http://bit.ly/2rCFyrD

Babies' DNA affects mothers' risk of pre-eclampsia in pregnancy, study finds

A major new international study has revealed for the first time that some features in a baby's DNA can increase the risk of its mother developing pre-eclampsia -- a potentially dangerous condition in pregnancy.

These results from the InterPregGen study are published in Nature Genetics. The work was carried out by genetics experts from the UK, Nordic countries and Central Asia and is the first to show an effect of DNA from the fetus on the health of its mother.

Pre-eclampsia affects up to 5% of pregnancies and is first suspected when a woman is found to have high blood pressure, usually in the second half of pregnancy. The condition can cause serious complications including fits, stroke, liver and blood problems and in some cases the death of mother and baby.

The 5-year study involved teams from the UK, Iceland, Finland, Norway, Kazakhstan and Uzbekistan. They studied the genetic make-up of 4,380 babies born from pre-eclamptic pregnancies and compared their DNA with over 300,000 healthy individuals.

Dr Linda Morgan, from the University of Nottingham's School of Life Sciences, coordinated the 5-year study, which included DNA samples contributed from Iceland, Norway and Finland as well as from over 20 universities and maternity units in the UK.

Dr Morgan says: "For many years midwives and obstetricians have known that a woman is more likely to develop pre-eclampsia if her mother or sister had the disorder. More recently research has shown that the condition also runs in the families of men who father pre-eclamptic pregnancies. We knew that faulty formation of the placenta is often found in pre-eclampsia. As it is the baby's genes that produce the placenta we set out to see if we could find a link between the baby's DNA and the condition. We found there were indeed some features in a baby's DNA that can increase the risk of pre-eclampsia."

Laboratory and statistical analysis performed at the Wellcome Trust Sanger Institute (UK) and deCODE Genetics (Iceland) pinpointed the location in the baby's DNA that increases risk of pre-eclampsia. This location was confirmed by other InterPregGen members to fit hand-in-glove with other medical information about pre-eclampsia.

Dr Ralph McGinnis, who led the analysis at the Sanger Institute, said: "Pre-eclampsia has been recognized since ancient Egypt and Greece as being a danger to the lives of mothers and babies. This first piece of the genetic jigsaw holds substantial promise for unlocking some of the mystery of how pre-eclampsia is caused. Our finding may also enable better prediction of mothers who will become pre-eclamptic when combined with clinical information and with other pieces of the genetic jigsaw that will also surely be discovered in the next few years."

The baby's DNA comes from both its mother's and its father's genes - in keeping with the inherited risk of pre-eclampsia. The DNA changes associated with pre-eclampsia are common -- over 50% of people carry this sequence in their DNA so the inherited changes are not sufficient in themselves to cause disease, but they do increase the risk of pre-eclampsia.

The research found DNA variations close to the gene that makes a protein called sFlt-1 with significant differences between the babies born from pre-eclamptic pregnancies and the control group. At high levels sFlt-1 released from the placenta into the mother's bloodstream can cause damage to her blood vessels, leading to high blood pressure and damage to her kidneys, liver and brain - all features of pre-eclampsia. If a baby carried these genetic variants it increased the risk of that pregnancy being pre-eclamptic.

Dr Morgan concludes: "Because pre-eclampsia has its origins in the very early stages of pregnancy, during the formation of the placenta, research into the causes and processes of the disease has always been challenging. Now modern genome wide screening and its data analysis allows us to look for clues in the mother's, father's and their

baby's DNA. We believe the new insights from this study could form the basis for more effective prevention and treatment of pre-eclampsia in the future, and improve the outcome of pregnancy for mother and child."

DNA from a further 4,220 babies from pre-eclamptic pregnancies in Kazakhstan and Uzbekistan is currently being analysed in an extended study to see if the same variations occur near sFlt-1.

The research was funded by a 6 million Euro grant from the European Commission.

http://bit.ly/2sTse6G

Psychiatric medication protects developing mouse brain from birth defects

A clinically available anxiety drug safely and effectively protects against brain defects caused by the mouse version of a common human virus, finds new research published in The Journal of Neuroscience.

More than half of U.S. adults are infected with cytomegalovirus (CMV), but most people do not experience any symptoms because a healthy immune system keeps the virus in check. However, CMV infection in babies can cause unusually small brain size (microcephaly) like the less common Zika virus, deafness, blindness, mental dysfunction, and other neurological problems that can last a lifetime. There is no effective CMV vaccine, and current treatments are not recommended during pregnancy or in newborns because of their potential to cause other birth defects and cancer.

