ8wx

More than 8 million babies born from IVF since the world's first in 1978

European IVF pregnancy rates now steady at around 36 percent, according to ESHRE monitoring

Barcelona - Forty years after the birth of Louise Brown, the world's first test-tube baby, an international committee monitoring progress in assisted reproduction reports today that the global total of babies born as a result of IVF and other advanced fertility treatments is "more than 8 million".(1) Dr David Adamson speaking at this congress on behalf of the International Committee for Monitoring ART (ICMART) said: "Based on ICMART's annual collection of global IVF data, it is estimated that since Louise Brown's birth in 1978 over 8 Million babies have been born from IVF around the world."

The figure, calculated from data collected from regional registries from 1991 to 2014, represent another steep rise in the cumulative use of IVF in the treatment of infertility. Estimates are that more than a half million babies are now born each year from IVF and ICSI from more than 2 million treatment cycles performed.

In Europe, Spain remains the most active country in assisted reproduction. ESHRE has collected the national registry data of ART cycles performed in Europe since 1997 and for its latest report (for 2015) found that a record 119,875 treatment cycles were performed in Spain, which now sets the pace of European treatment ahead of Russia (110,723 cycles), Germany (96,512) and former front runner France (93.918). The cycles monitored by ESHRE include treatments with IVF, ICSI, and egg donation.(2)

The report covers a total of almost 800,000 treatment cycles performed in 2015 and 157,449 babies born - and represents the largest and most accurate snapshot of ART in Europe.(3) Dr Christian de Geyter, chairman of ESHRE's European IVF Monitoring Consortium, will present the results today in Barcelona at the 34th Annual Meeting of ESHRE.

Dr de Geyter estimates that around 80% of all European assisted reproduction fertility treatments are included in the monitoring programme - but this year (ie, for 2015) without the data so far from the UK. The UK usually performs around 60,000 treatments a year.

Among other findings:

- ***Clinics in Europe continue to favour ICSI over IVF by around two-to-one (356,351 ICSI, 131,221 IVF), a pattern now evident throughout the world. ICSI was developed in the early 1990s as a specific treatment for male infertility (low sperm counts, poor sperm quality) but is now clearly used for fertilisation in non-male cases.***
- ***Pregnancy rates (as measured per embryo transfer) seem to have stabilised in Europe at about 36% for both IVF and ICSI. Pregnancy rates are higher with five-day old embryos (blastocysts) than with three-day.***
- ***Pregnancy rates from egg donation continue to rise (now at about 50%).***
- ***The rate of twin pregnancy continues to decline in Europe, in 2015 to around 14%. Similarly, the rate of single embryo transfers continues to rise - from 11% in 1997 to 38% in 2015.***

"Success rates have stabilised," said ESHRE's EIM committee chairman Christian De Geyter, "although outcome in egg donation and with use of frozen embryos is still moving upwards. The biggest upwards movement, however, is from treatments with frozen eggs, which have been revolutionised by the widespread introduction of vitrification."

Also gaining ground is embryo freezing. All embryos in 15% of all treatment cycles monitored in 2015 were frozen before thawing and

transfer in a subsequent cycle. Uptake of this "freeze-all" approach increased by 7% on the previous year. Freezing by vitrification would also explain the increase in egg donation treatments, no doubt made possible by egg banking and the greater availability of donor eggs.

De Geyter also noted that the availability of assisted reproduction treatment remains very patchy in Europe, with Denmark and Belgium each offering more than 2500 treatment cycles per million population, while others (such as Austria and Italy) offer considerably fewer. A study calculated that the global need for advanced fertility treatments was around 1500 cycles per million population per year. "Only a minority of European countries meet this need," said De Geyter.

Abstract 0-145, Tuesday 3 July 2017 O-145: European IVF monitoring of ART and development of a strategy for vigilance

1. Louise Brown, the world's first IVF baby, was born on 25 July 1978 at Oldham General Hospital, UK. Her in vitro conception - with an egg collected from a natural cycle - was led by the Cambridge reproductive biologist Robert Edwards (a later founder of ESHRE) and the Oldham gynaecologist Patrick Steptoe.

2. The data collection and monitoring of ESHRE's EIM Consortium have grown more complex with the progress of ART. IUI was added to the techniques monitored in 2002, while present data collections must include PGD, in vitro maturation, and frozen oocyte replacement. Collecting data on a single procedure is no longer a simple matter of recording a cycle, but must now acknowledge oocyte and/or embryo cryopreservation, transfer in a fresh or future (non-stimulated) cycle, and outcome, which may well be several years after the initial egg collection cycle.

3. The total number of cycles submitted to the ESHRE Consortium is now increasing by about 7% per year, meaning that the Consortium has monitored a cumulative total of almost 9 million cycles since its formation in 1997 and more than 1.6 million children born.

http://bit.ly/2J1vfoN

Finding suggest HPV testing detects cervical pre-cancer earlier, more accurately than Pap smear

Bottom Line: ***Nearly all cervical cancers are associated with persistent cervical infection from cancer-related human papillomavirus (HPV) strains. Testing for HPV alone, or combined with a Pap smear (cytology) for cervical screening, has been associated with increased detection of precancerous lesions compared with Pap smears alone.*** Some organizations have recommended primary HPV-based cervical cancer screening, while others have called for clinical trials of primary HPV testing alone. This study reports the results of a large randomized clinical trial of about 19,000 women that compared primary HPV testing alone versus Pap test for cervical screening. The study demonstrates that primary HPV testing of women detects precancerous lesions earlier, and more accurately than the Pap test. Furthermore, women who were HPV negative were less likely than women screened by Pap tests to have cervical pre-cancer after four years. More research is needed to understand the long-term outcomes and cost-effectiveness of HPV testing.

Authors: *Gina Suzanne Ogilvie, M.D., F.C.F.P., Dr.P.H., University of British Columbia, Vancouver, Canada, and coauthors*

Visual Abstract: JAMA *is introducing this new feature initially focused on randomized clinical trials. A predictive link to the abstract that will work when the embargo lifts is* ***here****.*

Related material: *The editorial, "**Replacing the Pap Test With Screening Based on Human Papillomavirus Assays,**" by L. Stewart Massad, M.D., Washington University School of Medicine, St. Louis, Missouri, is also available on the For The Media website.*

http://bit.ly/2m0n7Mn

This man was fired by a computer – real AI could have saved him

Ibrahim Diallo was allegedly fired by a machine.

July 3, 2018 by Adrian Hopgood,

Recent news reports relayed the escalating frustration he felt as his security pass stopped working, his computer system login was disabled, and finally he was frogmarched from the building by security personnel. His managers were unable to offer an explanation, and powerless to overrule the system.

Some might think this was a taste of things to come as artificial intelligence is given more power over our lives. Personally, I drew the opposite conclusion. Diallo was sacked because a previous manager hadn't renewed his contract on the new computer system

and various automated systems then clicked into action. The problems were not caused by AI, but by its absence.

The systems displayed no knowledge-based intelligence, meaning they didn't have a model designed to encapsulate knowledge (such as human resources expertise) in the form of rules, text and logical links. Equally, the systems showed no computational intelligence – the ability to learn from datasets – such as recognising the factors that might lead to dismissal. In fact, it seems that Diallo was fired as a result of an old-fashioned and poorly designed system triggered by a human error. AI is certainly not to blame – and it may be the solution.

