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Starting young vital to lifelong volunteering and social action, says new research

Children undertaking volunteering and service related activities from a young age, with strong support networks in place, are more likely to develop a habit of lifelong service, say researchers.

The University of Birmingham research found that participants who first engaged with service or volunteering under the age of 10 were more than twice as likely to have developed a 'habit' of social action than those who began from 16 to 18. Strong support networks and encouragement from schools were identified as key factors contributing to a lifelong 'habit of service' and social action.

The study, A Habit of Service, examined responses from over 4,500 young people - 3,300 of whom had been involved in youth social action programmes in the past 12 months. It was found those within the 'habit' group were more likely to be female and they participated more frequently in a wider range of 'service' activities – such as helping their local community, volunteering or mentoring.

Dr Tom Harrison, University of Birmingham and co-author of the report, published by the Jubilee Centre for Character and Virtues, stressed the practical importance of the research for social action providers across the country:

"These findings will help those in the voluntary sector plan and deliver youth social action programmes that support young people to cultivate a habit of service.

"The more people who contribute to the common good, the more likely we are to flourish as a nation."

The report found that the quality principles of social action, identified by charity Step Up To Serve, correlated with young people who have made a habit of service. In particular, those with a 'habit of service' were more likely to have volunteering opportunities embedded in their school, college or university, and were more likely to feel they had the time, skills and confidence to participate.

The findings highlight the role that schools and other institutions can play in facilitating young people's engagement in social action, particularly by embedding character education and other enrichment activities. Enjoyment of service activities was also found to be important, with participants who reported enjoying activities 'a great deal' 47 percent more likely to be in the habit group.

Those who had developed a 'habit' were also more likely to have parents and friends participating in similar activities.

Overall, friends' involvement had a more significant effect than parents," boosting participation by 14 percent within the habit group, and 12 percent amongst non-habit participants.

The report is launched in collaboration with the #iwill campaign, a longstanding partner of the Jubilee Centre in researching youth social action.

Writing in the report's foreword, Dame Julia Cleverdon and Amanda Jordan, co-founders of charity Step Up To Serve who oversee #iwill, emphasised both the societal and the personal benefits social action can have:

"…social action not only improves communities, but at the same time it improves the lives of the young people who undertake it, developing their character and skills in the process – what we call the 'double benefit' of youth social action."

http://bit.ly/2Bu9HPn

Microbe threat to Mars

Experiments suggest an ancient survival strategy on Earth could benefit bacterial hitch-hikers. Andrew Masterson reports.

The presence of water on Mars increases the possibility that human missions to the planet will inadvertently contaminate it with Earth species. And new research has uncovered the most likely potential threat.

Some planetary scientists have suggested the danger of microbial contamination on Mars is reduced because any water on the planet – such as that identified at the equatorial Gale Crater in 2015 – is hyper-

briny and likely shot through with bio-unfriendly ingredients such as high levels of sulfate.

Research led by astrobiologist Adam Stevens of the University of Edinburgh in Scotland, however, indicates that some types of terrestrial life might be tough enough to survive in such harsh conditions.

Stromatolites in northern Western Australia -- made by a biofilm-forming organism. **Ted Mead / Getty**

Stevens and his colleagues looked at biofilm-forming microbes. These are species that clump together on surfaces and embed themselves in a matrix of polysaccharides, proteins, DNA and fats (known collectively as "extracellular polymeric substances").

Biofilm-making microbes are found among bacteria and archaea, and the process is also conducted by some more complex species, including certain fungi and algae. Embedding in a biofilm offers increased protection from the environment, and typically affects gene regulation. Biofilm microbe colonies tend to grow very slowly, be highly resilient, and extremely long-lived.

These are qualities that might make them well suited to gaining a foothold in the wet areas of Mars, Stevens' team discovered.

In a series of experiments, the astrobiologists used a species of bacteria called *Sphingomonas desiccabilis*, found in the soil on the US Colorado Plateau. The microbe can survive in extremely dry conditions, and accumulates in self-made crusts.

The scientists created a number of brines thought to be identical to, or very similar to, those currently on Mars, and exposed the bacteria to them. Plankton cells were also exposed, as controls.

The results showed that while some brines were so concentrated that they killed everything put in them, others allowed *S. desiccabilis* to survive considerable lengths of time before succumbing. The longevity of the bacteria was extended if they were fully dried out before immersion.

In a paper currently on the pre-print server *biorix*, the researchers conclude that biofilms provide protection in conditions "potentially analogous" to those on Mars.

"Our results show that contaminant biofilm-forming microorganisms may have a greater chance of surviving," in briny areas on the planet, they write, "with implications for planetary protection in missions that aim to explore these regions."

http://bit.ly/2ADWpCB

Researchers develop world's first alcoholic beverage made from tofu whey

Successful transformation of liquid generated from tofu production into a tasty alcoholic beverage

A research team from the National University of Singapore (NUS) has successfully turned tofu whey, a liquid that is generated from the production of tofu and is often discarded, into a tasty alcoholic beverage which they named Sachi. The innovative fermentation technique also enriches the drink with isoflavones, which are antioxidants that have many health benefits.

Associate Professor Liu Shao Quan (right) and PhD student Mr Chua Jian Yong (left), both from the Food Science & Technology Programme under the NUS Faculty of Science, successfully turned tofu whey into a tasty alcoholic beverage which they named Sachi. **National University of Singapore**

The creation of Sachi was initiated a year ago by Associate Professor LIU Shao-Quan and his PhD student Mr CHUA Jian-Yong, who have an interest in sustainable food production. Both are from the Food Science and Technology Programme at the NUS Faculty of Science.

"The traditional way of manufacturing tofu produces a large amount of whey, which contains high levels of calcium and unique soya

nutrients such as isoflavones and prebiotics. Hence, disposing tofu whey is wasteful. Very little research has been done to transform tofu whey into edible food and beverage products. I had previously worked on alcohol fermentation during my undergraduate studies in NUS, so I decided to take up the challenge of producing an alcoholic beverage using the whey. The drink turned out to be tasty, which is a pleasant surprise," said Mr Chua.

Turning waste into a tasty beverage

Tofu, also known as bean curd, is a popular food made from soybeans. One of the most common methods of producing tofu is by curdling freshly boiled soya milk, cooling it, and pressing it into a solid block. During the pressing process to remove excess water, tofu whey is generated. However, when tofu whey is discarded as an untreated waste, it creates environmental pollution as the protein and soluble sugars in the whey could contribute to oxygen depletion in the waterways. In contrast, upcycling tofu whey can be a means of generating economic returns for businesses.

"The health benefits associated with soy products, coupled with changing preferences towards vegetarian diets, have fueled the growth of tofu production. As a result, the amount of tofu whey has also increased proportionally. Alcoholic fermentation can serve as an alternative method to convert tofu whey into food products that can be consumed directly. Our unique fermentation technique also serves as a zero-waste solution to the serious issue of tofu whey disposal," explained Assoc Prof Liu.

Under the guidance of Assoc Prof Liu, Mr Chua took about three months to come up with a unique recipe to make an alcoholic beverage from tofu whey. He first made fresh soya milk from soybeans, and then used the soya milk to make tofu. In the course of making tofu, he collected the whey. Sugar, acid and yeast were added to the tofu whey, and the concoction was fermented to produce the alcoholic beverage. Mr Chua also designed a novel fermentation technique which utilises the tofu whey fully without generating any waste. The whole process of making the alcoholic beverage takes about three weeks.

Biotransformation of tofu whey yields benefits

Altering the composition of tofu whey via biotransformation methods converts its strong beany odour into a fruity, sweet flavour, and extends the shelf life of tofu whey from less than one day to about four months. In addition, after fermentation, the bound isoflavones that were present in the tofu whey were transformed into free isoflavones that can be absorbed more easily by the human body. The result is a refreshing beverage that is a tad sweet, with fruity and floral notes, and has an alcohol content of about 7 to 8 per cent.

The team has filed a patent for the novel process of making Sachi, and they are looking to collaborate with industry partners to introduce the drink to consumers.

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Health Officials Agree Undetectable HIV Levels Likely Mean Uninfectious

Medical organizations endorse the "Undetectable = Untransmissible" campaign, which aims to raise awareness of scientific evidence showing that virally suppressed people living with HIV cannot infect others.

By Catherine Offord | November 27, 2017

More than 500 organizations from 67 countries have now endorsed a campaign promoting awareness that virally suppressed HIV-positive people cannot sexually transmit HIV. Launched in early 2016 to confront the stigma surrounding HIV infection, Prevention Access Campaign's Undetectable = Untransmissible (U=U) movement has received support from major medical organizations including the Centers for Disease Control and Prevention (CDC).

"The fact that people infected with HIV who are virally suppressed cannot sexually transmit the virus to others is now accepted in the HIV/AIDS community as a result of accumulating evidence since the

early 2000s," notes an editorial in *The Lancet HIV*, published earlier this month.

In particular, three large studies carried out in the last decade with couples practicing unprotected sex found zero reported cases of sexual transmission of the virus from a person with virally suppressed HIV to an HIV-negative partner. The findings support research showing that a daily dose of antiretroviral treatment (ART) can suppress the virus to undetectable levels and prevent spread to other people.

Jonathan Mermin, director of the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, outlined these findings in a statement published earlier this fall (September 27). However, he notes that there are still uncertainties surrounding transmission risk that need to be addressed with research.

"The public-health challenge now is moving from theory to implementation," he tells the *Washington Post*. "Many questions arise following the information that when a person with HIV has an undetectable viral load, he has effectively no risk of transmitting the virus."

The effect of missed medication on viral suppression, for example, is not currently well understood. And in some people, the viral load may fluctuate around the detectable limit, with unclear consequences for the risk of sexual transmission.

Nevertheless, the evidence-based message that effective treatment prevents HIV transmission has "already been successful in influencing public opinion, causing more people with HIV (and their friends and families) to comprehend that they can live long, healthy lives, have children, and never have to worry about passing on their infection to others," notes *The Lancet HIV*. "The clarity of the message will make it easier to promote the undeniable benefits of treatment," and to achieve "complete elimination of the entirely unfair and outdated stigma still faced by many people living with HIV today."

http://bit.ly/2zMI7PS

Removing chemical used to make Teflon-like coatings has led to fewer low birth weights and less brain damage

Has prevented more than 118,000 low-weight births and related brain damage in the United States

Government and industry efforts since 2003 to phase out chemicals used to make non-stick coatings, such as Teflon, have prevented more than 118,000 low-weight births and related brain damage in the United States.

This is the main finding of a new report -- based on analysis of new mothers' blood samples gathered for a national health study -- published Nov. 23 in the *International Journal of Hygiene and Environmental Health*.

Scientists behind the research, conducted at NYU School of Medicine, say that studies have long linked the chemicals -- famous for keeping food from sticking to pans -- with high blood pressure, birth defects, and lower-than-normal birth weights. These damaging health effects were major factors behind a 2006 agreement between the Environmental Protection Agency (EPA) and American manufacturers to curtail and eventually eliminate the harmful chemicals' production in 2014.

The study authors estimate that the drop in chemically linked low-birth weight babies saved the nation at least $13.7 billion by reducing infant hospital stays and the number of children in need of long-term care after cognitive damage; and by improving the prospects of children going on to achieve higher education levels and get better-paying jobs.

"The evidence is overwhelming that the EPA-industry accord to phase out chemicals once used in nonstick coatings has been a major success in protecting children's health," says study lead investigator and health epidemiologist Leonardo Trasande, MD, MPP, an associate professor at NYU Langone Health. "This policy designed to lessen human exposure has spared thousands of newborns from damage to their

health and saved U.S. taxpayers over a billion dollars in unnecessary health care costs."

Before 2006, the principal danger to fetuses and pregnant women, researchers say, came from chemicals used in the manufacture of the coating called perfluorooctanoic acid, or PFOA. Not occurring naturally in the environment, PFOA chemicals accumulate in the blood of marine mammals and in most humans exposed to them. Research over decades has linked even a nanogram (one-billionth of gram) increase in PFOA per milliliter of blood to an 18.9 gram reduction in birth weight.

A healthy newborn typically weighs about 8 pounds (3,600 grams), experts say, and a low birth weight -- associated with potential brain damage -- is considered anything less than 5.5 pounds (2,500 grams).

Trasande cautions that while the EPA-industry accord has greatly diminished blood PFOA levels, products manufactured before the phase-out are still in circulation. He also says that the health impact for chemical replacements for PFOA, related chemicals called perfluorinated compounds (PFCs) remain unknown. Both sets of chemicals are endocrine disruptors, a set of chemicals shown by recent studies to interfere with natural hormone function, says Trasande.