Anthony van den Pol and colleagues found that a daily low dose of the mood stabilizer valnoctamide reduced the amount of CMV in the body of infected newborn mice and suppressed further replication of the virus that had already reached the brain, without negative side effects. The treatment also normalized neurological and behavioral development in the infected mice, including impaired social interactions thought to link CMV infection and autism spectrum disorder. Finally, the authors show that the drug suppresses replication of CMV in human fetal brain cells.

Article: Valnoctamide inhibits cytomegalovirus infection in developing brain and attenuates neurobehavioral dysfunctions and brain abnormalities
URL: http://content/early/2017/06/19/JNEUROSCI.0970-17.2017

http://bit.ly/2tNQNhK

Smartphone app directs first responders to cardiac arrest 3 minutes before ambulance

Each minute increases the chance of survival by 10 percent

Vienna, Austria - A novel smartphone application (app) has been developed that can direct first responders to cardiac arrest victims more than three minutes before the emergency services arrive. Each minute increases the chance of survival by 10%.

The EHRA First Responder App was created by the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC).

"Sudden cardiac arrest is lethal within minutes if left untreated," said EHRA spokesperson Dr Christian Elsner. "In Europe, the emergency services arrive around nine minutes after a cardiac arrest. Every minute earlier raises the probability of survival by 10% and reduces the risk of brain injury, which starts four minutes after cardiac arrest."

If cardiopulmonary resuscitation (CPR) is initiated by a member of the public, this will in essence shorten the time between cardiac arrest and the urgently needed resuscitation measures. However, bystander resuscitation occurs in just of 30-60% of patients who have a cardiac arrest outside hospital.

The EHRA First Responder App was developed to increase the rate of bystander resuscitation and reduce the time between cardiac arrest and resuscitation. Based on GPS tracking technology, the app is used by existing emergency services (reached in many countries by dialling 112) to locate trained "app rescuers" and then automatically direct them to the scene of cardiac arrest. The target is for an app rescuer to arrive three to four minutes after the cardiac arrest.

In a typical scenario, after the cardiac arrest a bystander calls the emergency services. The operator dispatches an emergency crew and simultaneously locates nearby app rescuers. The nearest app rescuers

are notified on their smartphones and the quickest responder is given directions, via the app, to the patient and then performs CPR. Other app rescuers can then additionally bring a nearby automated external defibrillator (AED).

The app was tested in Lübeck, Germany, where around 600 app rescuers were recruited. In 36% of cardiac arrests an app rescuer arrived more than three minutes before the emergency services. App rescuers were recruited through a local media campaign and 70% were already medically trained. The 30% without medical training took a basic life support course and committed to retaking it every two years.

"Recruitment of the app rescuers was no problem at all because people want to help," said Dr Elsner.

Project organisers are now asking emergency dispatch units (fire departments and hospitals) across Germany to connect to the app so that they have free access to the fleet of app rescuers.

"The software has a standard interface and can be easily connected to most emergency alert systems in Europe in just a few steps," said Dr Elsner. "We provide insurance for app users and we have a guarantee of data security from the German Department for Data Security in Schleswig-Holstein."

Dr Elsner concluded: "Ultimately we will roll the app out across Europe. We hope to raise bystander resuscitation rates to 70-90% and for cardiac arrest patients to be resuscitated in three to four minutes on average."

For more information, visit: http://www.firstresponderapp.com

http://bit.ly/2sTOhdq

Discovery could lead to sustainable ethanol made from carbon dioxide

Recent discovery could lead to a new, more sustainable way to make ethanol

Most cars and trucks in the United States run on a blend of 90 percent gasoline and 10 percent ethanol, a renewable fuel made primarily from fermented corn. But to produce the 14 billion gallons of ethanol consumed annually by American drivers requires millions of acres of farmland.

A recent discovery by Stanford University scientists could lead to a new, more sustainable way to make ethanol without corn or other crops. This promising technology has three basic components: water, carbon dioxide and electricity delivered through a copper catalyst. The results are published in the Proceedings of the National Academy of Sciences (PNAS).

"One of our long-range goals is to produce renewable ethanol in a way that doesn't impact the global food supply," said study principal investigator Thomas Jaramillo, an associate professor of chemical engineering at Stanford and of photon science at the SLAC National Accelerator Laboratory.