The conclusion I would draw from this experience is that some human resources functions are ripe for automation by AI, especially as, in this case, dumb automation has shown itself to be so inflexible and ineffective. Most large organisations will have a personnel handbook that can be coded up as an automated, expert system with explicit rules and models. Many companies have created such systems in a range of domains that involve specialist knowledge, not just in human resources.

But a more practical AI system could use a mix of techniques to make it smarter. The way the rules should be applied to the nuances of real situations might be learned from the company's HR records, in the same way common law legal systems like England's use precedents set by previous cases. The system could revise its reasoning as more evidence became available in any given case using what's known as "Bayesian updating". An AI concept called "fuzzy logic" could interpret situations that aren't black and white, applying evidence and conclusions in varying degrees to avoid the kind of stark decision-making that led to Diallo's dismissal.

The need for several approaches is sometimes overlooked in the current wave of overenthusiasm for "deep learning" algorithms, complex artificial neural networks inspired by the human brain that can recognise patterns in large datasets. As that is all they can do, some experts are now arguing for a more balanced approach. Deep learning algorithms are great at pattern recognition, but they certainly do not show deep understanding.

Using AI in this way would likely reduce errors and, when they did occur, the system could develop and share the lessons with corresponding AI in other companies so that similar mistakes are avoided in the future. That is something that can't be said for human solutions. A good human manager will learn from his or her mistakes, but the next manager is likely to repeat the same errors.

So what are the downsides? One of the most striking aspects of Diallo's experience is the lack of humanity shown. A decision was made, albeit in error, but not communicated or explained. An AI may make fewer mistakes, but would it be any better at communicating its decisions? I think the answer is probably not.

Losing your job and livelihood is a stressful and emotional moment for anyone but the most frivolous employees. It is a moment when sensitivity and understanding are required. So, I for one would certainly find human contact essential, no matter how convincing the AI chatbot.

A sacked employee may feel that they have been wronged and may wish to challenge the decision through a tribunal. That situation raises the question of who was responsible for the original decision and who will defend it in law. Now is surely the moment to address the legal and ethical questions posed by the rise of AI, while it is still in its infancy.

http://bit.ly/2N0HbcL

The Gaia Sausage: The major collision that changed the Milky Way galaxy

An international team of astronomers has discovered an ancient and dramatic head-on collision between the Milky Way and a smaller object, dubbed the "Sausage" galaxy.

New York City -- The cosmic crash was a defining event in the early history of the Milky Way and reshaped the structure of our galaxy, fashioning both its inner bulge and its outer halo, the astronomers report in a series of new papers.

The astronomers propose that around 8 billion to 10 billion years ago, an unknown dwarf galaxy smashed into our own Milky Way. The dwarf did not survive the impact: It quickly fell apart, and the wreckage is now all around us.

An impression of the encounter between the Milky Way galaxy and the smaller Sausage galaxy about 8 billion to 10 billion years ago. The record of this ancient encounter is still preserved in the velocities and chemistry of the stars. **V. Belokurov (Cambridge, UK); Based on image by ESO/Juan Carlos Muñoz**

"The collision ripped the dwarf to shreds, leaving its stars moving in very radial orbits" that are long and narrow like needles, said Vasily Belokurov of the University of Cambridge and the Center for Computational Astrophysics at the Flatiron Institute in New York City. The stars' paths take them "very close to the centre of our galaxy. This is a telltale sign that the dwarf galaxy came in on a really eccentric orbit and its fate was sealed."

The new papers in the *Monthly Notices of the Royal Astronomical Society*, *The Astrophysical Journal Letters* and arXiv.org outline the salient features of this extraordinary event. Several of the papers were led by Cambridge graduate student GyuChul Myeong. He and colleagues used data from the European Space Agency's Gaia satellite. This spacecraft has been mapping the stellar content of our galaxy, recording the journeys of stars as they travel through the Milky Way. Thanks to Gaia, astronomers now know the positions and trajectories of our celestial neighbours with unprecedented accuracy.

The paths of the stars from the galactic merger earned them the moniker "the Gaia Sausage," explained Wyn Evans of Cambridge. "We plotted the velocities of the stars, and the sausage shape just jumped out at us. As the smaller galaxy broke up, its stars were thrown onto very radial orbits. These Sausage stars are what's left of the last major merger of the Milky Way."

The Milky Way continues to collide with other galaxies, such as the puny Sagittarius dwarf galaxy. However, the Sausage galaxy was much more massive. Its total mass in gas, stars and dark matter was more than 10 billion times the mass of our sun. When the Sausage crashed into the young Milky Way, its piercing trajectory caused a lot of mayhem. The Milky Way's disk was probably puffed up or even fractured following the impact and would have needed to regrow. And Sausage debris was scattered all around the inner parts of the Milky Way, creating the 'bulge' at the galaxy's centre and the surrounding 'stellar halo.'

Numerical simulations of the galactic mashup can reproduce these features, said Denis Erkal of the University of Surrey. In simulations run by Erkal and colleagues, stars from the Sausage galaxy enter stretched-out orbits. The orbits are further elongated by the growing Milky Way disk, which swells and becomes thicker following the collision.

Evidence of this galactic remodelling is seen in the paths of stars inherited from the dwarf galaxy, said Alis Deason of Durham University. "The Sausage stars are all turning around at about the same distance from the centre of the galaxy." These U-turns cause the density in the Milky Way's stellar halo to decrease dramatically where the stars flip directions. This discovery was especially pleasing for Deason, who predicted this orbital pileup almost five years ago. The new work explains how the stars fell into such narrow orbits in the first place.

The new research also identified at least eight large, spherical clumps of stars called globular clusters that were brought into the Milky Way by the Sausage galaxy. Small galaxies generally do not have globular clusters of their own, so the Sausage galaxy must have been big enough to host a collection of clusters.

"While there have been many dwarf satellites falling onto the Milky Way over its life, this was the largest of them all," said Sergey Koposov of Carnegie Mellon University, who has studied the kinematics of the Sausage stars and globular clusters in detail.

PAPERS

In http://adsabs.harvard.edu/abs/2018MNRAS.478..611B, the authors describe the local evidence but also outline explicitly and precisely what sort of event this was and how much debris it could contribute to the inner Milky Way halo. The researchers also analyse cosmological simulations to pin down the mass and the time of the accretion and point out that it may have produced the thick disk.

In http://adsabs.harvard.edu/abs/2018arXiv180510288D, the authors point out that the deposits of stellar debris from this event have similar apocenters and are naturally responsible for the stellar halo break.

In http://adsabs.harvard.edu/abs/2018arXiv180500453M, the authors demonstrate that this merger has brought a large number of globular clusters into the Milky Way, and that these stand out clearly from the rest of the galactic population.

In http://adsabs.harvard.edu/abs/2018ApJ...856L..26M, the authors point to the evidence for this merger in the distribution of actions and also highlight the existence of the large retrograde spray of debris.

In http://adsabs.harvard.edu/abs/2018arXiv180407050M, the authors discuss in detail the retrograde debris and provide comparisons to a simple model of a massive merger.

http://bit.ly/2KDQB1j

Global warming may be twice what climate models predict

Past warming events suggest climate models fail to capture true warming under business-as-usual scenarios

Future global warming may eventually be twice as warm as projected by climate models under business-as-usual scenarios and even if the world meets the 2°C target sea levels may rise six metres or more, according to an international team of researchers from 17 countries.