Senior study investigator Teresa M. Attina, MD, PhD, also of NYU Langone, says the detrimental health effects seen with the original nonstick chemical formulation warrant more thorough safety testing of PFCs before any more of them receive government approval.

For the new study, funded entirely by NYU Langone, the research team looked for PFOA levels in blood analyses kept on participants in the National Health and Nutrition Examination Survey. Since 1999, NHANES, as it is known, has gathered information about the prevalence of and risk factors for major diseases by annually surveying 5,000 volunteers.

Survey results showed that blood PFOA levels in women of child-bearing age, from 18 to 49, continued to rise from 2003 to 2008, when median levels peaked at 3.5 nanograms per milliliter. But the trend, investigators say, reversed in 2009, a few years after the phase-out was introduced, and hazardous blood levels began dropping from a median 2.8 nanograms per milliliter to 1.6 nanograms per milliliter by 2014.

Computer models were then used to project the percentage of low-weight births that could have been prevented from specific PFOA chemical exposure and to calculate the estimated health costs and lost income. According to the team's analysis, the number of low-birth weight babies in the United States attributable to such PFOA exposure dropped from a highpoint of 17,501 in 2008 to 1,491 in 2014.

In addition to Trasande and Attina, other members of the NYU research team are Julia Malits and Jan Blustein.

http://bit.ly/2Bucqbi

Autism and the smell of fear

Odors that carry social cues seem to affect volunteers on the autism spectrum differently

Autism typically involves the inability to read social cues. We most often associate this with visual difficulty in interpreting facial expression, but new research at the Weizmann Institute of Science suggests that the sense of smell may also play a central role in autism. As reported today in Nature Neuroscience, Weizmann Institute of Science researchers show that people on the autism spectrum have different - and even opposite - reactions to odors produced by the human body. These odors are ones that we are unaware of smelling, but which are, nonetheless, a part of the nonverbal communication that takes place between people, and which have been shown to affect our moods and behavior. Their findings may provide a unique window on autism, including, possibly, on the underlying developmental malfunctions in the disorder.

Researchers in the lab of Prof. Noam Sobel in the Institute's Neurobiology Department investigate, among other things, the smells that announce such emotions as happiness, fear or aggression to others.

Although this sense is not our primary sense, as it is in many other mammals, we still subliminally read and react to certain odors. For example "smelling fear," even if we cannot consciously detect its odor, is something we may do without thinking. Since this is a form of social communication, Sobel and members of his lab wondered whether it might be disrupted in a social disorder like autism.

To conduct their experiments, Sobel and lab members Yaara Endevelt-Shapira and Ofer Perl, together with other members of his lab, devised a series of experiments with a group of participants on the high functioning end of the autism spectrum who volunteered for the study. To begin with, the researchers tested the ability of both autistic and control volunteers to identify smells that can be consciously detected, including human smells like sweat. There was no significant difference between the groups at this stage, meaning the sense of smell in the autistic participants was not significantly different from that of controls.

Two groups were then exposed to either to the "smell of fear" or to a control odor. The smell of fear was sweat collected from people taking skydiving classes, and control odor was sweat from the same people, only this time it had been collected when they were just exercising -- without feeling fear.

This is where differences emerged: Although neither group reported detecting dissimilarities between the two smells, their bodies reacted to each in a different way. In the control group, smelling the fear-induced sweat produced measurable increases in the fear response, for example in skin conductivity, while the everyday sweat did not. In the autistic men, fear-induced sweat lowered their fear responses, while the odor of "calm sweat" did the opposite: It raised their measurable anxiety levels.

Next, the group created talking robotic mannequins that emitted different odors through their nostrils. These mannequins gave the volunteers, who were unaware of the olfactory aspect of the experiment, different tasks to conduct. Using mannequins enabled the researchers to have complete control over the social cues - odor-based or other - that the subjects received. The tasks were designed to evaluate the level of trust that the volunteers placed in the mannequins - and here, too, the behavior of autistic volunteers was the opposite of the control group: They displayed more trust in the mannequin that emitted the fear-induced odor and less in the one that smelled "calmer."

In continuing experiments, the researchers asked whether other subliminal "social odors" have a different impact in autism than in control groups. In one, the volunteers were exposed to sudden loud noises during their sessions while at the same time they were also exposed to a potentially calming component of body-odor named hexadecanal.

Another automatic fear response - blinking - was recorded using electrodes above the muscles of the eye. Indeed, the blink response in the control group was weaker when they were exposed to hexadecanal, while for those in the autistic group this response was stronger with hexadecanal.

In other words, the autistic volunteers in the experiment did not display an inability to read the olfactory social cues in smell, but rather they misread them. Sobel and his group think that this unconscious difference may point to a deeper connection between our sense of smell and early development.

Research in recent years has turned up smell receptors like those in our nasal passages in all sorts of other places in our bodies - from our brains to our uteri. It has been suggested that these play a role in development, among other things. In other words, it is possible that the sensing of subtle chemical signals may go awry at crucial stages in the brain's development in autism.

"We are still speculating, at this point," says Sobel, "but we are hoping that further research in our lab and others will clarify both the function of these unconscious olfactory social cues and their roots in such social disorders as autism."

Prof. Noam Sobel's research is supported by the Azrieli National Institute for Human Brain Imaging and Research, which he heads; the Carl and Micaela Einhorn-Dominic Institute for Brain Research, which he heads; the Nadia Jaglom Laboratory for the Research in the Neurobiology of Olfaction; the Adelis Foundation; the late H. Thomas Beck; the Rob and Cheryl McEwen Fund for Brain Research; the Mike Rosenbloom Foundation; European Research Council. Prof. Sobel is the incumbent of the Sara and Michael Sela Professorial Chair of Neurobiology.

http://bit.ly/2nbZBPR

Muscles can't get any faster than this ... a fundamental muscle speed limit

Superfast muscles have reached maximum speed attainable in any vertebrate muscle

When birds sing their elaborate songs, bats echolocate, rattlesnakes rattle and toadfish hum they use so-called superfast muscles, the fastest vertebrate muscles known. New research shows that these muscles have reached a maximum speed attainable in any vertebrate muscle.

Across all animals, different muscle types have evolved to perform vastly different tasks at different speeds.

Tortoise leg muscles move slow over several seconds, while hummingbird's flight muscles move fast dozens of times per second.

The speed record holders among vertebrates are the so-called superfast muscles, which can move up to 250 times per second.

Superfast muscles are all around us

- The iconic superfast muscles power the alarming rattle of rattlesnakes and courtship calls in fish, but over the last years we have discovered them to also power rapid echolocation calls essential to prey capture in bats and the elaborate vocal gymnastics of songbirds, says lead author of the study, Dr. Andrew Mead from the University of Vermont, USA.

- So although previously thought to be rare, these extreme muscles are all around us and seem to be typically used for the control of sound production, adds Dr. Coen Elemans, senior author on the study and head of the Sound Communication and Behavior group at University of Southern Denmark.

The study is published in eLife.

A common superfast ancestor?

In this work the team studied if all these superfast muscles use the same ways to achieve their extreme behavior and if they share a common ancestral superfast muscle.

- We show that all superfast muscles share certain specific adaptations that allow superfast contractions, says Dr. Mead.

Furthermore, the three fastest muscles - toadfish, songbird, and bat - have nearly identical maximum speed, which argued in favor of a shared ancestry.

Maximum speed limit reached

- Interestingly the story turned out otherwise, comments Dr. Elemans:

- By looking at presence of motor proteins we found that each of these three superfast muscles expresses a different one, arguing strongly in favor of independent ancestry.

Because superfast muscles converged in performance and mechanism this argues that they represent a maximum speed attainable in any vertebrate muscle.

- We also show that in songbirds the superfast muscles speed up as young animals learn to sing, but we don't yet know if this is due to a developmental program or maybe training.

Better understanding of normal muscles

- Animals that evolved some extreme physiological performance can teach us a lot about general mechanisms, says Elemans: - Any technical failure in a fine-tuned racecar most likely will noticeably slow it down, while the same failure in a robustly engineered family car may not be so noticeable.

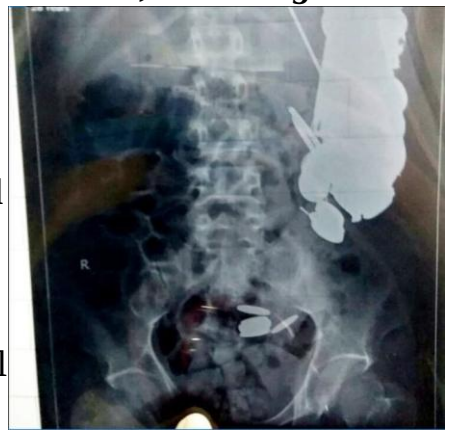
Superfast muscles are so interesting because extremely fast muscles allow us to gain a better understanding of how normal muscles contract.

http://bit.ly/2AfMlPn

Man Has Surgery to Remove 263 Coins, 100 Nails from Stomach

Doctors in India were shocked to find that a patient with stomach pain had swallowed hundreds of coins and nails, according to news reports.

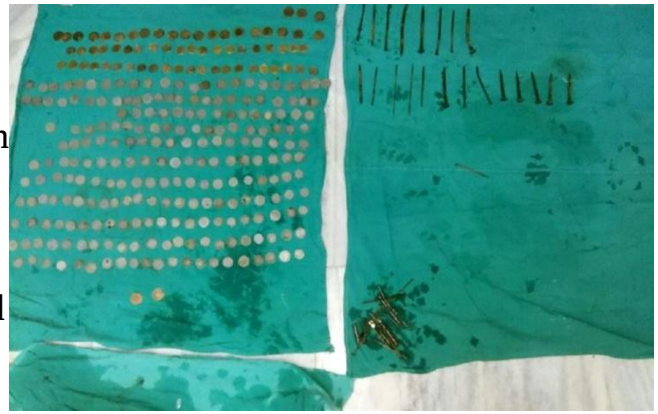
By Rachael Rettner, Senior Writer



The 35-year-old patient was recently admitted to the hospital with abdominal pain, and doctors initially thought he had food poisoning, according to the Independent. But an endoscopy exam - which uses a flexible tube to view the digestive tract - revealed numerous metal objects.

An image of coins and nails seen inside a man's gastrointestinal tract. **SWNS**

The doctors performed surgery, and eventually removed 263 coins, 100 nails, dozens of shaving blades and shards of glass, and a 6-inch piece of rusted iron shackle, the Independent said. In total, the collection of foreign objects removed from the patient weighed about 15 pounds (7 kilograms).



"We were shocked to discover that [there were] coins, nails and nut-bolts in his stomach," Dr. Priyank Sharma, of Sanjay Gandhi Hospital in Madhya Pradesh, India, who treated the patient, was quoted as saying.

Coins and nails that were found inside a man's stomach**: SWNS**

This is the first time the doctors had seen such a case in their careers, Sharma said.

The patient, Maksud Khan, is thought to have mental health problems, and didn't tell his friends or family about his strange eating behavior.

The new case is similar to one reported last month, in which a man in France was found to have more than 100 pieces of metal in his stomach, including coins and nails. In that case, the patient was diagnosed with psychosis, which means a person experiences a loss of touch with reality.

Another similar case occurred in 2016, when a 42-year-old man in India swallowed 40 knives. That patient said he felt "addicted" to the behavior, and he may have had pica, an eating disorder in which people eat nonfood materials such as metal for at least one month.

http://bit.ly/2i83os5

Beating heart patch is large enough to repair the human heart

Beating patch is as strong and electrically active as healthy adult heart

DURHAM, N.C. -- Biomedical engineers at Duke University have created a fully functioning artificial human heart muscle large enough to patch over damage typically seen in patients who have suffered a heart attack. The advance takes a major step toward the end goal of repairing dead heart muscle in human patients. The study appears online in Nature Communications on November 28, 2017.

"Right now, virtually all existing therapies are aimed at reducing the symptoms from the damage that's already been done to the heart, but no approaches have been able to replace the muscle that's lost, because once it's dead, it does not grow back on its own," said Ilya Shadrin, a biomedical engineering doctoral student at Duke University and first author on the study. "This is a way that we could replace lost muscle with tissue made outside the body."

Unlike some human organs, the heart cannot regenerate itself after a heart attack. The dead muscle is often replaced by scar tissue that can no longer transmit electrical signals or contract, both of which are necessary for smooth and forceful heartbeats.

The end result is a disease commonly referred to as heart failure that affects over 12 million patients worldwide. New therapies, such as the one being developed by Shadrin and his advisor Nenad Bursac, professor of biomedical engineering at Duke, are needed to prevent heart failure and its lethal complications.