Scientists would like to design copper catalysts that selectively convert carbon dioxide into higher-value chemicals and fuels, like ethanol and propanol, with few or no byproducts. But first they need a clear understanding of how these catalysts actually work. That's where the recent findings come in.

Copper crystals

For the PNAS study, the Stanford team chose three samples of crystalline copper, known as copper (100), copper (111) and copper (751). Scientists use these numbers to describe the surface geometries of single crystals.

"Copper (100), (111) and (751) look virtually identical but have major differences in the way their atoms are arranged on the surface," said Christopher Hahn, an associate staff scientist at SLAC and co-lead lead author of the study. "The essence of our work is to understand how these different facets of copper affect electrocatalytic performance."

In previous studies, scientists had created single-crystal copper electrodes just 1-square millimeter in size.

"With such a small crystal, it's hard to identify and quantify the molecules that are produced on the surface," Hahn explained. "This

leads to difficulties in understanding the chemical reactions, so our goal was to make larger copper electrodes with the surface quality of a single crystal."

To create bigger samples, Hahn and his co-workers at SLAC developed a novel way to grow single crystal-like copper on top of large wafers of silicon and sapphire.

"What Chris did was amazing," Jaramillo said. "He made films of copper (100), (111) and (751) with 6-square centimeter surfaces. That's 600 times bigger than typical single crystals.

Catalytic performance

To compare electrocatalytic performance, the researchers placed the three large electrodes in water, exposed them to carbon dioxide gas and applied a potential to generate an electric current.

The results were clear. When a specific voltage was applied, the electrodes made of copper (751) were far more selective to liquid products, such as ethanol and propanol, than those made of copper (100) or (111). The explanation may lie in the different ways that copper atoms are aligned on the three surfaces.

"In copper (100) and (111), the surface atoms are packed close together, like a square grid and a honeycomb, respectively" Hahn said. "As a result, each atom is bonded to many other atoms around it, and that tends to make the surface more inert."

But in copper (751), the surface atoms are further apart.

"An atom of copper (751) only has two nearest neighbors," Hahn said. "But an atom that isn't bonded to other atoms is quite unhappy, and that makes it want to bind stronger to incoming reactants like carbon dioxide. We believe this is one of the key factors that lead to better selectivity to higher-value products, like ethanol and propanol."

Ultimately, the Stanford team would like to develop a technology capable of selectively producing carbon-neutral fuels and chemicals at an industrial scale.

"The eye on the prize is to create better catalysts that have game-changing potential by taking carbon dioxide as a feedstock and converting it into much more valuable products using renewable electricity or sunlight directly," Jaramillo said. "We plan to use this method on nickel and other metals to further understand the chemistry at the surface. We think this study is an important piece of the puzzle and will open up whole new avenues of research for the community."

Jaramillo also serves at deputy director of the SUNCAT Center for Interface Science and Catalysis, a partnership of the Stanford School of Engineering and SLAC.

The study was also written by co-lead author Toru Hatsukade, Drew Higgins and Stephanie Nitopi at Stanford; Youn-Geun Kim at SLAC; and Jack Baricuatro and Manuel Soriaga at the California Institute of Technology.

http://bit.ly/2tNTP5z

Vaccine that lowers cholesterol offers hope of immunizing against cardiovascular disease

Study conducted in mice, but phase I clinical trial now started

A vaccine to immunise people against high levels of cholesterol and the narrowing of the arteries caused by build-up of fatty material (atherosclerosis) may be possible following successful results in mice. Now, a phase I trial in patients has started to see if the findings translate to humans.

The study, which is published today (Tuesday) in the European Heart Journal [1], is the first to show that it is possible to immunise genetically modified mice with a molecule that causes the body to produce antibodies against an enzyme called PCSK9 (Proprotein covertase subtilisin/kexin type 9), which plays a role in preventing the clearance of low density lipoprotein cholesterol ("bad" cholesterol) from the blood.

People with high levels of LDL cholesterol, either due to their genetic inheritance, or to poor diet and lifestyles, are at much greater risk of developing cardiovascular disease prematurely. These diseases of the heart and blood vessels, caused by atherosclerosis, have overtaken infections as the main cause of illness and death throughout the world.

At present, drugs such as statins can be used to lower LDL cholesterol, but they have to be taken on a daily basis and although they are generally well-tolerated they can cause adverse side effects in some people. The most recently approved cholesterol-lowering compounds are monoclonal antibodies targeting PCSK9, which are highly effective, but their effect is short-lived, resulting in frequent re-application and high costs.