The findings published last week in *Nature Geoscience* are based on observational evidence from three warm periods over the past 3.5 million years when the world was 0.5°C-2°C warmer than the pre-industrial temperatures of the 19th Century.

The research also revealed how large areas of the polar ice caps could collapse and significant changes to ecosystems could see the Sahara Desert become green and the edges of tropical forests turn into fire dominated savanna. "Observations of past warming periods suggest that a number of amplifying mechanisms, which are poorly represented in climate models, increase long-term warming beyond climate model projections," said lead author, Prof Hubertus Fischer of the University of Bern.

"This suggests the carbon budget to avoid 2°C of global warming may be far smaller than estimated, leaving very little margin for error to meet the Paris targets."

To get their results, the researchers looked at three of the best-documented warm periods, the Holocene thermal maximum (5000-9000 years ago), the last interglacial (129,000-116,000 years ago) and the mid-Pliocene warm period (3.3-3 million years ago).

The warming of the first two periods was caused by predictable changes in the Earth's orbit, while the mid-Pliocene event was the result of atmospheric carbon dioxide concentrations that were 350-450ppm - much the same as today.

Combining a wide range of measurements from ice cores, sediment layers, fossil records, dating using atomic isotopes and a host of other established paleoclimate methods, the researchers pieced together the impact of these climatic changes.

In combination, these periods give strong evidence of how a warmer Earth would appear once the climate had stabilized. By contrast, today our planet is warming much faster than any of these periods as human caused carbon dioxide emissions continue to grow. Even if

our emissions stopped today, it would take centuries to millennia to reach equilibrium.

The changes to the Earth under these past conditions were profound - there were substantial retreats of the Antarctic and Greenland ice sheets and as a consequence sea-levels rose by at least six metres; marine plankton ranges shifted reorganising entire marine ecosystems; the Sahara became greener and forest species shifted 200 km towards the poles, as did tundra; high altitude species declined, temperate tropical forests were reduced and in Mediterranean areas fire-maintained vegetation dominated.

"Even with just 2°C of warming - and potentially just 1.5°C - significant impacts on the Earth system are profound," said co-author Prof Alan Mix of Oregon State University.

"We can expect that sea-level rise could become unstoppable for millennia, impacting much of the world's population, infrastructure and economic activity."

Yet these significant observed changes are generally underestimated in climate model projections that focus on the near term. Compared to these past observations, climate models appear to underestimate long term warming and the amplification of warmth in Polar Regions.

"Climate models appear to be trustworthy for small changes, such as for low emission scenarios over short periods, say over the next few decades out to 2100. But as the change gets larger or more persistent, either because of higher emissions, for example a business-as-usual-scenario, or because we are interested in the long term response of a low emission scenario, it appears they underestimate climate change.," said co-author Prof Katrin Meissner, Director of the University of New South Wales Climate Change Research Centre.

"This research is a powerful call to act. It tells us that if today's leaders don't urgently address our emissions, global warming will bring profound changes to our planet and way of life - not just for this century but well beyond."

http://bit.ly/2MUpnjJ

Were Our Ancestors Sleeping in Trees 3 Million Years Ago?

That's only one question posed by a new analysis of an extraordinary* Australopithecus *skeleton.

Robinson Meyer Jul 6, 2018

Selam, the most complete juvenile skeleton of an early-human ancestor ever discovered DeSilva et al. / Science Advances

It happened fast—that's all we know.

Perhaps the young girl fell out of a tree or was struck by an illness. Maybe she drowned. But 3.3 million years ago, a roughly 3-year-old *Australopithecus afarensis* died in modern-day Ethiopia.

From her misfortune has sprung a wealth of knowledge. She fossilized quickly, likely because she tumbled into a stream bed or rushing floodwaters. The movement of rocks and water were kind to her skeleton, leaving it largely intact and whole. And soon after her skull was spotted sticking out of a cliff wall in 2000, anthropologists realized they had something unprecedented on their hands.

The girl is the most complete juvenile skeleton of an early-human ancestor ever discovered. Her skull, neck, vertebrae, rib cage, and lower body are almost entirely preserved. Even her brain left a cast of its shape on the rock. Scientists call her Selam, after the Amharic word for "peace."

"The presentation is remarkable—it's like nothing I've ever seen before," said Jeremy DeSilva, a professor of anthropology at Dartmouth College. "Adult bones are larger, denser, and more easily discovered. Kid bones are often quite fragile, and they don't preserve.

Every so often, we find a fragmentary piece of a kid's mandible, or some teeth. But this discovery is just extraordinary."

Selam's discovery was first announced in 2006: After first spotting her in 2000, it took the paleontologist Zeresenay Alemseged and his team more than half a decade just to unearth her skeleton intact. It has taken another 12 years for a related team to image and reveal the chunks of rock that contained her foot bones.

On Wednesday, the latter team published the first results of their work, in the journal *Science Advances*.

Their analysis matters because it gets to one of the most important questions in piecing together humans' origin story: When did we learn to walk on two feet? *Australopithecus*, whose dozens of subspecies roamed Africa before the Ice Age, seems to provide a key phase in that story.

And Selam's skeleton is presented in a way like very few other early-human fossils. "The bones are still in anatomical association," said Kim Congdon, an anthropologist at Touro University Nevada who was not connected to the new paper. In other words, Selam's foot bones still connect as they connected in life.

"Mostly, when we find fossils, they're scattered. Lucy's skeleton was scattered over a wide area. Nothing was found with one bone connecting to the next—but in this skeleton, her foot is still held together, which allows us to really see how these bones in life were oriented," said DeSilva, an author of the new paper.

Take Selam's big toe, which is somewhat larger and bendier than a modern-day human child's. Anthropologists have long argued that the shape of a primate's big toe implies a kind of evolutionary trade-off: A large, curved big toe makes it easy to climb trees; a short, stubby one makes it easier to walk on two feet. Compare a human's foot to a chimpanzee's, for instance. Chimpanzees have a long, grasping big toe, positioned on the foot in roughly the same place as an opposable thumb. Chimps also "almost sprint up trees," DeSilva said.

Humans, meanwhile, have short, stubby big toes. We're adept at walking, but when it's time to ascend trees, we have to lift ourselves slowly and carefully. "It appears that as you acquire the adaptations for upright walking, you necessarily lose some of the anatomies that are good for climbing," DeSilva told me.

These chimp-human differences are more than happenstance. Chimpanzees are modern humans' closest living relatives, and we share a common ancestor 7 million years in the past. "Humans and chimps also have the same 26 foot bones—they're just shaped a little bit differently. It's those subtle differences that make *all* the difference in how we use our foot," he said.

The new paper argues that Selam's toe was somewhere in between. It wasn't as long as a chimp's toe, but it had more grasping ability than a modern human's. DeSilva and his colleagues argue that young *Australopithecus* like Selam had long, big toes because they were climbing around a lot—even if they weren't as skilled at the arboreal life as chimpanzees.

"These kiddos would be scrambling up trees if they got spooked by a predator, or they'd be climbing up on their moms to be carried," DeSilva told me. "In the absence of strollers and Baby Björns, moms had to carry their kids. And if the kids can grab onto you a little bit, when you pick them up, that reduces the energy needed to carry them."

"I don't think they're climbing like chimpanzees do," he added. "They don't have the anatomies for it—but they do have the anatomy to climb slightly better than we do."