Current clinical trials are testing the tactic of injecting stem cells derived from bone marrow, blood or the heart itself directly into the affected site in an attempt to replenish some of the damaged muscle. While there do seem to be some positive effects from these treatments, their mechanisms are not fully understood. Fewer than one percent of the injected cells survive and remain in the heart, and even fewer become cardiac muscle cells.

Heart patches, on the other hand, could conceivably be implanted over the dead muscle and remain active for a long time, providing more strength for contractions and a smooth path for the heart's electrical signals to travel through. These patches also secrete enzymes and growth factors that could help recovery of damaged tissue that hasn't yet died.

For this approach to work, however, a heart patch must be large enough to cover the affected tissue. It must also be just as strong and electrically active as the native heart tissue, or else the discrepancy could cause deadly arrhythmias.

This is the first human heart patch to meet both criteria. "Creating individual cardiac muscle cells is pretty commonplace, but people have been focused on growing miniature tissues for drug development," said Bursac. "Scaling it up to this size is something that has never been done and it required a lot of engineering ingenuity."

The cells for the heart patch are grown from human pluripotent stem cells -- the cells that can become any type of cell in the body. Bursac and Shadrin have successfully made patches using many different lines of human stem cells, including those derived from embryos and those artificially forced or "induced" into their pluripotent state.

Various types of heart cells can be grown from these stem cells: cardiomyocytes, the cells responsible for muscle contraction; fibroblasts, the cells that provide structural framework for heart tissue; and endothelial and smooth muscle cells, the cells that form blood vessels. The researchers place these cells at specific ratios into a jelly-like substance where they self-organize and grow into functioning tissue.

Finding the right combination of cells, support structures, growth factors, nutrients and culture conditions to grow large, fully functional patches of human heart tissue has taken the team years of work. Every container and procedure had to be sized up and engineered from scratch. And the key that brought it all together was a little bit of rocking and swaying.

"It turns out that rocking the samples to bathe and splash them to improve nutrient delivery is extremely important," said Shadrin. "We obtained three-to-five times better results with the rocking cultures compared to our static samples."

The results improved on the researchers' previous patches, which were one square centimeter and four square centimeters. They successfully scaled up to 16 square centimeters and five to eight cells thick. Tests show that the heart muscle in the patch is fully functional, with electrical, mechanical and structural properties that resemble those of a normal, healthy adult heart.

"This is extremely difficult to do, as the larger the tissue that is grown, the harder it is to maintain the same properties throughout it," said Bursac. "Equally challenging has been making the tissues mature to adult strength on a fast timescale of five weeks while achieving properties that typically take years of normal human development."

Bursac and Shadrin have already shown that these cardiac patches survive, become vascularized and maintain their function when implanted onto mouse and rat hearts. For a heart patch to ever actually replace the work of dead cardiac muscle in human patients, however, it would need to be much thicker than the tissue grown in this study.

And for patches to be grown that thick, they need to be vascularized so that cells on the interior can receive enough oxygen and nutrients. Even then, researchers would have to figure out how to fully integrate the heart patch with the existing muscle.

"Full integration like that is really important, not just to improve the heart's mechanical pumping, but to ensure the smooth spread of electrical waves and minimize the risk of arrhythmias," said Shadrin.

"We are actively working on that, as are others, but for now, we are thrilled to have the 'size matters' part figured out," added Bursac.

The research is part of a seven-year, $8.6 million grant from the National Institutes of Health. With the large heart patches in hand, the Bursac team is collaborating with researchers at the University of Alabama at Birmingham to develop procedures to successfully integrate the patch onto the hearts of pigs. Another affiliated team of researchers at the University of Wisconsin-Madison is working to develop improved stem cells for creating the main cell types that compose these heart patches, in the hopes of minimizing an immune response to the delivery of the engineered tissues.

This research was supported by Foundation Leducq and the National Institutes of Health (R01HL104326, R01HL12652, UG3TR002142, U01HL134764, 5T32GM007171, F30HL122079).

CITATION: "Cardiopatch platform enables maturation and scale-up of human pluripotent stem cell-derived engineered heart tissues," Ilya Y. Shadrin, Brian W. Allen, Ying Qian, Christopher P. Jackman, Aaron L. Carlson, Mark E. Juhas, and Nenad Bursac. Nature Communications, 2017. DOI: 10.1038/s41467-017-01946-x

http://bit.ly/2BtPYhE

Critical link between obesity and diabetes has been identified

Identification of major mechanism by which obesity causes type 2 diabetes

DALLAS - UT Southwestern researchers have identified a major mechanism by which obesity causes type 2 diabetes, which is a common complication of being overweight that afflicts more than 30 million Americans and over 400 million people worldwide.

Researchers found that in obesity, insulin released into the blood by the pancreas is unable to pass through the cells that form the inner lining of blood vessels. As a result, insulin is not delivered to the muscles, where it usually stimulates most of the body's glucose to be metabolized. Blood glucose levels rise, leading to diabetes and its related cardiovascular, kidney and vision problems, said Dr. Philip Shaul, Director of the Center for Pulmonary and Vascular Biology in the Department of Pediatrics at UT Southwestern.

"It was totally unpredicted that a major problem in obesity is the delivery of circulating insulin to your muscle. It was even more surprising that this problem involves immunoglobulins, which are the proteins that make up circulating antibodies," said Dr. Chieko Mineo, Associate Professor of Pediatrics, who is a co-senior author on the report with Dr. Shaul.

The researchers found that obese mice have an unexpected chemical change in their immunoglobulins. "The abnormal immunoglobulins then act on cells lining blood vessels to inhibit an enzyme needed to transfer insulin from the bloodstream into the muscle," said Dr. Shaul, who holds the Associates First Capital Corporation Distinguished Chair in Pediatrics. "Type 2 diabetes patients have the same chemical change, and if we give a mouse immunoglobulins from a type 2 diabetic individual, the mouse becomes diabetic."

The findings reported in The Journal of Clinical Investigation may lead to new tools for diabetes risk screening and new avenues for diabetes prevention or treatment. The researchers identified an agent that they could administer to mice that prevents the chemical change in immunoglobulins that occurs with obesity and preserves healthy glucose status. The researchers plan to test this strategy in humans in the near future.

Funding for the study came from the American Diabetes Association, the American Heart Association, The Hartwell Foundation, the Cancer Prevention and Research Institute of Texas (CPRIT) and the National Institutes of Health (NIH). Further research on both adults and children is under way with support from The Hartwell Foundation and the National Institutes of Health.

Other researchers involved were Dr. Keiji Tanigaki, senior research scientist and first author; Dr. Wanpen Vongpatanasin, Director of the Hypertension Section and holder of the Norman and Audrey Kaplan Chair in Hypertension Research at UT Southwestern; Dr. Jennifer Kohler, Associate Professor of Biochemistry; Dr. William Holland, Assistant Professor of Internal Medicine in the Touchstone Diabetes Center at UT Southwestern; and

collaborators from the University of Texas at Dallas, University of Alabama, University of Georgia, and Imperial College London.

http://bit.ly/2AEbxiM

Hip steroid injections associated with bone changes

Receiving steroid injection in the hip yields significantly greater incidence of bone death and collapse compared with control groups

CHICAGO - Osteoarthritis patients who received a steroid injection in the hip had a significantly greater incidence of bone death and collapse compared with control groups, according to new research presented today at the annual meeting of the Radiological Society of North America (RSNA).

Receiving an injection of a steroid and anesthetic is a common treatment for patients who are experiencing pain and inflammation in a joint, such as the hip, knee or shoulder.

"Changes due to osteoarthritis, such as narrowing in the space between joints and the development of bony proliferations, typically develop slowly over time," said Connie Y. Chang, M.D., radiologist at Massachusetts General Hospital and assistant professor of radiology at Harvard Medical School in Boston. "When reading follow-up radiographs of patients who had received a hip injection, we noticed changes had developed rapidly in some patients."

To determine whether arthritis worsened in patients following a hip steroid/anesthetic injection, Chang and a team of radiologists specializing in musculoskeletal diagnostic imaging and intervention, including hip injections, conducted a study involving 102 patients (age range 19-92, including 62 women) who received X-ray images of the treated hip at the time of the injection and during a follow-up three to nine months later.

Two musculoskeletal radiologists independently reviewed the X-ray images of the patients who received the injections and those of two control groups matched to demographics and follow-up imaging duration. The control groups consisted of 102 patients who had hip X-rays without steroid/anesthetic injection and 44 patients who underwent imaging and a steroid/anesthetic injection in the shoulder.

The radiologists reported new osteonecrosis in 22-24 percent of hip injection patients, compared to 5-9 percent in the hip control group and 5 percent in the shoulder injection control group. They observed bone collapse in the head of the femur bone, located at the top of the femur at the articulation with the pelvic bone, in 15-17 percent of hip injection patients, versus 4 percent of hip control patients and 2 percent of shoulder control patients.

Hip injection patients also showed increased imaging findings of osteoarthritis compared to the control groups, but the differences were not statistically significant.

Dr. Chang noted that patients receiving hip injections have symptoms of hip pain severe enough to require the injection and may be prone to faster progression of bony changes compared to the control groups. These considerations may be important as some orthopedists are requesting higher steroid doses and injections in younger patients.

"We need to look at what's going on with the steroid/anesthetic injectate and osteoarthritis patients to determine what's causing the changes that occur in some patients," Dr. Chang said. "However, we don't want to deter patients from getting an injection. These results are enough to warrant an investigation, but not enough to cancel a procedure."

Co-authors are F. Joseph Simeone, M.D., Joao Rafael T. Vicentini, M.D., and Susan V. Kattapuram, M.D.

http://bit.ly/2j9bUYS

Minimally invasive treatment provides relief from back pain

Majority of patients were pain free after receiving a new image-guided pulsed radiofrequency treatment

CHICAGO - The majority of patients were pain free after receiving a new image-guided pulsed radiofrequency treatment for low back pain and

sciatica, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

Low back pain is an extremely common problem that affects at least 80 percent of the population at some point in their lifetime. It is the most common cause of job-related disability. Low back pain affects men and women equally.

Most back pain is short-term, but about 20 percent of people affected by acute low back pain go on to develop chronic low back pain lasting a year or more. A compressed and herniated disk, in which the rubbery cushion between vertebrae impinges on and irritates nearby nerves, is a major cause of low back pain that can radiate to the legs.

"The nerve root is a sensitive structure that when pinched becomes inflamed and causes pain," said lead investigator Alessandro Napoli M.D., Ph.D., an interventional radiologist at Sapienza University of Rome. "The body reacts with muscle constriction, which decreases the distance between vertebrae, and a vicious cycle is created."

The single-center prospective study included 80 patients experiencing at least three months of low back pain due to a herniated disk that had not responded to conservative treatments including exercise and medication.

The patients underwent a minimally invasive interventional radiology procedure in which, with the help of CT imaging, a needle is guided to the location of the bulging disc and nerve root. A probe is then inserted through the needle tip and delivers pulsed radiofrequency energy to the area over a 10-minute period. Even without touching the disc, the pulsation serves to resolve the herniation.

"The probe delivers a gentle electrical energy, so there's no thermal damage," Dr. Napoli said. "The results have been extraordinary. Patients have been relieved of pain and resumed their normal activities within a day."

Of the 80 patients treated, 81 percent were pain free one year after a single 10-minute treatment session. Six patients required a second pulsed radiofrequency session. Ninety percent of the patients were able to avoid surgical treatment. "Following this treatment, inflammation and pain go away. With relaxation of the muscles, the distance between the vertebrae returns," Dr. Napoli explained.

Dr. Napoli said no patients experienced side effects after receiving the minimally invasive outpatient treatment.

"There's a big gap between conservative treatments for disc compression and herniation and surgical repair, which can lead to infection, bleeding and a long recovery period," Dr. Napoli said. "Evolving technologies like this image-guided treatment may help a substantial number of patients avoid surgery."

Co-authors are Roberto Scipione, M.D., Hans Peter Erasmus, M.D., Cristina Marrocchio, M.D., Susan Dababou, M.D., and Carlo Catalano, M.D.

http://bit.ly/2nocjuY

Prehistoric women had stronger arms than today's elite rowing crews

Average prehistoric agricultural woman had stronger upper arms than living female rowing champions

A new study comparing the bones of Central European women that lived during the first 6,000 years of farming with those of modern athletes has shown that the average prehistoric agricultural woman had stronger upper arms than living female rowing champions.

Researchers from the University of Cambridge's Department of Archaeology say this physical prowess was likely obtained through tilling soil and harvesting crops by hand, as well as the grinding of grain for as much as five hours a day to make flour.