The research published today shows that the AT04A vaccine, when injected under the skin in mice that have been fed fatty, Western-style food in order to induce high cholesterol and the development of atherosclerosis, reduced the total amount of cholesterol by 53%, shrank atherosclerotic damage to blood vessels by 64%, and reduced biological markers of blood vessel inflammation by 21-28%, compared to unvaccinated mice. Furthermore, the induced antibodies remained functional over the whole study period and concentrations were still high at the end of the study.

Dr Günther Staffler, chief technology officer at AFFiRis (the company that developed AT04A) and one of the authors of the study, said: "AT04A was able to induce antibodies that specifically targeted the enzyme PCSK9 throughout the study period in the circulation of the treated mice. As a consequence, levels of cholesterol were reduced in a consistent and long-lasting way, resulting in a reduction of fatty deposits in the arteries and atherosclerotic damage, as well as reduced arterial wall inflammation.

"The reduction in total cholesterol levels was significantly correlated with induced antibody concentration, proving that induced antibodies caused the reduction in cholesterol and also are ultimately responsible for the reduction of atherosclerosis development. As antibody concentrations remained high at the end of the study, it can be assumed they would continue to reduce cholesterol levels for some time afterwards, resulting in a long-lasting effect, as has been shown in previous studies.

"If these findings translate successfully into humans, this could mean that, as the induced antibodies persist for months after a vaccination, we could develop a long-lasting therapy that, after the first vaccination, just needs an annual booster. This would result in an effective and more convenient treatment for patients, as well as higher patient compliance."

The enzyme PCSK9 is made in the liver and it locks on to LDL cholesterol receptors, reducing their ability to get rid of LDL cholesterol from the blood. When injected, AT04A causes the body to produce antibodies that block the function of PCSK9, so that the activity of the LDL cholesterol receptors is increased.

"The way that AT04A is administered is comparable to a vaccine," explained Dr Staffler. "However, the difference between a conventional vaccine and our approach is that a vaccine induces antibodies that are specific to bacterial or viral proteins that are foreign to the body - pathogens - whereas AT04A induces antibodies against a target protein that is produced by the body - endogenous proteins. This it is really an immunotherapeutic approach rather than a vaccine approach."

In 2015, a phase I clinical study [2] started at the Department of Clinical Pharmacology, Medical University of Vienna, Austria, studying AT04A and another molecule AT06A in 72 healthy people to assess its safety and activity. The study is expected to complete at the end of this year.

In an accompanying editorial [3], Professor Ulrich Laufs, of Saarland University, Germany, and Professor Brian Ference, of the University of Bristol, UK, and the Wayne State University School of Medicine, Detroit, USA, write: "It appears promising to further evaluate long-term LDL cholesterol lowering by vaccination against PCSK9 for the prevention of atherosclerotic events." However, they say that "safety, the response in humans and the very important but unknown long-term immune effects need to be very carefully addressed during the course of clinical development". In particular, reductions in total

cholesterol via statins and other drugs are associated with an increase in new onset diabetes. "Therefore, one potential safety concern for long-term lowering of LDL cholesterol with a vaccine directed against PCSK9 is the potential for an increased risk of new onset diabetes. In the short term, the LDL cholesterol lowering effect of statins and PCS9 inhibitors appears to far outweigh the risks of new onset diabetes."

Notes:

*[1] "The AT04A vaccine against proprotein convertase subtilisin/kexin type 9 reduces total cholesterol, vascular inflammation, and atherosclerosis in APOE*3Leiden. CETP mice", by Christine Landlinger et al. European Heart Journal. doi:10.1093/eurheartj/ehx260.*

[2] Study Assessing Safety, Immunogenicity and LDLc -Lowering Activity of 2 PCSK9 Targeting AFFITOPE Vaccines in Healthy Subjects (AFF012)".
ClinicalTrials.gov Identifier: NCT02508896

[3] "Vaccination to prevent atherosclerotic cardiovascular disease", by Ulirich Laufs and Brian Ference. European Heart Journal. doi:10.1093/eurheartj/ehx302

http://bit.ly/2sy800G

Buyer beware: Antimicrobial products can do more harm than good

Global call to action on antimicrobials from scientists published today

BERKELEY, CA: Are you buying antimicrobial or antibacterial soaps? According to over 200 scientists and medical professionals, you may want to save your money. A consensus statement published today in the peer-reviewed scientific journal Environmental Health Perspectives concludes that common antimicrobial products do not provide health benefits and cause health and environmental harm. The statement also calls for greater caution in using antimicrobial chemicals in everyday products.