He and his colleagues argue that Selam's toe helps resolve a long-running puzzle about this era of human ancestors. By 3.3 million years ago, *Australopithecus* adults seem to have had very "humanlike" feet. Their feet were well adapted for walking. Even young kids would have been bipedal. But even adult *Australopithecus* still have

curved, apelike big toes. Hence the debate: Perhaps *Australopithecus* was both climbing trees *and* walking around. Perhaps large toes were—like the modern human appendix—a mostly useless, vestigial feature that had not yet been lost to evolution's dynamo.

DeSilva proposed a third choice: "The adults look the way they do because those very adults were once kids, and their bones were once growing. Now, bones were living tissue, and they're going to respond to what you're doing—so if you're climbing a whole lot, those bones are going to respond and they're going to curve."

Australopithecus also probably climbed trees at night, though not to hunt. As the sun set on the savanna, family units or larger social groups would have avoided predators by climbing into trees at night to sleep. "They're likely slowly going up into the trees, passing the babies up, and building night nests," DeSilva told me. "But they're much better suited for living on the ground and walking like we do."

Michelle Drapeau, an anthropologist at the University of Montreal who was not involved in this research, told me that she agreed that Selam's longer toe probably allowed for "a little more movement than there is in modern humans."

But she doubted whether big toes helped *Australopithecus* babies cling to their mothers. Researchers have found that modern-day monkeys hold on to their mothers by flexing their smaller toes. Why would *Australopithecus* children be any different? "You don't really need this prehensile big toe to grab to your mom's hair," she said.

The many overlapping interpretations of the big toe point to the difficulty of tracking human evolutionary history—particularly of "primitive" traits, features that once existed but are now lost.

"When you look at traits that you *know* have changed from the ancestor, then you know there was natural selection, because the trait became different. But if a trait is still there, you don't know if it [remained] because there was no reason to get rid of it, or because it was still important," Drapeau said.

All of which didn't make the paper's interpretation unreasonable, she added: "It's just not the only one."

And note this entire discussion follows from just one of Selam's features. There are dozens more hypotheses and theories to be gleaned from the foot. The new paper also asserts that Selam's foot had an arch; Drapeau wasn't so sure about that interpretation, either. The paper also finds that Selam's heel bone wasn't as well developed and bony as a human adult's. This is less of a surprise, as modern-day human children have softer, smaller heel bones that enlarge and harden as they grow. Since *Australopithecus* adults seem to have large heel bones, this suggests that *Australopithecus* kids developed similarly to how human children do today.

https://go.nature.com/2zqGWbL

Contagious cancer could have wiped out America's first dogs

Ancient-genome study finds that indigenous dogs in North and South America split from other domestic canines around 15,000 years ago.

Colin Barras

A vast population of indigenous domestic dogs once roamed the Americas, concludes one of the largest studies yet of ancient dog DNA, published in *Science* on 5 July[1]. Today, almost nothing remains of this dog family, apart from a bizarre transmissible cancer.

Ceramic sculptures, including this roughly 2,000-year-old figure from a burial in western Mexico, show the importance of dogs to ancient humans.
The Walters Art Museum/CC0 1.0

The oldest known domestic-dog remains in the Americas are approximately 9,900-year-old skeletons from a site in Illinois; they were deliberately buried, implying that the animals were important to their owners[2]. But exactly when those dogs arrived in the Americas or how they relate to domestic dogs elsewhere has been unclear, says Angela Perri, an archaeologist at Durham University, UK.

To find out, Perri and her colleagues analysed DNA from 71 ancient dogs that lived across North America and Siberia over the past 10,000 years. On the basis of the animals' mitochondrial genomes — which are inherited maternally — the researchers found that all of the ancient American dogs belonged to the same population, distinct from modern and ancient Eurasian dogs. Analysis of the nuclear genomes of seven of the canines confirmed this.

Isolated population

From the genome data, the researchers estimate that the last common ancestor of the ancient American dogs lived about 14,600 years ago — and that it separated from Siberian dogs roughly 1,000 years before that. Humans first crossed into Alaska from Asia around 20,000 years ago, and the dogs may have been imported by later waves of hunter-gatherers.

To study the legacy of the first American dogs, the researchers examined the DNA of more than 5,000 modern dogs from across North and South America. The team concluded that these animals traced only 2-4% of their ancestry to indigenous American dogs.

The researchers speculate that when Europeans arrived in the New World in the 15th century, they favoured their own dogs and prevented them from breeding with indigenous ones, and so the indigenous dogs died out. That would make sense, says Elaine Ostrander, a geneticist at the National Human Genome Research Institute in Bethesda, Maryland. "You're going to believe what you bring with you is better than what's already there," she says.

Canine cancer

Elinor Karlsson, a geneticist at the Broad Institute in Cambridge, Massachusetts, isn't persuaded. "It seems ridiculous to me, given the scale of loss of the dogs, to argue this came down to human preference," she says. In an essay[3] accompanying the research paper, she suggests that a contagious cancer contributed to the indigenous dogs' demise.

Canine transmissible venereal tumour (CTVT) is one of a handful of known contagious cancers — more famous are the two forms that threaten Tasmanian devils with extinction. CTVT is a parasitic clone of a tumour that emerged in a single dog and has since gone global, largely owing to contact between dogs during mating. It creates large tumours on the genitals of males and females.

Karlsson's idea emerges from the paper's discovery that CTVT originated as early as 8,225 years ago, in a dog that was more closely related to indigenous American dogs than to modern Eurasian dogs. Despite its close genetic ties with indigenous American dogs, the researchers think the tumour emerged in Asia in a relative of the dog population that had entered the Americas several millennia earlier. Other evidence suggests that the tumour diversified in Asian dogs, before spreading to Europe and Africa in the past 2,000 years[4]. It probably reached the Americas only 500 years ago, with the arrival of Europeans and their dogs.

Karlsson speculates that the close genetic relationship between the tumour and indigenous American dogs might explain the dogs' disappearance. CTVT isn't fatal in most dogs, because their immune system recognizes the tumour cells as foreign and limits the damage they cause. Perhaps, Karlsson says, the immune systems of indigenous American dogs overlooked the tumour cells because the cells' DNA was so similar to their own. The tumours might, then, have grown more aggressively in indigenous dogs, eventually killing them or stopping them from mating.

Elizabeth Murchison, a geneticist at the University of Cambridge, UK, who co-led the latest study, finds that to be a plausible explanation for the disappearance of indigenous American dogs. “The last remaining vestige of this dog’s group might have contributed to its downfall,” she says. *doi: 10.1038/d41586-018-05645-5*

http://bit.ly/2u15jVW

Ancient genome analyses reveal mosaic pattern of goat domestication thousands of years ago

Goat domestication was a mosaic -- not a singular -- process, with capture from the wild impacting genetic diversity in different regions of the Fertile Crescent

An international team of scientists, led by geneticists from Trinity College Dublin, have sequenced the genomes from ancient goat bones from areas in the Fertile Crescent where goats were first domesticated around 8,500 BC. They reveal a 10,000-year history of local farmer practices featuring genetic exchange both with the wild and among domesticated herds, and selection by early farmers.

This genetic data - including 83 mitochondrial sequences and whole genome data from 51 goats - is published today by PhD Researcher in Genetics, Kevin Daly, and colleagues, in leading international journal Science.