Until now, bioarchaeological investigations of past behaviour have interpreted women's bones solely through direct comparison to those of men. However, male bones respond to strain in a more visibly dramatic way than female bones. The Cambridge scientists say this has resulted in the systematic underestimation of the nature and scale of the physical demands borne by women in prehistory.

"This is the first study to actually compare prehistoric female bones to those of living women," said Dr Alison Macintosh, lead author of the

study published today in the journal Science Advances. "By interpreting women's bones in a female-specific context we can start to see how intensive, variable and laborious their behaviours were, hinting at a hidden history of women's work over thousands of years."

The study, part of the European Research Council-funded ADaPt (Adaption, Dispersals and Phenotype) Project, used a small CT scanner in Cambridge's PAVE laboratory to analyse the arm (humerus) and leg (tibia) bones of living women who engage in a range of physical activity: from runners, rowers and footballers to those with more sedentary lifestyles.

The bones strengths of modern women were compared to those of women from early Neolithic agricultural eras through to farming communities of the Middle Ages.

"It can be easy to forget that bone is a living tissue, one that responds to the rigours we put our bodies through. Physical impact and muscle activity both put strain on bone, called loading. The bone reacts by changing in shape, curvature, thickness and density over time to accommodate repeated strain," said Macintosh.

"By analysing the bone characteristics of living people whose regular physical exertion is known, and comparing them to the characteristics of ancient bones, we can start to interpret the kinds of labour our ancestors were performing in prehistory."

Over three weeks during trial season, Macintosh scanned the limb bones of the Open- and Lightweight squads of the Cambridge University Women's Boat Club, who ended up winning this year's Boat Race and breaking the course record. These women, most in their early twenties, were training twice a day and rowing an average of 120km a week at the time.

The Neolithic women analysed in the study (from 7400-7000 years ago) had similar leg bone strength to modern rowers, but their arm bones were 11-16% stronger for their size than the rowers, and almost 30% stronger than typical Cambridge students.

The loading of the upper limbs was even more dominant in the study's Bronze Age women (from 4300-3500 years ago), who had 9-13% stronger arm bones than the rowers but 12% weaker leg bones.

A possible explanation for this fierce arm strength is the grinding of grain. "We can't say specifically what behaviours were causing the bone loading we found. However, a major activity in early agriculture was converting grain into flour, and this was likely performed by women," said Macintosh.

"For millennia, grain would have been ground by hand between two large stones called a saddle quern. In the few remaining societies that still use saddle querns, women grind grain for up to five hours a day.

"The repetitive arm action of grinding these stones together for hours may have loaded women's arm bones in a similar way to the laborious back-and-forth motion of rowing."

However, Macintosh suspects that women's labour was hardly likely to have been limited to this one behaviour.

"Prior to the invention of the plough, subsistence farming involved manually planting, tilling and harvesting all crops," said Macintosh. "Women were also likely to have been fetching food and water for domestic livestock, processing milk and meat, and converting hides and wool into textiles.

"The variation in bone loading found in prehistoric women suggests that a wide range of behaviours were occurring during early agriculture. In fact, we believe it may be the wide variety of women's work that in part makes it so difficult to identify signatures of any one specific behaviour from their bones."

Dr Jay Stock, senior study author and head of the ADaPt Project, added: "Our findings suggest that for thousands of years, the rigorous manual labour of women was a crucial driver of early farming economies. The research demonstrates what we can learn about the human past through better understanding of human variation today."

http://bit.ly/2jE38la

Study shows lower lung cancer rates in communities with strong smoke-free laws

Communities with strong smoke-free workplace laws have fewer

A recent study by University of Kentucky BREATHE (Bridging Research Efforts and Advocacy Toward Healthy Environments) researchers shows that fewer new cases of lung cancer were found in communities with strong smoke-free workplace laws.

The study, "Lung Cancer Incidence and the Strength of Municipal Smoke-free Ordinances" was published in Cancer, an American Cancer Society journal dedicated to providing clinicians with information on diagnosis, treatment and prevention.

Ellen Hahn, Ph.D., director of BREATHE and professor in the University of Kentucky College of Nursing, and her team studied whether new cases of lung cancer in Kentucky were lower, higher, or stable in communities with smoke-free laws.

"Kentucky has one of the highest adult cigarette smoking rates and the highest rate of new lung cancer cases in the nation," said Hahn. "Only one-third of Kentuckians are protected by strong smoke-free workplace laws."

Strong smoke-free laws are known to improve public health by lowering heart attacks, stroke, asthma and emphysema. This study is the first to show that new cases of lung cancer are lower when communities enact strong smoke-free laws covering all workers and the public.

Kentucky has more cases of lung cancer than any other state, and its mortality rate is 50 percent higher than the national average. Though other environmental factors play a part in the development of lung cancer, smoking and secondhand smoke exposure are the root cause of the disease.

"The mission of the UK Markey Cancer Center is to reduce the overwhelming burden of cancer in our state," said Dr. Mark Evers, Markey director. "This new study shows that having strong smoke-free workplace laws in place to prevent exposure to secondhand smoke is one more way we can help protect our citizens from this devastating disease."

Using data compiled from the Kentucky Cancer Registry, the Cancer Research Informatics Shared Resource Facility, and the UK Markey Cancer Center, researchers looked at 20 years of new lung cancer diagnoses among Kentuckians age 50 and over in communities with strong, moderate and weak smoke-free laws. They found that lung cancer incidence was eight percent lower in communities with strong smoke-free workplace laws in comparison to communities without smoke-free laws. Researchers did not find differences in lung cancer rates between communities with moderate or weak smoke-free laws and those without any smoke-free laws.

These findings could be used to prompt legislation to create more communities with strong smoke-free workplace laws in Kentucky.

"Local government can play a critical role in preventing lung cancer," said Hahn. "Elected officials can ensure that all workers and the public are protected from secondhand smoke by passing strong smoke-free laws with few or no exceptions."

BREATHE is a multi-disciplinary research, outreach, and practice collaborative of the UK College of Nursing. Its mission is to promote lung health and healthy environments to achieve health equity through research, community outreach and empowerment, advocacy and policy development and access to health services.

http://bbc.in/2AOyO1Y

Trophy hunting removes 'good genes' and raises extinction risk

Hunting animals that stand out from the crowd because of their impressive horns or lustrous manes could lead to extinction, according to a study.

By Helen Briggs BBC News

Research predicts that removing even 5% of high-quality males risks wiping out the entire population, for species under stress in a changing

world. Animals prized by trophy hunters for their horns, antlers or tusks usually have the best genes, say UK scientists.

Removing these could push a species over the edge, they warn.

There is intense global debate over trophy hunting. Some argue that it should be banned or restricted, while others say it can provide valuable revenue for conservation.

Cecil the lion, killed in 2015, was a major attraction at a national park in Zimbabwe. His black-fringed mane was an identifying characteristic **Getty Images**

Dr Rob Knell of Queen Mary, University of London, who led the research, said the assumption that so-called selective harvesting is not especially threatening to a population of animals does not take into account recent work.

"Because these high-quality males with large secondary sexual traits tend to father a high proportion of the offspring, their 'good genes' can spread rapidly, so populations of strongly sexually selected animals can adapt quickly to new environments," he said. "Removing these males reverses this effect and could have serious and unintended consequences."

Human hunting is different from natural predation in that big-game trophy hunters target large animals, usually males. They may be awarded prizes for killing animals with exceptionally large antlers, horns or manes. And illegal poaching of animals such as elephants for the ivory trade also targets animals with the biggest tusks.

Using a computer simulation model, the scientists were able to predict the impact of selectively targeting males on the basis of their secondary sexual traits.

"If the population is having to adapt to a new environment and you remove even a small proportion of these high quality males, you could drive it to extinction," said Dr Knell. "You're removing the genes from the population that would otherwise allow the population to adapt."

In the past, human hunting has led to the extinction of many animals, from the zebra-like Quagga, which was once common in Southern Africa, to the Tasmanian tiger of mainland Australia and Tasmania.

Hunting is still legal in many countries; trophy hunting takes place over a larger area in Sub-Saharan Africa than is conserved in national parks. In the US and Canada, there is also a lucrative trophy hunting industry, for the likes of deer and big-horn sheep.

Some argue that revenue from trophy hunting can support conservation efforts and local livelihoods.

The scientists said age restrictions that allow males to breed before being removed could reduce the impact of trophy hunting. This is already recommended with some species, such as lions.

"When properly regulated trophy hunting can be a powerful force for conservation which is why we're suggesting a different management approach as opposed to calling for a ban," said Dr Knell.

The study is published in Proceedings of the Royal Society B: Biological Sciences.

http://bit.ly/2BB5zNv

Smartphone addiction creates imbalance in brain

Researchers have found an imbalance in the brain chemistry of young people addicted to smartphones and the internet

CHICAGO - Researchers have found an imbalance in the brain chemistry of young people addicted to smartphones and the internet, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

According to a recent Pew Research Center study, 46 percent of Americans say they could not live without their smartphones. While this sentiment is clearly hyperbole, more and more people are becoming increasingly dependent on smartphones and other portable electronic devices for news, information, games, and even the occasional phone call.

Along with a growing concern that young people, in particular, may be spending too much time staring into their phones instead of

interacting with others, come questions as to the immediate effects on the brain and the possible long-term consequences of such habits.

Hyung Suk Seo, M.D., professor of neuroradiology at Korea University in Seoul, South Korea, and colleagues used magnetic resonance spectroscopy (MRS) to gain unique insight into the brains of smartphone- and internet-addicted teenagers. MRS is a type of MRI that measures the brain's chemical composition.

The study involved 19 young people (mean age 15.5, 9 males) diagnosed with internet or smartphone addiction and 19 gender- and age-matched healthy controls. Twelve of the addicted youth received nine weeks of cognitive behavioral therapy, modified from a cognitive therapy program for gaming addiction, as part of the study.

Researchers used standardized internet and smartphone addiction tests to measure the severity of internet addiction. Questions focused on the extent to which internet and smartphone use affects daily routines, social life, productivity, sleeping patterns and feelings.

"The higher the score, the more severe the addiction," Dr. Seo said.

Dr. Seo reported that the addicted teenagers had significantly higher scores in depression, anxiety, insomnia severity and impulsivity.

The researchers performed MRS exams on the addicted youth prior to and following behavioral therapy and a single MRS study on the control patients to measure levels of gamma aminobutyric acid, or GABA, a neurotransmitter in the brain that inhibits or slows down brain signals, and glutamate-glutamine (Glx), a neurotransmitter that causes neurons to become more electrically excited. Previous studies have found GABA to be involved in vision and motor control and the regulation of various brain functions, including anxiety.

The results of the MRS revealed that, compared to the healthy controls, the ratio of GABA to Glx was significantly increased in the anterior cingulate cortex of smartphone- and internet-addicted youth prior to therapy.

Dr. Seo said the ratios of GABA to creatine and GABA to glutamate were significantly correlated to clinical scales of internet and smartphone addictions, depression and anxiety. Having too much GABA can result in a number of side effects, including drowsiness and anxiety.

More study is needed to understand the clinical implications of the findings, but Dr. Seo believes that increased GABA in the anterior cingulate gyrus in internet and smartphone addiction may be related to the functional loss of integration and regulation of processing in the cognitive and emotional neural network.

The good news is GABA to Glx ratios in the addicted youth significantly decreased or normalized after cognitive behavioral therapy. "The increased GABA levels and disrupted balance between GABA and glutamate in the anterior cingulate cortex may contribute to our understanding the pathophysiology of and treatment for addictions," Dr. Seo said.

Co-authors are Eun-Kee Jeong, Ph.D., Sungwon Choi, Yunna Kwon, Hae-Jeong Park, and InSeong Kim.

http://bit.ly/2zHaiLY

Barrow researchers validate five new genes responsible for ALS

New study suggests early findings accelerated with augmented intelligence

Barrow Neurological Institute researchers have completed additional experiments that validate the identification of five new genes linked to Amyotrophic Lateral Sclerosis (ALS) - also known as Lou Gehrig's disease. The new study results, validated through five different methods, were published in a full length manuscript in Acta Neuropathologica, validating earlier findings in the project.

ALS is a fatal neurological disorder affecting more than 220,000 patients worldwide1 with no cures and few treatments. Dr. Robert Bowser, who led the research, directs the Gregory W. Fulton ALS Research Center at Barrow, located at Dignity Health St. Joseph's Hospital and Medical Center and considered one of the world's leading neuroscience centers.