"People think antimicrobial hand soaps offer better protection against illness. But generally, antimicrobial soaps perform no better than plain soap and water," said Barbara Sattler, RN, DrPH, FAAN, environmental health professor at the University of San Francisco. Last fall, the U.S. Food and Drug Administration (FDA) determined that 19 different antimicrobial chemicals, including infamous triclosan and triclocarban, were not effective and should not be marketed for use in over-the-counter consumer wash products. Now, 200 scientists say the FDA's decision does not go far enough to protect consumers and the environment.

In consumer soaps and washes, brands are using different additives. "I was happy that the FDA finally acted to remove these chemicals from soaps. But I was dismayed to discover at my local drugstore that most products now contain substitutes that may be worse," said Arlene Blum, PhD, Executive Director of Green Science Policy Institute. Antimicrobials are also commonplace in products where you wouldn't expect them, including paints, exercise mats, flooring, apparel, food storage containers, home textiles, electronics, kitchenware, school supplies, and countertops.

"Customers may think added antimicrobials are a way to reduce infections, but in most products there is no evidence that they do," said Ted Schettler, MD, MPH, Science Director of the Science and Environmental Health Network. In 2016, Dr. Schettler authored a report on antimicrobials in hospital furnishings for the nonprofit Health Care Without Harm.

"Added antimicrobials are marketed as beneficial in building products from countertops to doorknobs and light switches" said Bill Walsh, President of Healthy Building Network, which recently produced a white paper on antimicrobial building products. "Antimicrobial preservatives are useful in certain products like paints, but we found claims about health benefits to be largely invalid." Nevertheless, sales of "antimicrobial" performance products are projected to grow.

Scientists and health professionals agree that non-medical uses of antimicrobials should be reduced. "Environmental and human exposures to triclosan and triclocarban are widespread, affecting pregnant women, developing fetuses, and breast-feeding babies," said Rolf Halden, PhD, PE professor of engineering at Arizona State University. "We must develop better alternatives and prevent unneeded exposures to antimicrobial chemicals."

http://bit.ly/2rYyda1

DNA variants that are bad for health may also make you stupid

Could CRISPR give us better health and an IQ boost?

By Michael Le Page

What makes some people smarter than others? A genetic analysis of families in Scotland, UK, hints that brainier people have fewer DNA mutations that impair intelligence and general health, rather than having more genetic variants that make them smarter.

"This is one of the most exciting studies on the genetics of intelligence I've seen for a while," says Steve Stewart-Williams of the University of Nottingham Malaysia Campus, who was not involved in the work.

One implication is that using gene editing to fix the hundreds of mutations that slightly damage people's health would make them smarter as well as healthier. "I think this strengthens the moral case for pursuing genome editing technologies," says ethicist Christopher Gyngell of the University of Oxford. "It would be killing two birds with one stone, and that would be a good thing."

Missing intelligence

There is no doubt that intelligence depends partly on the environment in which we grow up. Well-nourished children brought up in safe, unpolluted and stimulating environments on average score better in IQ tests than deprived children, for instance.

But our genes also play a role. Studies of twins have suggested that 50 to 80 per cent of the variation in general intelligence between people could be down to genes. However, finding the gene variants responsible for intelligence has proven tricky. So far, studies of the DNA of hundreds of thousands of unrelated people suggest that only around 30 per cent of the variation in intelligence is inherited. This big discrepancy between the results of twin studies and genome studies has become known as the mystery of the missing heritability.

Now a team including David Hill of the University of Edinburgh, UK, has analysed data from 20,000 people taking part in a study called Generation Scotland, which is looking at the health and genomes of families. The team used a statistical method to work out how much effect rare genetic variants shared by most of the members of a family have on intelligence. Because these variants are so rare in unrelated people, other studies have missed their effect.

They found that rare genetic variants missed by other studies explain the discrepancy between the two types of study. "If the result stands up, they've solved the missing heritability problem for intelligence," says Stewart-Williams. "Pretty impressive."

Brighter babies?