One of our first domesticates and a source of meat, milk and hides, goats now number almost a billion animals. They have been a partner animal since c. 8,500 BC. The earliest evidence for domestic goats occurs in the Fertile Crescent region of Southwest Asia, where crop farming and animal herding began. Before herding, local hunters targeted wild goats - also known as bezoar - and this local practice eventually became the basis of goat management and livestock keeping. However, reading the past from examining modern genetics is difficult due to thousands of years of migration and mixture.

"Just like humans, modern goat ancestry is a tangled web of different ancestral strands. The only way to unravel these and reach reliably into the past is to sequence genomes from actual ancient animals; a kind of molecular time travel," said Professor of Population Genetics and ERC Advanced Investigator at Trinity College Dublin, Dan Bradley, who led the project.

Using genetic data from over 80 ancient wild and domestic goats, the group has charted the initial patterns of domestication, demonstrating a surprising degree of genetic differentiation between goats across the Fertile Crescent and the surrounding regions.

Research Fellow at Trinity, and joint first author of the paper, Pierpaolo Maisano Delser, said: "Goat domestication was a mosaic rather than a singular process with continuous recruitment from local wild populations. This process generated a distinctive genetic pool which evolved across time and still characterises the different goat populations of Asia, Europe and Africa today."

Using ancient samples, the group was able to analyse the genetic diversity of different goat populations back in time and reconstruct the history of early domesticates. Domestic animals have changed human society and humans have also moulded livestock into hundreds of different types and breeds - this study has the earliest genetic discovery yet of this process. It seems that, like modern breeders, ancient farmers were interested in animal appearance.

PhD Researcher at Trinity, and first author of the paper, Kevin Daly, said: "Whole genome sequences from the past allowed us directly analyse some of the earliest goat herds. We found evidence that at least as far back as 8,000 years ago herders were interested in or valued the coat colour of their animals, based on selection signals at pigmentation genes." Furthermore, distinct but parallel patterns of this selection were observed in different early herds, suggesting this was a repeated phenomenon. There are also indications that these early animals had been selected for liver enzymes that gave better tolerance to new toxins, possibly from fungus growing on fodder, and also production traits such as fertility and size.

This research was funded by the European Research Council project CodeX.

http://bit.ly/2lZBSPk

Amyloid beta protein protects brain from herpes infection by entrapping viral particles

Chronic viral infection could induce overproduction of Alzheimer's-disease-associated protein and cause damaging inflammation

A Massachusetts General Hospital (MGH) study has found the mechanism by which amyloid beta (A-beta) - the protein deposited into plaques in the brains of patients with Alzheimer's disease - protects from the effects of herpes viruses commonly found in the brain. Along with another study appearing in the same July 11 issue of Neuron, which found elevated levels of three types of herpes viruses in the brains of patients with Alzheimer's disease, the MGH team's results support a potential role for viral infection in accelerating A-beta deposition and Alzheimer's progression.

"There have been multiple epidemiological studies suggesting people with herpes infections are at higher risk for Alzheimer's disease, along with the most recent findings from Icahn School of Medicine at Mt. Sinai that are being published with our study," says Rudolph Tanzi, PhD, director of the Genetics and Aging Research Unit in the MassGeneral Institute for Neurodegenerative Disease (MIND) and co-corresponding author of the *Neuron* paper. "Our findings reveal a simple and direct mechanism by which herpes infections trigger the deposition of brain amyloid as a defense response in the brain. In this way, we have merged the infection hypothesis and amyloid hypothesis into one 'Antimicrobial Response Hypothesis' of Alzheimer's disease."

Previous studies led by Tanzi and co-corresponding author Robert Moir, PhD, also of the MIND Genetics and Aging Research Unit, found evidence indicating that A-beta - long thought to be useless "metabolic garbage" - was an antimicrobial protein of the body's innate immune system, capable of protecting animal models and cultured human brain cells from dangerous infections. Given that brain infection with herpes simplex - the virus that causes cold sores - is known to increase with aging, leading to almost universal presence of that and other herpes strains in the brain by adulthood, the MGH team set out to find whether A-beta could protect against herpes infection and, if so, the mechanism by which such protection takes place.

After first finding that transgenic mice engineered to express human A-beta survive significantly longer after injections of herpes simplex into their brains than do nontransgenic mice, the researchers found that A-beta inhibited infection of cultured human brain cells with herpes simplex and two other herpes strains by binding to proteins on the viral membranes and clumping into fibrils that entrap the virus and prevent it from entering cells. Further experiments with the transgenic mice revealed that introduction of herpes simplex into the brains of 5- to 6-week-old animals induced rapid development of A-beta plaques, which usually appear only when the animals are 10 to 12 weeks old.

"Our findings show that amyloid entrapment of herpes viruses provides immediate, effective protection from infection," says Moir. "But it's possible that chronic infection with pathogens like herpes that remain present throughout life could lead to sustained and damaging activation of the amyloid-based immune response, triggering the brain inflammation that drives a cascade of pathologies leading to the onset of Alzheimer's disease. A key insight is that it's not direct killing of brain cells by herpes that causes Alzheimer's, rather it's the immune response to the virus that leads to brain-damaging neuroinflammation."

He continues, "Our data and the Mt. Sinai findings suggest that an antimicrobial protection model utilizing both anti-herpes and anti-amyloid drugs, could be effective against early Alzheimer's disease.

Later on when neuroinflammation has begun, greater benefit may come from targeting inflammatory molecules. However, it remains unclear whether infection is the disease's root cause. After all, Alzheimer's is a highly heterogeneous disease, so multiple factors may be involved in its development.

Tanzi says, "We are currently conducting what we call the 'Brain Microbiome Project,' to characterize the population of microbes normally found in the brain. The brain used to be considered sterile but it turns out to have a resident population of microbes, some of which may be needed for normal brain health. Our preliminary findings suggest that the brain microbiome is severely disturbed in Alzheimer's disease and that bad players - including herpes viruses - seem to take advantage of the situation, leading to trouble for the patient. We are exploring whether Alzheimer's pathogenesis parallels the disrupted microbiome models seen in conditions like inflammatory bowel disease, and the data generated to date are both surprising and fascinating."

Tanzi is the Joseph P. and Rose F. Kennedy Professor of Neurology, and Moir is an assistant professor of Neurology at Harvard Medical School. The lead author of the Neuron paper is William Eimer, PhD, of the MIND Genetics and Aging Unit. Additional co-authors are Deepak K.V. Kumar, PhD, Nanda K. N. Shanmugam, PhD, Alex S. Rodriguez, Teryn Mitchell and Kevin J. Washicosky, MIND Genetics and Aging Unit; and Bence György and Xandra O. Breakefield, PhD, MGH Neurology. The study was funded by grants from the Cure Alzheimer's Fund, Good Ventures and the Open Philanthropy Project.

http://bit.ly/2J91TFm

Bacterial survival in salty antifreeze raises hope for life on Mars and icy moons

New research by a trans-Atlantic team of scientists suggests that bacteria could survive in briny chemicals that exist on Mars, Enceladus, Europa, Pluto and possibly elsewhere.

Joelle Renstrom, Astrobiology Magazine, Astrobiology Magazine

The discovery of plumes and subsurface oceans on Jupiter's moon Europa, organic materials on Mars, and the likelihood of hydrothermal vents in the oceans of Saturn's moon Enceladus, inches humanity closer to discovering life elsewhere. Such life would have to withstand extreme environments, and previous studies indicate that various types of bacteria can.