Dr. Bowser's team used technologies provided by IBM Watson Health, including Watson for Drug Discovery, a novel research platform that harnesses the text of more than 28 million MEDLINE abstracts and other data sources.

The solution applies advanced natural language processing, machine learning and predictive analytics to identify new relationships between genes, proteins, drugs and disease.

"Further validating and expanding on our earlier findings has been exciting, because in research of this nature, time is of the essence," says Dr. Bowser, one of the nation's top ALS researchers. "We could have individually looked at the 1,500 proteins and genes but it would have taken us much longer to do so. These findings inspire hope that, with this technology, we may someday identify new and more effective treatments for ALS."

This research is important because it demonstrates the ability of artificial intelligence algorithms to accelerate wet lab research discoveries. It also provides further evidence that RNA metabolism plays an important role in ALS.

More than 30 genes have been linked to ALS, and mutations in the 11 genes that encode RNA binding proteins cause familial forms of ALS. These RNA binding proteins play a critical role in how genes encoded within the DNA in every cell are converted to the proteins that perform all the functions within a cell. Alterations in these proteins can lead to altered RNA metabolism and the generation of toxic protein aggregates within motor neurons that contribute to motor dysfunction and ultimately paralysis and death.

A person's DNA encodes for over 1,500 RNA binding proteins, and it is unknown if other RNA binding proteins may contribute to ALS. With so many RNA binding proteins encoded in our genome, the cost and time required to examine all these RNA binding proteins would prohibitive.

The Barrow laboratory studied whether IBM Watson for Drug Discovery could accelerate the identification of additional RNA binding proteins linked to ALS by helping scientists focus research efforts on the proteins that Watson ranked high and predicted to be altered in ALS.

Dr. Bowser and his team provided a list of 11 RNA binding proteins with known mutations that cause ALS. Watson for Drug Discovery used the list of proteins and cross referenced medical literature from 28 million MEDLINE abstracts to rank order all other 1,500 RNA binding proteins encoded by our genome to attempt to identify new RNA binding proteins linked to ALS.

The Barrow team validated the top 10 RNA binding proteins using five different methods that included use of patient tissue samples and patient derived stem cells differentiated into motor neurons.

They also examined a smaller set of RNA binding proteins near the bottom of the list to demonstrate that any changes detected in the top 10 were not observed for those at the bottom of the list, demonstrating the ability of Watson for Drug Discovery to correctly predict RNA binding proteins linked to ALS.

The results were groundbreaking - and a painstaking process that would have taken researchers years was completed in only a few months.

Eight of the top 10 candidates were successfully validated and shown to be altered in ALS. Five of these genes had never been examined in ALS, indicating that IBM's artificial intelligence platform could predict novel genes and proteins linked to this disease. RNA binding proteins at the bottom of the list were not altered in ALS.

By accelerating cell biological research, scientists hope to speed the discovery of new therapies for ALS.

For more information about Barrow's partnership with IBM Watson Health, please view this short video: https://youtu.be/F-qBLH6EfR8.

Sources:

1) National Center for Biotechnology Information, Nature Communications, "Projected increase in amyotrophic lateral sclerosis from 2015 to 2040," August 2016: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4987527/

http://bbc.in/2AD0nL7

Migraine therapy that cut attacks hailed as 'huge deal'

A new approach to preventing migraines can cut the number and severity of attacks, two clinical trials show.

By James Gallagher Health and science correspondent, BBC News

About 50% of people on one study halved the number of migraines they had each month, which researchers at King's College Hospital called a "huge deal". The treatment is the first specifically designed for preventing migraine and uses antibodies to alter the activity of chemicals in the brain. Further trials will need to assess the long-term effects.

- ***One in seven people around the world live with the regular agony of migraine***
- ***Migraine is up to three times more common in women than men***
- ***The Migraine Trust estimates there are more than 190,000 migraine attacks every day in the UK***
- ***People with headaches for fewer than 15 days a month have episodic migraine***
- ***If it is on more than 15 days it is classed as chronic migraine***

Research has shown a chemical in the brain - calcitonin gene-related peptide or CGRP - is involved in both pain and sensitivity to sound and light in migraine.

Four drug companies are racing to develop antibodies that neutralise CGRP. Some work by sticking to CGRP, while others block the part of a brain cell with which it interacts.

Clinical trials on two of the antibodies have now been published in the New England Journal of Medicine.

One antibody, erenumab made by Novartis, was trialled on 955 patients with episodic migraine. At the start of the trial the patients had migraines on an average of eight days a month.

The study found 50% of those given the antibody injections halved their number of migraine days per month. About 27% did have a similar effect without treatment, which reflects the natural ebb and flow of the disease.

Another antibody, fremanezumab made by Teva pharmaceuticals, was trialled on 1,130 patients with chronic migraine.

About 41% of patients halved their number of migraine days compared with 18% without treatment.

Prof Peter Goadsby, who led the erenumab trials at the NIHR research centre at King's College London, told the BBC: "It's a huge deal because it offers an advance in understanding the disorder and a designer migraine treatment. "It reduces the frequency and severity of headaches. "These patients will have parts of their life back and society will have these people back functioning."

He said other data, not published in the latest studies, suggested a fifth of patients had no migraines at all after treatment.

Better option?

The antibodies are not the only preventative drugs for migraine. Others include former epilepsy and heart disease pills as well as botox.

But Simon Evans, the chief executive of Migraine Action, said those drugs came with a lot of side-effects and did not work for everyone.

"Some doctors give patients a choice of being angry or fat-and-dosey and the drug they give them depends on their answer," he said.

The hope is discovering CGRP and precisely targeting it with antibodies should lead to fewer side-effects. Both studies say long-term safety data still needs to be studied. The problem with antibodies is they tend to be more expensive to make than other therapies.

Prof Goadsby thinks patients who get no benefit from existing treatments or cannot cope with the side-effects are those most likely to benefit.

Dr Andy Dowson, who runs headache services in Kent and London, said: "I am really enthusiastic we have something new that's coming, but we need to know cost, who will respond and a lot more detail as we go down the line. "Chronic migraine is in the top seven conditions for lifetime disability and yet nothing much is done about it, maybe this is going to help us to make some progress."

http://bit.ly/2ARXy9I

This Flu Season Could Be a Whopper, Officials Warn

U.S. health officials said they are concerned the upcoming flu season could be a bad one, based on reports from the Southern Hemisphere, where the flu season recently ended for the year.

By Rachael Rettner, Senior Writer | November 30, 2017 04:03pm ET

In Australia, for example, there were record-high numbers of laboratory-confirmed flu cases this year — more than 2.5 times the number last year, according to the Australian Government Department of Health. And flu hospitalizations and deaths in Australia were also higher than average this past season.

That does not bode well for the United States, experts say.

"As clinicians in the United States prepare for the start of another influenza season, experts have been watching the Southern Hemisphere winter for hints of what might be in store for us in the north," Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, and colleagues wrote in a recent paper published in The New England Journal of Medicine.

"Reports from Australia have caused mounting concern" about the upcoming flu season, the authors wrote. [6 Myths About the Flu Vaccine]

Australia's bad flu season may have been due, in part, to a mismatch between the flu strains included in this year's flu vaccine and the flu strains that were circulating in the public.

According to preliminary estimates from Australia, the flu vaccine was 33 percent effective at preventing the flu and only 10 percent effective at preventing infection with H3N2, the predominate flu strain in circulation during the country's flu season.

The U.S. will use the same flu vaccine this year as the one used in Australia, and early data show that H3N2 is also the predominate flu strain in circulation in the United States so far this season, according to the Centers for Disease Control and Prevention.

Still, there's no way to predict for certain how severe or mild the flu season will be in any given year. So, health officials still recommend that everyone ages 6 months and older get a flu shot this season.

"However imperfect, though, current influenza vaccines remain a valuable public health tool, and it is always better to get vaccinated than not to get vaccinated," the paper said.

The paper also noted that the flu vaccine "mismatch" seen in Australia this year could be related to the way most flu vaccines are currently made: using chicken eggs to "grow" the flu virus strains. During this egg-based production process, flu strains may acquire changes that facilitate their replication in eggs but that reduce their effectiveness at preventing flu, the paper said.

The possibility of a low-effectiveness flu vaccine this year "underscores the need to strive toward a 'universal' influenza vaccine that will protect against seasonal influenza drift variants, as well as potential pandemic strains, with better durability than current annual vaccines," the officials said in their paper. "In all likelihood, such a vaccine would not be subject to the limitations of egg-based vaccine technology," the authors said.

http://bit.ly/2AO9o4B

Hundreds of fossilized eggs sheds light on pterosaur development

An invaluable collection of more than 200 eggs is providing new insights into the development and nesting habits of pterosaurs.

To date, only a small handful of pterosaur eggs with a well-preserved 3-D structure and embryo inside have been found and analyzed - three eggs from Argentina and five from China. This sparse sample size was dramatically increased upon the discovery of 215 eggs of the pterosaurs species Hamipterus tianshanensis from a Lower Cretaceous site in China. Xiaolin Wang et al. used computed tomography scanning to peer inside the eggs, 16 of which contain embryonic remains of varying intactness. The most complete embryo contains a partial wing and cranial bones, including a complete lower jaw. The

samples of thigh bones that remain intact are well-developed, suggesting that the species benefited from functional hind legs shortly after hatching. However, the structure supporting the pectoral muscle appears to be underdeveloped during the embryonic stage, suggesting that newborns were likely not able to fly. Therefore, the authors propose that newborns likely needed some parental care. Based on growth marks, the team estimates one of the individuals to be at least 2 years old and still growing at the time of its death, supporting the growing body of evidence that pterosaurs had long incubation periods. Lastly, the fact that a single collection of embryos exhibits a range of developmental stages hints that pterosaurs participated in colonial nesting behavior, the authors say. Denis Deeming discusses these findings in a related Perspective.

http://bit.ly/2AOLaY6

New vaccine technique effectively fights breast cancer in mice

The body's own immune system can effectively fight breast cancer with the help of a new vaccine technique

A new vaccine technique can fight a certain type of breast cancer in mice. So-called HER2-positive breast cancer accounts for between 20 and 30 per cent of all cases of breast cancer in humans. Researchers from the University of Copenhagen and the University of Bologna now show that the same type of cancer can be fought in mice with help of their new vaccine.

In cases of breast cancer, the immune system has difficulties distinguishing between cancer cells and healthy cells. Therefore, it normally does not launch a protective immune response that can prevent cancer cells from growing and spreading. But the research group at the University of Copenhagen is able to change that by adding an antigen which is normally expressed on the cancer cells onto the surface of a virus-like particle. They thus inject the particle into the bodies of the mice.

'Our virus-like particle with the added cancer antigen makes the body believe it is under attack. This makes the immune system produce large amounts of antibodies targeted at the cancer antigen, which then fights the cancer cells in the mice', says Associate Professor and author of the study Adam F. Sander from the Department of Immunology and Microbiology.

In the study, which was published today in the scientific journal OncoImmunology, the researchers have documented the beneficial effect of their vaccine technique in several ways. Because their vaccine both has a preventive effect and works when cancer has already developed.

They have given the vaccine to two different groups of mice genetically coded to spontaneously develop two different types of breast cancer. In one group only half of the mice developed cancer, which was characterised by significantly fewer and smaller tumours than usual. In the second group none of the vaccinated mice developed cancer.

Depending on the genetic variation in the mice the vaccine thus prevented breast cancer from developing in 50-100 per cent of the cases. In addition, the researchers examined the vaccine's effect on two groups of mice already suffering from cancer. They had either been injected with fragments of a tumour or human cancer cells.

The vaccine cured 80 per cent of the mice with tumour fragments. In the group with human cancer cells all of the mice developed cancer, but at a much slower pace than usual.

The researchers also took blood from the mice that produced the relevant antibodies and tested it on human cancer cells. Here too the effect was hard to miss. All the human cancer cells bound to the antibodies in the right way.

The present treatment of HER2-positive breast cancer involves administering large amounts of antibodies fighting the cancer over a long period of time. The treatment is expensive and has side effects, and the immune system may become intolerant to the antibodies,

which eventually have no effect. The researchers believe their vaccine by comparison will cost markedly less if its effect translates to humans.

'What is exciting about our treatment technique is that it makes the body do the work. We do not inject foreign antibodies, but leave it to the body to produce them', says Postdoc and author of the study Susan Thrane.

The Danish research group behind the study is headed by Associate Professor Adam F. Sander, who last year helped establish the spinout NextGen Vaccines Aps based on their research into vaccine techniques. This summer they established a joint venture company named AdaptVac Aps together with the company ExpreS2ion.

This study is one of the first large results of this collaboration, and the researchers hope they will be able to go on to conducting clinical trials on humans before long.

http://bit.ly/2j93Eb4

Cancer drug leads to 'drastic decrease' in HIV infection in lung cancer patient

Doctors in France have found the first evidence that a cancer drug may be able to eradicate HIV-infected cells in humans.

In a letter published in the leading cancer journal Annals of Oncology [1] today (Friday), researchers led by Professor Jean-Philippe Spano, head of the medical oncology department at Pitie-Salpetriere Hospital AP-HP in Paris, France, report that while treating an HIV-infected lung cancer patient with the cancer drug nivolumab, they observed a "drastic and persistent decrease" in the reservoirs of cells in the body where the human immunodeficiency virus (HIV) is able to hide away from attack by anti-retroviral therapy.

These reservoirs of HIV-infected cells are found in the immune system in organs such as the brain, bone marrow and genital tract. They lie dormant and cannot be eliminated by anti-retroviral therapy, nor by the weakened immune system, so that if treatment is stopped at any time, the virus starts to replicate and infect more cells again, while the immune system cannot suppress this rebound of HIV infection. If scientists could find a way of clearing away the reservoirs of HIV-infected cells, then it might enable them to eradicate the virus completely, making it possible to cure HIV patients.

HIV primarily infects CD4 T cells, which are a type of white blood cell that plays an important role in regulating the immune response. When under attack from HIV they not only become infected but also exhausted, meaning they are less able to fight the infection.

Professor Spano explained: "Dormant CD4 T cells infected with HIV are not actively producing HIV: they are latently infected. Latent HIV reservoirs are established during the earliest stage of HIV infection and throughout the course of the disease. When a latently infected cell is reactivated, the cell begins to produce HIV again. However, this re-activation is blocked in most latently-infected cells by cellular molecules called immune check-points. One of these check-points is programmed death-1 (PD-1), which also blocks the functions of CD4 T cells in fighting the virus.

"Increasingly, researchers have been looking into the use of certain drugs that appear to re-activate the latent HIV-infected cells. This could have the effect of making them visible to the immune system, which could then attack them. Drugs that inhibit immune check-points such as PD-1 are well known in the cancer field as being very efficient at restoring immune defences by removing the brake, enabling the immune cells to spring into action to reject the cancer cells. It was thought, but until now not demonstrated, that inhibitors of immune check-points could, in a similar way, wake up dormant HIV-infected cells and also the immune defences against the virus."

Nivolumab is PD-1 inhibitor, which is used to treat several cancers in their advanced stages, including melanoma, non-small cell lung cancer and kidney cancer. The researchers used it to treat an HIV-infected patient with non-small cell lung cancer after he relapsed following surgery and chemotherapy for his tumour. So far, the 51-year-old man has received 31 injections of nivolumab every 14 days since

December 2016. He was diagnosed as HIV-positive in 1995 and the cancer was diagnosed in May 2015.

When the researchers first gave nivolumab to the patient, HIV was undetectable in blood samples. It then increased progressively up to day 45 before decreasing again. At the same time T cell activity increased, with a marked increase in the activity of another T cell, CD8, from day 30 to 120. By day 120 the reservoirs of HIV-infected cells "showed a drastic and persistent decrease", report the researchers in their letter to Annals of Oncology.

Professor Spano said: "In this patient we observed, as expected, both a re-activation of HIV and an increase in CD8 T cell responses against HIV, which resulted in the drastic decrease in the HIV reservoir, thus leading to a sustained reduction of the HIV reservoirs.

"This is the first demonstration of this mechanism working in humans. It could have implications for HIV patients, both with and without cancer, as it can work on HIV reservoirs and tumour cells independently. The absence of side effects in this patient is also good news, and suggests this could be an optimum treatment for HIV-infected patients with cancer."

However, the researchers are also cautious about their results. Professor Spano continued: "Firstly, this is the first case of such a drastic decrease of the HIV reservoir, and we must remain careful, especially because this is only one case; we have published details of another case where there was no decrease of the HIV reservoir.

"Secondly, we have to evaluate - in clinical trials and in a group of 50 French patients we are treating currently - the potential toxicities of these drugs in HIV infected people. And finally, we have to identify markers that can predict HIV response to the anti-PD-1 therapy so that treatment can be personalised, especially as we observed one responder and one non-responder."

Editor-in-chief of Annals of Oncology, Fabrice André, Professor in the Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, commented: "Although this is a single case study, it is an exciting result. Anti-HIV drugs usually stop virus replication but don't cure the patients who still have reservoirs of the virus. This study generates the hypothesis that drugs that make the virus disappear could, perhaps, cure patients."

The patient will be treated with more nivolumab later this month and his cancer will also be assessed then. "For the moment, he is doing quite well and doesn't show any signs of disease, even though the cancer is progressing slowly, which suggests it is not optimally controlled," said Professor Spano.

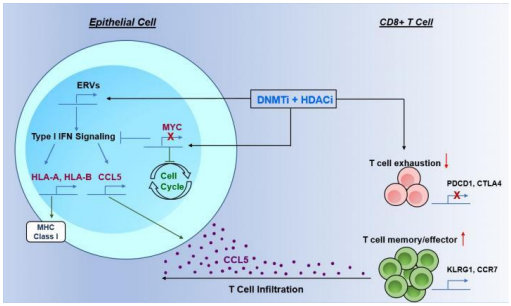
[1] *"Drastic decrease of the HIV reservoir in a patient treated with nivolumab for lung cancer", Letter to the editor from Amélie Guihot et al. Annals of Oncology. doi:10.1093/annonc/mdx696*

http://bit.ly/2kiaDlq

Two-drug combination may boost immunotherapy responses in lung cancer patients

Novel drug combination therapy that could prime nonsmall cell lung cancers to respond better to immunotherapy

Johns Hopkins Kimmel Cancer Center researchers and colleagues have identified a novel drug combination therapy that could prime nonsmall cell lung cancers to respond better to immunotherapy. These so-called epigenetic therapy drugs, used together, achieved robust anti-tumor responses in human cancer cell lines and mice.



Combination therapy attracts immune cells to fight tumors and blocks cancer gene MYC Johns Hopkins Kimmel Cancer Center researchers and colleagues have identified a novel drug combination therapy that could prime nonsmall cell lung cancers to respond better to immunotherapy. These so-called epigenetic therapy drugs, used together, achieved robust anti-tumor responses in human cancer cell lines and mice. **Michael Topper and Michelle Vaz**

During the study, published Nov. 30, 2017, in the journal *Cell*, a team of researchers led by graduate student Michael Topper; research

associate Michelle Vaz, Ph.D.; and senior author Stephen B. Baylin, M.D., combined a demethylating drug called 5-azacytidine that chemically reignites some cancer suppressor genes' ability to operate, with one of three histone deacetylase inhibitor drugs (HDACis). The HDACis work against proteins called histone deacetylases that are involved in processes, such as cell copying and division, and can contribute to cancer development. The combination therapy triggered a chemical cascade that increased the attraction of immune cells to fight tumors and diminished the work of the cancer gene MYC. Based on these findings, investigators have launched a clinical trial of the combination therapy in patients with advanced, nonsmall cell lung cancer.

The development of therapeutic approaches for patients with lung cancer has been a critical medical need, says Baylin, the Virginia and Daniel K. Ludwig Professor of Cancer Research at the Kimmel Cancer Center. While immune checkpoint therapy has been "a tremendous step forward, less than half of patients with lung cancer have benefited to date," he says.

"In our study, the two-drug epigenetic therapy combination worked exceedingly well, even before putting in the immune checkpoint inhibitors," Baylin says. "In animal models of lung cancer, the two agents either prevented cancer from emerging or blunted the effects of more aggressive cancers. In both scenarios, a large component of the results involved an increase in immune recognition of the tumors."

In a series of experiments, researchers studied the combination of 5-azacytidine with the HDACis entinostat, mocetinostat or givinostat in human cancer cell lines and in mouse models of nonsmall cell lung cancers. The treatments were found to alter the tumor microenvironment. In cancer cell lines, 5-azacytidine worked against the cancer gene MYC, causing down regulation of the entire MYC signaling program. Adding the HDACis further depleted MYC, and together the drugs subsequently caused actions that prevented cancer cell proliferation, simultaneously attracted more immune system T cells to the area of the tumor and activated these cells for tumor recognition.

In mouse models, the strongest response was observed when using 5-azacytidine plus givinostat. In one mouse model with a mutant form of nonsmall cell lung cancer, this drug combination given for three months yielded prevention of benign, precursor tumors from becoming cancers and caused 60 percent reduction of overall area of benign tumor appearance in the lungs. By contrast, a group of mice with the same form of lung cancer that were given a mock treatment universally developed large, cancerous lesions in the lungs.

In a second model of mice with established, aggressive, nonsmall cell lung cancer, treatment with an alternating schedule of 5-azacytidine with givinostat and of 5-azacytidine with mocetinostat not only reduced the growth of established, rapidly growing primary tumors but also dramatically reduced metastatic occurrence.

Baylin and colleagues at Memorial Sloan Kettering Cancer Center in New York and Fox Chase Cancer Center in Philadelphia have started a phase I/Ib clinical trial to evaluate if giving mocetinostat with a 5-azacytidinelike drug called guadecitabine can boost immune checkpoint therapy responses in patients with advanced, nonsmall cell lung cancers. The trial is part of the Van Andel Research Institute-Stand Up To Cancer Epigenetics Dream Team and is funded by Merck through the Stand Up To Cancer (SU2C) Catalyst program, an initiative led by SU2C to bring innovative cancer treatments to patients quickly. Matthew Hellmann, M.D., an author on the paper, will lead this trial at Memorial Sloan Kettering, and Jarushka Naidoo, M.B.B.Ch., assistant professor of oncology, will lead at Johns Hopkins. For more information, click here.

In addition to Topper, Vaz and Baylin, other scientists contributing to the Cell *paper include Michael J. Christina DeStefano Shields, Noushin Niknafs, Ray-Whay Chiu Yen, Alyssa Wenzel, Jessica Hicks, Matthew Ballew, Meredith Stone, Phuoc T. Tran, Cynthia A. Zahnow, Valsamo Anagnostou and Victor E. Velculescu of Johns Hopkins; Katherine B. Chiappinelli of the George Washington University Cancer Center; Matthew D. Hellmann of Memorial Sloan Kettering Cancer Center; and Pamela L. Strissel and Reiner Strick of the University-Clinic Erlangen in Germany.*

The work was supported by grants from the Hodson Trust, the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation, Stand Up To Cancer's Jim Toth Sr. Breakthrough Lung Cancer Research Award, the Commonwealth Foundation for Cancer Research and the Samuel Waxman Cancer Research Foundation Collaboration for a Cure. It also was supported by National Institutes of Health grants (CA12113, CA006973, CA180950) and the Van Andel Research Institute-Stand Up To Cancer Epigenetics Dream Team.

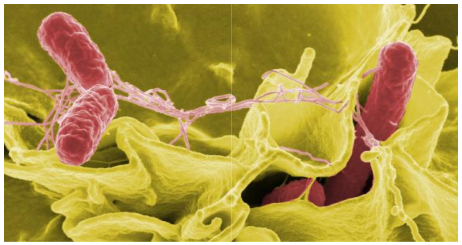
http://bit.ly/2iKjtYR

Historical diarrhea bacteria blasted past antibiotics, scooped pre-resistance

Researchers suspect use of a similar antibiotic in food animals primed them for defense.

Beth Mole - 12/1/2017, 4:54 AM

As soon as scientists figured out how to harness the power of antibiotic drugs, bacteria hit back. Following clinical trials of penicillin around 1941, doctors documented the spread of penicillin-resistant *Staphylococcus aureus* among hospital patients in 1942. By the late 1960s, more than 80 percent of *S. aureus* bacteria isolated in and out of hospitals turned up resistant to the revolutionary drug.



Color-enhanced scanning electron micrograph showing Salmonella Typhimurium (red) invading cultured human cells. **Rocky Mountain Laboratories, NIAID, NIH**

It's a common pattern that has led to the crisis of antibiotic resistance the world is now facing. In 1945, Alexander Fleming himself—the discoverer of penicillin—even warned of such "an era... of abuses," in which strong public demand for antibiotics would drive bacterial resistance that render the "miraculous" drugs impotent.

But the problem is not just overuse in people. And sometimes, bacteria aren't just one step behind—they may be one step ahead, according to a new study in the *Lancet Infectious Diseases*.

Genetic analyses of 288 bacterial isolates collected between 1911 and 1969 from 31 countries show that *Salmonella* developed resistance to an antibiotic several years before that drug even hit the market. The finding suggests that the diarrhea-causing bacteria were somehow primed to withstand the semi-synthetic antibiotic ampicillin before doctors could prescribe it in the early 1960s. Thus, overuse in humans didn't drive the emergence of that resistance.