Liquid oceans on some bodies far from the Sun have lower freezing points because of chemicals and salts that amount to antifreeze, so microbial life would have to survive both the temperatures and the elements. To zoom in on parameters for microbial survivability, researchers from the Technical University of Berlin, Tufts University, Imperial College London, and Washington State University conducted tests with Planococcus halocryophilus, a bacteria found in the Arctic permafrost.

They subjected the bacteria to sodium, magnesium and calcium chloride cocktails, as well as solutions of perchlorate, which is a chemical compound that may help Mars sustain liquid water during the summer. Lead author Jacob Heinz, of the Technical University of Berlin's Center of Astronomy and Astrophysics, says that the researchers expanded beyond the conventional sodium chloride solution because "there's much more than that on Mars."

Toxic to life

Since perchlorates are toxic in large concentrations, researchers wanted to determine whether, how much and at what concentrations they might inhibit bacterial survivability. Survival rates for bacteria in perchlorate were far lower than in all the other solutions, although at temperatures as low as –30 degrees Celsius (–22 degrees Fahrenheit), the rates were slightly better.

Heinz explains that the lowest freezing point depression – the extent to which a solute can lower a solution's freezing temperature – for perchlorate requires roughly 50 percent of the mass of the total solution, which is incredibly high compared to the freezing-point depression of other chlorides. Given its toxicity, the low survivability of bacteria in concentrated perchlorate solutions isn't surprising.

Does that mean that Mars can't support microbial life? According to Heinz, life is still a possibility there. The presence of perchlorate "wouldn't preclude life on Mars or elsewhere," he says. "Bacteria in ten percent mass perchlorate solutions can still grow." Mars's surface soil contains less than one weight percent of perchlorate, but Heinz points out that salt concentrations in solutions are different than those in soil.

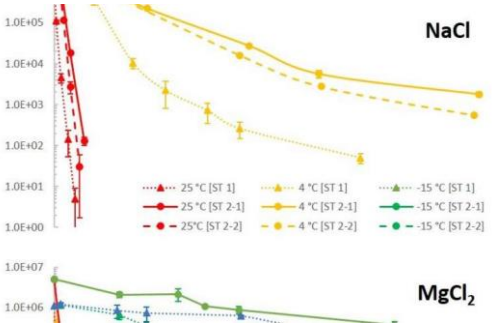
Adapted to survive

Liquid perchlorate solutions can also be diluted to increase the bacteria's ability to survive, though a balance between concentration and temperature would have to be maintained.

Theresa Fisher, a Ph.D. student at Arizona State University's School of Earth and Space Exploration who focuses on microbial ecology and planetary habitability, agrees that the study's results don't rule out bacterial survival on Mars – in fact, perhaps the opposite.

Places such as the Atacama Desert (the world's driest environment) in Chile and parts of Antarctica have relatively high perchlorate levels, Fisher tells Astrobiology Magazine. "I'd be surprised if microbes haven't evolved a way to deal with that toxicity," she says. Generally, colder temperatures boost microbial survivability, but temperature isn't a "one-size-fits-all" factor– the type of microbe and the composition of the chemical solution also determine the sweet spot for survivability. The researchers found that bacteria in a sodium chloride (NaCl) solution died within two weeks at room temperature. At four degrees Celsius, survival increased, and once temperatures hit –15 degrees Celsius (5 degrees Fahrenheit), almost all the bacteria survived. NaCl has a higher freezing point (–21 degrees Celsius/–5.8 degrees Fahrenheit) than the other salts; bacteria in the magnesium and calcium-chloride solutions had high survival rates at –30 degrees Celsius (–22 degrees Fahrenheit).

This isn't surprising because "all reactions, including those that kill cells, are slower at lower temperatures," says Heinz, "but bacterial survivability didn't increase much at lower temperatures in the perchlorate solution, whereas lower temperatures in calcium chloride solutions yielded a marked increase in survivability."



The survival rates of bacteria in various types of salt – sodium chloride (NaCl), magnesium chloride (MgCl2) and calcium chloride (CaCl2). In general, the cooler the temperature, the longer they survived. **J. Heinz et al**

Results also varied between the three more conventional saline solvents. Bacteria in calcium chloride (CaCl2) had significantly lower survival rates than those in sodium chloride (NaCl) and magnesium chloride (MgCl2) between 4 and 25 degrees Celsius, but lower temperatures boosted survival in all three.

Researchers subjected the bacteria to numerous freeze/thaw cycles ranging from 25 degrees Celsius (77 degrees Fahrenheit) to –50 degrees Celsius (–58 degrees Fahrenheit). Mars can undergo some pretty dramatic surface temperature changes, both diurnal and seasonal, depending on the location on the planet says Heinz. The average temperature on Mars is roughly –60 degrees Celsius (–76 degrees Fahrenheit), with temperatures at the poles dropping to –125 degrees Celsius (–193 degrees Fahrenheit). Consequently, bacteria need to be able to endure extreme fluctuations in order to survive.

Generally, saltier solutions improved freeze/thaw survival rates. According to Fisher, "bacteria, when stressed, have shock responses. They manufacture specific proteins that help them adjust, survive, and cope with detrimental environments." Adding 10 percent sodium chloride decreased the microbial death rate from 20 percent to 7

percent and increased the number of freeze/thaw cycles the bacteria could sustain from 70 to 200. Bacteria manufacture stabilizing proteins as a shock response to severe environments, Fisher explains, "but there are only so many shock proteins bacteria can produce."

Survival versus growth

While the study provides insight into extraterrestrial microbial possibilities, Heinz emphasizes the difference between surviving and thriving. Just because bacteria subsist in certain conditions doesn't mean they actually grow. Heinz is currently working on another study to determine how different concentrations of salts across different temperatures affect bacterial propagation.

"Survival versus growth is a really important distinction," Fisher affirms, "but life still manages to surprise us. Some bacteria can not only survive in low temperatures, but require them to metabolize and thrive. We should try to be unbiased in assuming what's necessary for an organism to thrive, not just survive."

Studies that explore various salt solutions, concentrations, and temperatures help scientists focus the search for life, or at least not rule out possibilities, such as microbial survival in toxic perchlorate. Other variables affect the search for life, such as a bacteria's ability to withstand radiation or extreme atmospheric pressure. There may even be factors we don't know about yet, but with each study, there's one fewer haystack to search.

https://bbc.in/2udZlQQ

Yes! We have no bananas: Why the song may come true again

A wild banana that may hold the key to protecting the world's edible banana crop has been put on the extinction list.

By Helen Briggs BBC News

It is found only in Madagascar, where there are just five mature trees left in the wild. Scientists say the plant needs to be conserved, as it may hold the secret to keeping bananas safe for the future.

Most bananas consumed around the world are of a type known as the Cavendish, which is vulnerable to a plant pest.

The race is on to develop new banana varieties that are both tasty to eat and resilient enough to survive attack from Panama disease.

The Madagascan banana has evolved in isolation on an island cut off from the mainland, and may have special properties.

Richard Allen, senior conservation assessor at the Royal Botanic Gardens, Kew, said the species (*Ensete perrieri*) could have in-built tolerance to drought or disease.

"It doesn't have Panama disease in it, so perhaps it has genetic traits against the disease," he said.

"We don't know until we actually do research on the banana itself, but we can't do the research until it's saved." Kew scientists searched for the banana plant in Madagascar and found it was almost extinct in the wild.

Floral haven

They hope that its inclusion on the latest official Red List of the IUCN (International Union for Conservation of Nature) will highlight its plight.

Dr Hélène Ralimanana of the Kew Madagascar Conservation Centre says the plant is part of the island's rich floral heritage. "It is very important to conserve the wild banana because it has large seeds which can offer an opportunity to find a gene to improve the cultivated banana," she said.

If the wild banana can be protected, there will be opportunities to collect the seeds and look at the plant's genetic make-up.

The Madagascan banana produces seeds within the fruit, which means it is not palatable to eat. But cross-breeding could lead to a new type of banana that would be both edible and resilient.

The banana grows on the edge of forests, where it is vulnerable to damage from severe weather events as well as from logging, fires and the clearing of forests for farming.

Why are bananas vulnerable to disease?

Bananas are clones - which means they are all the same. So, if the disease is present in one plant it can spread quickly throughout the whole population.

What's the problem? I can still buy bananas in the shops

That is the case for now, but it may not be so in the future.

The disease affecting the Cavendish is currently confined to Asia, but if it were to spread to the Americas, it could wipe out the world's banana crop. This actually happened in the 1950s with a type of banana known as the Gros Michel (often known as Big Mike).

The song, "Yes! We Have No Bananas," is said to have been inspired by a shortage of Gros Michel bananas, which began with an outbreak of the fungus behind Panama disease.

Gros Michel bananas were replaced by Cavendish bananas, which are named after William Cavendish, the 6th Duke of Devonshire, who lived at Chatsworth House in Derbyshire. Bananas have been grown at Chatsworth since 1830 when head gardener Joseph Paxton propagated a specimen imported from Mauritius.

Nearly every banana now eaten is directly descended from this plant.

What do we know about the Madagascan banana?

It goes by the scientific name, *Ensete perrieri*, and is listed as Critically Endangered. It is found in the tropical forests of the country's western region where it is under threat from deforestation: only five mature trees are now reported to remain in the wild.

http://bit.ly/2u4XIWf

Novel HIV vaccine candidate is safe and induces immune response in healthy adults and monkeys

Mosaic HIV vaccine may have the potential to protect against wide variety of HIV strains worldwide

Phase 1/2 results have led to the initiation of a phase 2b clinical efficacy trial in southern Africa to determine whether vaccine candidate can prevent HIV infection in humans

New research published in *The Lancet* shows that an experimental HIV-1 vaccine regimen is well-tolerated and generated comparable and robust immune responses against HIV in healthy adults and rhesus monkeys. Moreover, the vaccine candidate protected against infection with an HIV-like virus in monkeys.

Based on the results from this phase 1/2a clinical trial that involved nearly 400 healthy adults, a phase 2b trial has been initiated in southern Africa to determine the safety and efficacy of the HIV-1 vaccine candidate in 2,600 women at risk for acquiring HIV. This is one of only five experimental HIV-1 vaccine concepts that have progressed to efficacy trials in humans in the 35 years of the global HIV/AIDS epidemic.

Previous HIV-1 vaccine candidates have typically been limited to specific regions of the world. The experimental regimens tested in this study are based on 'mosaic' vaccines that take pieces of different HIV viruses and combine them to elicit immune responses against a wide variety of HIV strains.

"These results represent an important milestone. This study demonstrates that the mosaic Ad26 prime, Ad26 plus gp140 boost HIV vaccine candidate induced robust immune responses in humans and monkeys with comparable magnitude, kinetics, phenotype, and durability and also provided 67% protection against viral challenge in monkeys", says Professor Dan Barouch, Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center and Professor of Medicine at Harvard Medical School, Boston, USA who led the study. [1]

He adds: "These results should be interpreted cautiously. The challenges in the development of an HIV vaccine are unprecedented, and the ability to induce HIV-specific immune responses does not necessarily indicate that a vaccine will protect humans from HIV infection. We eagerly await the results of the phase 2b efficacy trial

called HVTN705, or 'Imbokodo', which will determine whether or not this vaccine will protect humans against acquiring HIV." [1]

Almost 37 million people worldwide are living with HIV/AIDS, with an estimated 1.8 million new cases every year. A safe and effective preventative vaccine is urgently needed to curb the HIV pandemic.

In the 35 years of the HIV epidemic, only four HIV vaccine concepts have been tested in humans, and only one has provided evidence of protection in an efficacy trial--a canarypox vector prime, gp120 boost vaccine regimen tested in the RV144 trial in Thailand lowered the rate of human infection by 31% but the effect was considered too low to advance the vaccine to common use.

A key hurdle to HIV vaccine development has been the lack of direct comparability between clinical trials and preclinical studies. To address these methodological issues, Barouch and colleagues evaluated the leading mosaic adenovirus serotype 26 (Ad26)-based HIV-1 vaccine candidates in parallel clinical and pre-clinical studies to identify the optimal HIV vaccine regimen to advance into clinical efficacy trials.

The APPROACH trial recruited 393 healthy, HIV-uninfected adults (aged 18-50 years) from 12 clinics in east Africa, South Africa, Thailand, and the USA between February 2015 and October 2015. Volunteers were randomly assigned to receive either one of seven vaccine combinations or a placebo, and were given four vaccinations over the course of 48 weeks.

To stimulate, or 'prime', an initial immune response, each volunteer received an intramuscular injection of Ad26.Mos.HIV at the start of the study and again 12 weeks later. The vaccine containing 'mosaic' HIV Env/Gag/Pol antigens was created from many HIV strains, delivered using a nonreplicating common-cold virus (Ad26).

To 'boost' the level of the body's immune response, volunteers were given two additional vaccinations at week 24 and 48 using various combinations of Ad26.Mos.HIV or a different vaccine component called Modified Vaccinia Ankara (MVA) with or without two different doses of clade C HIV gp140 envelope protein containing an aluminium adjuvant.

Results showed that all vaccine regimens tested were capable of generating anti-HIV immune responses in healthy individuals and were well tolerated, with similar numbers of local and systemic reactions reported in all groups, most of which were mild-to-moderate in severity. Five participants reported at least one vaccine-related grade 3 adverse event such as abdominal pain and diarrhoea, postural dizziness, and back pain. No grade 4 adverse events or deaths were reported.

In a parallel study, the researchers assessed the immunogenicity and protective efficacy of the same Ad26-based mosaic vaccine regimens in 72 rhesus monkeys using a series repeated challenges with simian-human immunodeficiency virus (SHIV)--a virus similar to HIV that infects monkeys.

The Ad26/Ad26 plus gp140 vaccine candidate induced the greatest immune responses in humans and also provided the best protection in monkeys--resulting in complete protection against SHIV infection in two-thirds of the vaccinated animals after six challenges.

The authors note several limitations, including the fact that that the relevance of vaccine protection in rhesus monkeys to clinical efficacy in humans remains unclear. They also note that there is no definitive immunological measurement that is known to predict protection against HIV-1 in humans.

Writing in a linked Comment, Dr George Pavlakis and Dr Barbara Felber from the National Cancer Institute at Frederik, Maryland, USA say: "Efficacy studies are necessary to determine protective ability in humans and also for the discovery of correlates of protection and for determining whether the same or different immune correlates apply for different vaccine regimens. It remains to be determined whether improved efficacy over RV144 will be achieved

by either of the present efficacy trials (NCT02968849; NCT03060629). New vaccine concepts and vectors are in development and can progress to efficacy trials, which is an important process since development of an AIDS vaccine remains urgent. Despite unprecedented advances in HIV treatment and prophylaxis, the number of people living with HIV infection continues to increase worldwide. Implementation of even a moderately effective HIV vaccine together with the existing HIV prevention and treatment strategies is expected to contribute greatly to the evolving HIV/AIDS response. It is therefore essential that a commitment to pursue multiple vaccine development strategies continues at all stages."