Instead, the authors speculate that overuse of a related antibiotic—penicillin G—in animals may be to blame. During the 1950s and 1960s, farmers used low doses of penicillin G to enhance the growth of poultry and pigs, as well as prevent infections in pigs. The authors, led by bacteriologist François-Xavier Weill of the Institut Pasteur in Paris, suspect that the low doses of the drug that lingered in the waste, water, and soil around farms may have spurred the development and spread of genes that make bacteria resistant to the antibiotic. Because ampicillin is a derivative of penicillin, it may have helped make them resistant to the newer drug, too.

"Although our study cannot identify a causal link between the use of penicillin G and the emergence of transmissible ampicillin-resistance in livestock, our results suggest that the non-clinical use of penicillins like [penicillin G] may have encouraged the evolution of resistance genes in the late 1950s," Weill said in a press statement.

History of drugs

Ampicillin was discovered in 1958 and commercialized as the first "broad spectrum" penicillin in 1961. But, like its predecessor, it quickly hit resistance. In the latter half of 1962, doctors encountered an outbreak of ampicillin-resistant *Salmonella enterica* serotype Typhimurium in the UK. Several such outbreaks followed in subsequent years, and researchers reported finding several strains in humans and pigs that were multi-drug resistant (including ampicillin resistant).

The timeline might suggest that use of ampicillin in humans spurred the resistance and outbreaks—they followed the drug's 1961 release. But *S. enterica* serotype Typhimurium is a zoonotic germ, meaning it can cause gastrointestinal infections in a range of mammals, including livestock. The quick appearance of ampicillin-resistant strains on farms raised suspicions among scientists. In the late 1960s, researchers in the UK warned that use of penicillins on farms may indeed be behind the rapid rise in resistance.

To better understand the emergence of ampicillin resistance, Weill and colleagues gathered up 288 *S. enterica* serotype Typhimurium isolates collected between 1911 and 1969 in Europe from humans, animals, and feed. Each isolate was tested to see what antibiotics it could resist. The researchers also decoded the entire genome—performing whole-genome sequencing—for 225 of the isolates (skipping redundant ones).

Of the 288 isolates, 253 (88 percent) were susceptible to all antibiotics, leaving 35 that were resistant to at least one type of antibiotic. Eleven of those were resistant to ampicillin—and all of those were also resistant to penicillin G. Three of the ampicillin-resistant isolates were archived before ampicillin was released in 1961. All three were collected from humans. One was collected in France in 1959 and the other two from Tunisia in 1960.

Rebels without a cause

Genetic sequencing revealed that the 11 ampicillin-resistant isolates had a variety of ampicillin-resistance genes, which were in a variety of genome positions and on different types of shareable DNA loops, called plasmids. Yet, the plasmids in the study's isolates were different from the ones implicated in the first ampicillin-resistant bacterial outbreaks in the UK.

As for the three isolates that were ampicillin resistant before there was ampicillin to resist, they all had a common resistance gene called $bla_{\text{TEM-1B}}$. But the two from Tunisia had their *bla* genes located on a different plasmid than the French isolate.

"Thus, the early emergence of ampicillin resistance in *S enterica* serotype Typhimurium was not due to single expansion of a clonal population that had acquired a particular plasmid encoding a β lactamase [*bla*], but to multiple independent acquisitions of bla_{TEM} gene-carrying plasmids by different bacterial populations," the authors concluded.

In an accompanying commentary, researchers at the Institute of Tropical Medicine Antwerp, Belgium conclude:

Despite limitations inherent to the retrospective nature of the study... [the authors] clearly show the existence of ampicillin resistance before the drug's commercial introduction... The findings underline the importance of One Health approaches to tackling antibiotic resistance, which state that the health of people is connected to the health of animals and the environment.

Use of antibiotics for growth promotion and prophylaxis was completely banned in Europe in 2006, but it continues elsewhere in the world. The US Food and Drug Administration has put forward guidelines to end the practice on American farms, but those guidelines are not mandatory.

Earlier this month, the World Health Organization called for an all-out ban on the use of antibiotics on healthy animals.

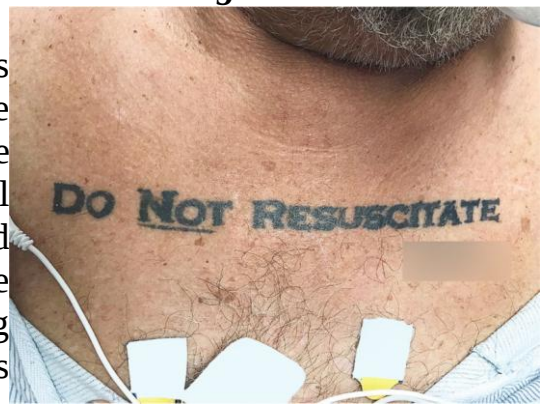
The Lancet Infectious Disease, 2017. DOI: 10.1016/S1473-3099(17)30705-3 (About DOIs).

http://bit.ly/2BtH6J5

Real wish or drunken regret? A "Do Not Resuscitate" tattoo throws doctors

Luckily, they dug up the paperwork in time to get the real answer.

Beth Mole - 12/1/2017, 6:46 AM



Enlarge **NEJM**

It's well known that patients struggle to clearly communicate their end-of-life wishes to those calling the shots at critical moments—generally doctors and family members. But, in case anyone was wondering, tattooing your wishes onto your body does not clear things up.

Emergency medicine doctors in Florida struggled to figure out how to respectfully care for an unconscious 70-year-old man with a chest tattoo that read "Do Not Resuscitate" followed by what appeared to be his signature.

In a case report published Thursday in the *New England Journal of Medicine*, the doctors recounted:

This patient's tattooed DNR request produced more confusion than clarity, given concerns about its legality and likely unfounded beliefs that tattoos might represent permanent reminders of regretted decisions made while the person was intoxicated.

The unresponsive patient was brought to the emergency department by paramedics. He had high blood-alcohol levels and no identification or family with him. After a few hours, hospital staff saw his condition slipping. His blood pressure dropped and acids were building up in his blood.

Despite the prominent tattoo, the doctors didn't know if they should trust it. They contacted social workers to try to find his next of kin and made several attempts to revive him enough to get him to confirm his wishes. But the revival attempts failed.

"We initially decided not to honor the tattoo, invoking the principle of not choosing an irreversible path when faced with uncertainty," the doctors reported. But the effort with which the patient seemed to take to have the message inked onto his body nagged at them. After stabilizing him, they called for an ethics consultation.

The ethics consultants sided with honoring the tattoo. "They suggested that it was most reasonable to infer that the tattoo expressed an authentic preference, that what might be seen as caution could also be seen as standing on ceremony, and that the law is sometimes not nimble enough to support patient-centered care and respect for patients' best interests," the doctors recalled.

Luckily, at the same time, social workers located his patient information, including a copy of his Florida Department of Health "out-of-hospital" DNR order, which matched the wishes of his tattoo. "We were relieved to find his written DNR request, especially because a review of the literature identified a case report of a person whose DNR tattoo did not reflect his current wishes," the authors note.

The patient, who had a history of chronic obstructive pulmonary disease, diabetes mellitus, and atrial fibrillation, continued to decline in health throughout the night. He died without further efforts of resuscitation, as requested.

NEJM, *2017. DOI: 10.1056/NEJMc1713344 (About DOIs).*

http://bit.ly/2AJRMq6

Researchers ID bacteria tied to esophageal cancer

Researchers at NYU Langone Health's Perlmutter Cancer Center report that at least three kinds of bacteria in the mouths of Americans may heighten or lower their risk of developing esophageal cancer.

Publishing online Dec. 1 in the journal Cancer Research, an analysis of data from two national studies involving more than 120,000 patients finds a 21 percent increased cancer risk tied to the presence of Tannerella forsythia, bacteria commonly linked to gum disease. By contrast, types of Streptococcus and Neisseria bacteria were associated with as much as a 24 percent decrease in risk for esophageal cancer. Neisseria are known to break down the toxins in tobacco smoke, and smokers are known to have lower amounts of these bacteria in their mouths than nonsmokers.

The mouth's overall bacterial make-up -- which can be changed by smoking, heavy drinking, diet, and gum disease or gastric reflux -- has long been thought to influence risk of esophageal adenocarcinoma or squamous cell carcinoma, say the researchers. But they add that the new study, which monitored healthy patients for as long as 10 years, is the first to identify which among nearly 300 kinds of bacteria commonly found in the mouth are statistically linked to the risk of getting either of the two most common forms of the disease.

"Our study brings us much closer to identifying the underlying causes of these cancers because we now know that at least in some cases disease appears consistently linked to the presence of specific bacteria in the upper digestive tract," says study senior investigator and epidemiologist Jiyoung Ahn, PhD. "Conversely, we have more

evidence that the absence or loss of other bacteria in the mouth may lead to these cancers, or to gut diseases that trigger these cancers."

That said, the researchers emphasized that their findings do not demonstrate that the bacteria directly cause or prevent esophageal cancer.

Cancer of the "food pipe" that connects the mouth and stomach is a top-10 cause of cancer death in the United States, killing some 13,000 annually, mostly men.

Study participants were men and women already enrolled in the National Cancer Institute Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, and the American Cancer Society Cancer Prevention Study II Nutrition Cohort. All were between the ages of 50 and 75, and were considered healthy and cancer free when they enrolled in either study and had the bacteria in their mouths sampled.

Among study participants, 106 developed esophageal cancer. The bacteria in the mouth of each of these patients at the beginning of these studies were compared to those of another study participant of similar age, sex, and race who remained cancer free.

Ahn says the latest findings may lead to guidelines to help physicians in the risk assessment and early detection of esophageal cancers. Ahn is an associate director of population science at Perlmutter and an associate professor in the departments of Population Health and Environmental Medicine at NYU School of Medicine.

"Early diagnosis could really help because esophageal cancers are often diagnosed in the later stages when the disease is harder to treat," says Ahn.

Postdoctoral fellow and study lead investigator Brandilyn Peters, PhD, says the team next plans to study whether use of probiotic pill supplements could be used to alter the oral microbiome and possibly decrease esophageal cancer risk.

She says the team also has plans to analyze the main biological functions of some bacteria in the mouth to see how these metabolic pathways may influence cancer risk. Further studies are planned to look at fungi and various viruses in the mouth to see if they also may influence who does and does not get esophageal cancer.

Funding support for the study, which took two years to complete, was provided by National Cancer Institute (NCI) grants R01 CA159036, U01 CA182370, R01 CA164964, and P30 CA016087.

Besides Ahn and Peters, other NYU Langone scientists involved in this research were study co-investigators Richard Hayes, DDS, PhD; Zhiheng Pei, MD; Jing Wu, PhD; and Liying Yang, MD. Additional research support was provided by Neal Freedman, PhD, and Mark Purdue, PhD, at the NCI; and by Eric Jacobs, PhD, and Susan Gapstur, PhD, at the American Cancer Society.

http://bit.ly/2zKhuqO

Study finds reading information aloud to yourself improves memory

You are more likely to remember something if you read it out loud, a study from the University of Waterloo has found.

A recent Waterloo study found that speaking text aloud helps to get words into long-term memory. Dubbed the "production effect," the study determined that it is the dual action of speaking and hearing oneself that has the most beneficial impact on memory.

"This study confirms that learning and memory benefit from active involvement," said Colin M. MacLeod, a professor and chair of the Department of Psychology at Waterloo, who co-authored the study with the lead author, post-doctoral fellow Noah Forrin. "When we add an active measure or a production element to a word, that word becomes more distinct in long-term memory, and hence more memorable."

The study tested four methods for learning written information, including reading silently, hearing someone else read, listening to a recording of oneself reading, and reading aloud in real time. Results from tests with 95 participants showed that the production effect of reading information aloud to yourself resulted in the best remembering.

"When we consider the practical applications of this research, I think of seniors who are advised to do puzzles and crosswords to help

strengthen their memory," said MacLeod. "This study suggests that the idea of action or activity also improves memory.

"And we know that regular exercise and movement are also strong building blocks for a good memory."

This research builds on previous studies by MacLeod, Forrin, and colleagues that measure the production effect of activities, such as writing and typing words, in enhancing overall memory retention.

This latest study shows that part of the memory benefit of speech stems from it being personal and self-referential.

The study was recently published in the journal Memory.

http://bit.ly/2Bxtr3Q

Evolution: In the beginning there was the sponge

Which group of animals evolved first? This problem has become a bone of contention among biologists.