NOTES TO EDITORS

This study was funded by Janssen Vaccines & Prevention BV, US National Institutes of Health, Ragon Institute of MGH, MIT and Harvard, Henry M Jackson Foundation for the Advancement of Military Medicine, US Department of Defense, and International AIDS Vaccine Initiative.

http://bit.ly/2ufi0vn

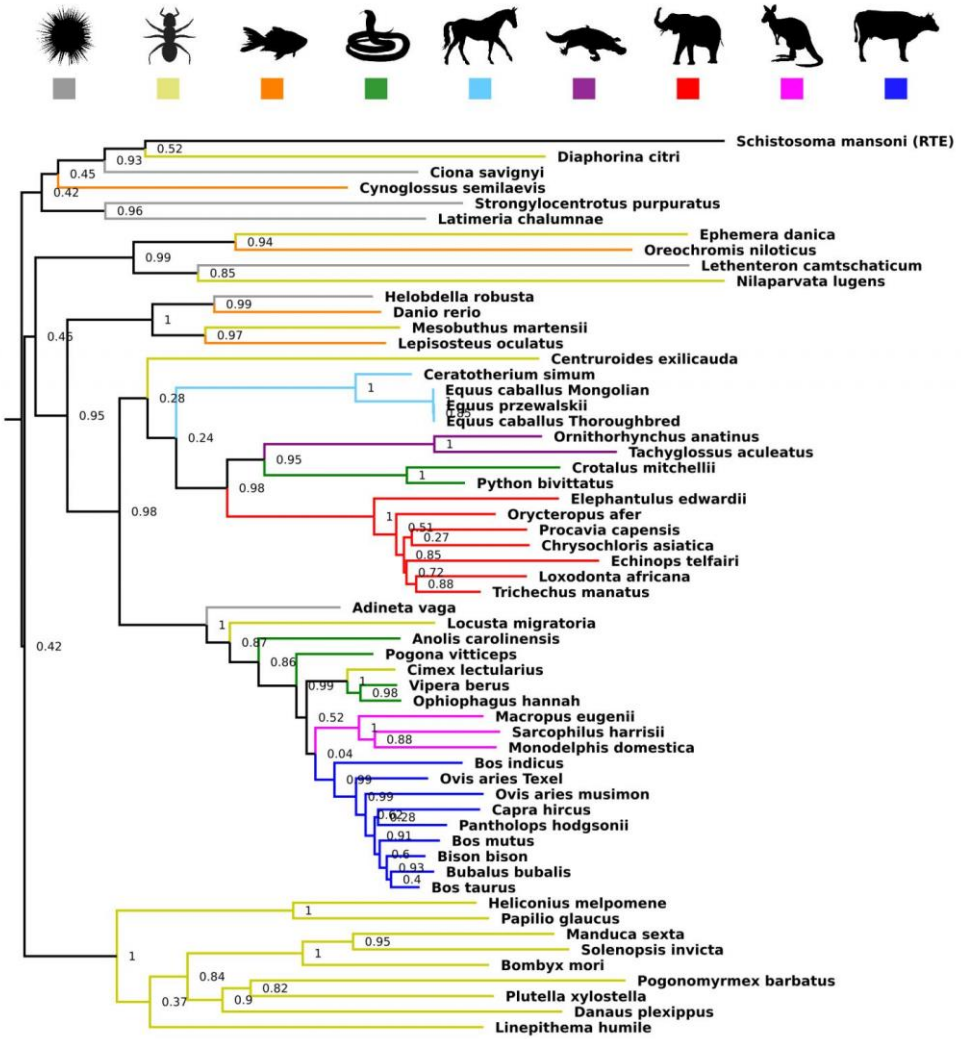
Cross species transfer of genes has driven evolution

Far from just being the product of our parents, University of Adelaide scientists have shown that widespread transfer of genes between species has radically changed the genomes of today's mammals, and been an important driver of evolution.

In the world's largest study of so-called "jumping genes", the researchers have traced two particular jumping genes across 759 species of plants, animals and fungi. These jumping genes are actually small pieces of DNA that can copy themselves throughout a genome and are known as transposable elements.

They have found that cross-species transfers, even between plants and animals, have occurred frequently throughout evolution.

Both of the transposable elements they traced - L1 and BovB - entered mammals as foreign DNA. This is the first time anyone has shown that the L1 element, important in humans, has jumped between species.



A graphic representation of the BovB element which shows how it has appeared in species that are wide apart on the evolutionary tree -- for example sea urchins and elephants, cows and snakes. **University of Adelaide**

"Jumping genes, properly called retrotransposons, copy and paste themselves around genomes, and in genomes of other species. How

they do this is not yet known although insects like ticks or mosquitoes or possibly viruses may be involved - it's still a big puzzle," says project leader Professor David Adelson, Director of the University of Adelaide's Bioinformatics Hub.

"This process is called horizontal transfer, differing from the normal parent-offspring transfer, and it's had an enormous impact on mammalian evolution."

For example, Professor Adelson says, 25% of the genome of cows and sheep is derived from jumping genes.

"Think of a jumping gene as a parasite," says Professor Adelson. "What's in the DNA is not so important - it's the fact that they introduce themselves into other genomes and cause disruption of genes and how they are regulated."

Published today in the journal *Genome Biology*, in collaboration with the South Australian Museum, the researchers found horizontal gene transfer was much more widespread than had been thought.

"L1 elements were thought to be inherited only from parent to offspring," says lead author Dr Atma Ivancevic, postdoctoral researcher in the University of Adelaide's Medical School. "Most studies have only looked at a handful of species and found no evidence of transfer. We looked at as many species as we could."

L1 elements in humans have been associated with cancer and neurological disorders. The researchers say that understanding the inheritance of this element is important for understanding the evolution of diseases.

The researchers found L1s are abundant in plants and animals, although only appearing sporadically in fungi. But the most surprising result was the lack of L1s in two key mammal species - the Australian monotremes (platypus and echidna) - showing that the gene entered the mammalian evolutionary pathway after the divergence from monotremes.

"We think the entry of L1s into the mammalian genome was a key driver of the rapid evolution of mammals over the past 100 million years," says Professor Adelson.

The team also looked at the transfer of BovB elements between species. BovB is a much younger jumping gene: it was first discovered in cows, but has since been shown to jump between a bizarre array of animals including reptiles, elephants and marsupials. Earlier research, led by Professor Adelson, found that ticks were the most likely facilitators of cross-species BovB transfer.

The new research extended the analysis to find that BovB has jumped even more widely than previously anticipated. BovB has transferred at least twice between frogs and bats, and new potential vector species include bed bugs, leeches and locusts.

The team believes that studying insect species will help find more evidence of cross-species transfer. They also aim to study other jumping genes and explore the possibility of aquatic vectors, such as sea worms and nematodes.

"Even though our recent work involved the analysis of genomes from over 750 species, we have only begun to scratch the surface of horizontal gene transfer," says Professor Adelson. "There are many more species to investigate and other types of jumping genes."