An international research team is now confident that the definitive answer is at hand: Sponges appeared before comb jellies.

Which came first - the sponges or the comb jellies? The consensus view among taxonomists has long been that the sponges (Porifera) represent the oldest surviving animal phylum. However, recent studies of their genomes have suggested that this title rightly belongs to the comb jellies (Ctenophora). The issue has become one of the most hotly debated problems in evolutionary biology, because the answer has profound implications for our understanding of the entire history of animal evolution. Several studies of the question in recent years have come to discordant conclusions: Some have supported the conventional model, which favors the sponges, while others pointed to the comb jellies as being at the root of the animal kingdom. Researchers led by Professor Gert Wörheide (Chair of Palaeontology and Geobiology, Ludwig-Maximilians-Universitaet (LMU) in Munich) and Professor Davide Pisani (Bristol University, UK) have now used a refined method to re-examine the datasets employed in these investigations, and their results are unequivocal: The sponges form the earliest branch on the animals' family tree. The new study supports the idea that the results which suggested otherwise were based on the use of inadequate - and hence misleading - analytical methods.

All biologists accept that sponges and comb jellies are very ancient groups, which emerged more than 600 million years ago. Sponges are comparatively simple multicellular organisms, which lack clearly defined tissues, such as muscles, and organs like the brain. Comb jellies are structurally much more complex. They use so-called cilia to propel themselves through the oceans, and they possess nerve cells and muscle cells. "If Ctenophora were indeed the oldest animal phylum, one would have to assume either that precursors of these organ systems were already present in the common ancestor of all animals but were lost prior to the emergence of the sponges, or that nerves and muscles evolved independently at least twice," Wörheide points out. "That would necessitate a complete revision of our picture of the evolution of the organs and the nervous system. That is the reason why it is so important to correctly define the sequence of animal emergence early in evolution."

In order to elucidate the genetic relationships between animal phyla, biologists compare the amino acid sequences of modern species with one another, and construct family trees based on the degree of difference between them. The most likely phylogenomic tree should then faithfully reflect the order in which the different phyla diverged from their common ancestor and from each other. "Two of the important datasets used in the modelling studies which identified the comb jellies as the oldest extant animal group were made up of very heterogeneous data. We have now shown that none of the conventionally used statistical methods is capable of adequately analyzing such datasets," Wörheide explains. To minimize the compositional heterogeneity of the data, the authors of the new study employed a procedure in which the amino acid sequence data were first divided into groups based on the biochemical functions of the proteins they form, and then subjected to the modelling process. The

analysis of these datasets - including those derived from the data that had previously ranked the comb jellies as the older phylum - demonstrated with high statistical confidence that the sponges are in fact the oldest of the animal groups. "Our results confirm the classical assumptions concerning early animal evolution, and should help to put an end to the recent controversy over the origin of multicellular animals," Wörheide concludes.

Related Journal Article *http://dx.doi.org/10.1016/j.cub.2017.11.008*

http://nyti.ms/2nrZmjW

Philippines Suspends Dengue Shots After Drug Firm's Warning

Sanofi's flagship dengue vaccine, Dengvaxia, been found to pose health risks in people not previously infected

By FELIPE VILLAMORDEC. 1, 2017

Receiving a dengue vaccine at an elementary school near Manila in April. Noel Celis/Agence France-Presse — Getty Images

MANILA — The Philippines suspended its school-based dengue immunization program on Friday after the French pharmaceutical giant Sanofi warned that its flagship vaccine, Dengvaxia, had been found to pose health risks in people not previously infected.

The suspension came after health experts expressed worries about Sanofi's announcement this week.

The company said further clinical studies had revealed that, in those who had previously had dengue, the vaccine could prevent repeat infection.

But for those who had not had dengue, and were vaccinated and later became infected, "more cases of severe disease could occur," Sanofi said in the advisory. With more than 740,000 elementary school students in the Philippines having already received Dengvaxia vaccinations, the government decided to halt the program for the time being.

The Philippine health secretary, Francisco Duque, said the program would be "on hold while review consultations are on the way."

He added that the government would seek help from medical experts outside the Philippines, including from the World Health Organization.

Dengue is the most widespread mosquito-borne disease in the world, with nearly 400 million people infected every year.

There are four dengue viruses, or serotypes, and most people who are infected recover and become immune to the first serotype they had. In some cases, a later infection with a different serotype can lead to a severe hemorrhagic fever. About 25,000 people die every year from hemorrhagic fevers arising from the disease.

Mr. Duque said that, with an average of 200,000 people infected with dengue every year in the Philippines, vaccination was "essential."

He said that the Department of Health would be stepping up its monitoring efforts to ensure public safety and that the department's legal division was studying what to do with the Sanofi contract and how to deal with the hundreds of thousands of children who may have been put at risk.

Mr. Duque said that government officials had been asked to coordinate with community health experts to identify and monitor the children. He said a post-vaccination surveillance program would last for five years.

"I hope that this development will not in any way affect the expanded program of immunization because there are countless number of lives that have been saved," Mr. Duque said, adding that 7 billion Philippine pesos, or about $140 million, had been budgeted for all government vaccination programs for the year, up from 340 million pesos in 2006.

He would not say when the program was likely to be restarted or what steps would be necessary to allow resumption.

"We need to go back quite a long way to really put the facts together," Mr. Duque said. "Until that is available, we can't answer all your questions with definitive responses."

He said the vaccines that were now in stock would not be allowed to be sold unless the labels were changed to reflect the latest advisory.

Sanofi, manufacturer of Dengvaxia, said the drug posed a risk to people who had not previously been infected. **Noel Celis/Agence France-Presse — Getty Images**

Sanofi representatives in Manila were not immediately available to comment on Friday.

The Philippines became the first country in Asia to approve the commercial sale of Dengvaxia, in December 2015. Dengvaxia is the first dengue vaccine developed by Sanofi.

Health advocates in the Philippines first raised the alarm over Dengvaxia when the government announced in April last year that it would be used in the school immunization program despite the fact that it was a relatively new drug with possible unknown effects.

But the government continued, budgeting about $70 million for the program.

The government has defended its use of the vaccine, saying that the treatment had undergone extensive studies and stressing that it was approved for use by the World Health Organization.

The first hint that there could be something wrong was in April last year, when an 11-year-old boy with congenital heart disease died after receiving a Dengvaxia shot, but the government worked to distance the drug from the death.

Nancy Binay, a legislator in the Philippine Senate, said she was alarmed at the drug's potential impact on public health and urged the health authorities and Sanofi to "launch a nationwide medical advisory and information drive" to contact parents whose children had been given Dengvaxia.

The recently released Sanofi medical report was "deeply shocking and disturbing," Senator Binay said.

She said it was "sad" that the health department ignored the warnings about the lack of patient safety and research integrity in the Dengvaxia tests. "Safety should always be the paramount concern when it comes to any immunization program," she said.

Senator Binay called on the pharmaceutical giant to explain what it meant when it warned of "severe disease."

"We don't want the warning to the public to come too little, too late," she said.

"Obviously, there were shortfalls and gaps in the vaccine's safety profile, and I believe Sanofi is morally and ethically obliged to inform the public what severe diseases came out in their clinical tests."

Dr. Anthony Leachon, an independent director at PhilHealth, a government medical insurance body, said the Philippine medical community had expressed alarm at the government's use of the vaccine.

He said that as early as last year medical experts had told the government that there was "lingering uncertainty" about the long-term effects of the vaccine, but that their concerns had apparently been ignored.

"Evidence from manufacturer's trials shows that there may be a paradoxical increase in the incidence of severe dengue beginning a few years after children are vaccinated, and possibly continuing for the rest of their lives," Dr. Leachon said.

The clinical trials on the dengue vaccine were designed specifically to assess this "and sadly, this danger has been confirmed," he said.

"Many parents, teachers and health care workers claim they were never fully informed about the benefits and potential side effects of the vaccine," Dr. Leachon added.

http://bit.ly/2ApUosz

It's time to talk about who can access your digital genomic data

We are approaching a time when you might be too scared to have your genome sequenced.

Caitlin Curtis James Hereward

Only last week, a US senator called for an investigation into the privacy policies of direct-to-consumer DNA companies. But this is only one piece of a puzzle that is about to get much more connected.

As with any kind of personal data there are a number of concerns regarding collection, transmission, storage and use. But unlike most other data, your genome reveals intimate information about not only you, but also the people to whom you are related.

It's time to talk about who can access that data, how, when and why.

The current situation

Genetic databases are not new. For a while we have had law enforcement DNA databases, medical genetic databases, and ancestry DNA databases, among others.

Historically there has been a natural separation between these databases, because they tend to contain different types of genetic data. Medical genetic databases, for example, have typically screened specific genes, and this data is usually not variable enough to be useful in law enforcement.

Additionally, some databases have been governed by specific rules, such as those that limit who can be included in law enforcement DNA databases.

This is changing. The unit of genetic "currency" is becoming the same thing: the sequence of the entire human genome.

The rise of the genomes

The rate of genome sequencing is increasing rapidly. Massive genomics projects are set to emerge in the United Kingdom, Canada, France, and elsewhere.

The US National Institutes of Health has launched a Precision Medicine Initiative that aims to combine genetic and health data for one million people. China is investing more than US$9 billion in a similar initiative – the pilot stage alone includes one million human genomes.

It's not just governments. Private companies have also set their sights on massive human genome datasets. Craig Venter's Human Longevity Inc. is planning to sequence a million genomes by 2020 and has partnered with pharmaceutical giant AstraZeneca to work towards this goal.

The marketplace of corporate, direct-to-consumer genomics companies is also rapidly expanding. Amazon (which claimed 45% of online sales on a record-breaking Black Friday) reported the 23andMe DNA testing kit as one of its top 5 bestselling items.

It's impossible to put a precise figure on the number of genomes that have been sequenced to date. Projects like BabySeq in the US point to a future in which genome sequencing may be a routine screen at birth.

Genome data is not anonymous

Keeping databases separate and anonymous may seem like a solution but this will be very difficult to accomplish. It is already possible, at least in some instances, to use information from a complete genome to locate the donor through searches of publicly available ancestry databases.

More recently, a controversial study claimed to be able to de-anonymise genomic data using facial reconstruction. In reality this isn't possible yet – but the application of AI will certainly accelerate our understanding of these links.

Who wants your data, and why?

Your genetic data could be useful to three main groups in society.

1. Law enforcement

Law enforcement queries to commercial ancestry DNA databases have already begun to blur the lines that have typically kept these databases apart. The controversial process of familial searching shows

how data may be used from ancestry databases to make inferences about a suspect. In the US, the existence of federally unregulated genetic databases may create further complication.

The establishment of mandatory DNA testing seems far-fetched, however that may not be the case everywhere. In 2015, Kuwait passed a law mandating DNA collections from all citizens and residents, although this was revoked earlier this year.

Closer to home, NSW Police Minister Michael Gallacher proposed that mandatory DNA collection from all newborns in Australia was "something that needs to happen". Australia is not averse to surveillance of its population, as we have discovered with the national facial recognition system. This system goes into effect in 2018, and both law enforcement and private companies are pushing for access.

2. Private industry

Commercial DNA test providers can be legally required to hand over customer data to law enforcement. The privacy policies that consumers agree to make it impossible to know who else will have access to the data.

What is clear is that a digitised genome has monetary value. Genetic data from direct-to-consumer companies has already reportedly been sold to pharmaceutical companies.

3. Insurance companies

Our digital genomes provide information about our predisposition to various medical conditions and this is attractive to insurance companies. The predictive power of the genome is only going to increase over time. Once a consumer has taken a genetic test, they may be required to disclose that fact to an insurer or risk fraud charges. What's more, legislation protecting consumers from genetic discrimination is inadequate, and may be eroding in the US. Access to insurance is already being impacted in Australia.

Let's talk about the future

Australia just created its first National Health Genomics Policy Framework, for 2018-20, and this begins to create guidelines for genomic data. This policy is geared towards medical research, however, so would not apply to consumer DNA services, and does not make provisions for law enforcement access requests.

Blockchain and "genome cloaking" cryptography approaches are being explored as a way to give people control over their genomic data and who can access it. A new company claims to offer a commercial, decentralised, blockchain system based on buying genetic services and selling access to genetic information.

Perhaps these approaches are part of the technological solution. But the central issue is this: should we own our genetic data, and should we as individuals be able to decide who can access it?

What is absolutely clear is that the future of genomic databases is almost here, and now is the time to figure out how we are going to allow this information to be used.

Disclosure statement ***The authors do not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and have disclosed no relevant affiliations beyond their academic appointment.***