The findings help us understand how our genomes determine intelligence. In theory, smart people may be that way because they have beneficial variants of genes that boost IQ. But we would expect beneficial gene variants to spread by natural selection, becoming common in a population. Hill's findings suggest an important role for very rare gene variants. These are more likely to be slightly harmful mutations that also impair health. Evolution isn't very good at getting rid of such mutations, so they build up, creating a "mutational load" that varies from person to person. The findings suggest people's intelligence depends on their mutational load, says Rosalind Arden of the London School of Economics, who studies intelligence and genetics.

Attempts to link intelligence to genes are controversial – many people do not like the idea that IQ is mostly determined by a person's DNA. But Arden argues that genetic influence on intelligence is a good thing. "If intelligence differences were all environmental, that would be absolutely catastrophic," she says. If that was the case, all those raised in deprived circumstances would be less intelligent than those from more privileged backgrounds, which would make societies even more unequal than they are now. Smarter people tend to be healthier and live longer, although it's not yet clear why. Intelligent people may be more likely to live a better lifestyle, but Hill's study suggest they are also genetically healthier too.

We are still some way from using techniques like CRISPR to edit the genomes of our embryos, but some believe it's inevitable we will one day take this step, and expert reports in countries including the US and UK have been suggested it could be used to prevent diseases.

If Hill's findings hold up in further studies, it suggests that attempts to remove mutations that are slightly harmful for health should also raise intelligence. "We're not talking about making people way, way smarter than the smartest people today – it's just bringing the average up," says Gyngell.

Journal reference: bioRxiv, DOI: 10.1101/106203

http://bit.ly/2s2Wc2Y

Bacterial superantigens turn our immune cells to the dark side

A subpopulation of immune cells that normally fend off pathogens can turn against the host during certain infections, a new study publishing on June 20 in the open access journal PLOS Biology reveals.

The researchers led by Dr. Mansour Haeryfar at Western University's Schulich School of Medicine & Dentistry, Canada, in collaboration with researchers from France, Australia and the United States, found for the first time that these immune cells, called mucosa-associated invariant T (MAIT) cells, can mount a rapid and robust inflammatory response that may contribute to severe organ damage or even death due to infections that lead to toxic shock syndrome.

Toxic shock syndrome is a life-threatening inflammatory response brought on by exposure to bacterial superantigens, which are toxins harbored and secreted by certain common bacteria, namely Staphylococcus ("staph") and Streptococcus ("strep") bacteria. Counterintuitively, it is not the bacteria or its toxins that make toxic shock fatal, but rather the overzealous inflammatory response triggered and perpetuated by the immune system.

Researchers used both animal models and human cells to demonstrate the hyper-responsiveness of MAIT cells to systemic exposure to bacterial superantigens. The team also demonstrated that as MAIT cells responded to superantigens, they also began to develop signs of exhaustion and failure to participate in antimicrobial host defense. This exhaustion may lead to immunosuppression, which can also have fatal consequences due to increased susceptibility to secondary, opportunistic infections.

"In this context, MAIT cells are actually disease-causing as opposed to protective," said Haeryfar. "We have shown that MAIT cells are the most powerful source of an inflammatory mediator called interferon-γ, thus likely contributing to morbidity associated with toxic shock syndrome and similar superantigen-mediated illnesses."

"Based on our findings, we propose that timely and efficient therapies that target MAIT cells will likely benefit the patients by preventing uncontrolled inflammation and also by relieving immunosuppression," said Haeryfar.

Citation: Shaler CR, Choi J, Rudak PT, Memarnejadian A, Szabo PA, Tun-Abraham ME, et al. (2017) MAIT cells launch a rapid, robust, and distinct hyperinflammatory response to bacterial superantigens and quickly acquire an anergic phenotype that impedes their cognate antimicrobial function: Defining a novel mechanism of superantigen-induced immunopathology and immunosuppression. PLoS Biol 15(6): e2001930. https://doi.org/10.1371/journal.pbio.2001930

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http://bit.ly/2rZ281R

Plant reveals anti-Alzheimer's compounds

Japanese scientists develop a new technique to isolate active therapeutic compounds for Alzheimer's disease from plants

Japanese scientists have developed a method to isolate and identify active compounds in plant medicines, which accurately accounts for drug behavior in the body. Using the technique, they have identified several active compounds from Drynaria Rhizome, a traditional plant medicine, which improve memory and reduce disease characteristics in a mouse model of Alzheimer's disease.

Traditional plant medicines have been used by humans for a long time, and these therapies are still popular in many countries. Plants typically contain a huge variety of compounds, many of which have no effect in the body, and some which can have significant effects. If a plant medicine shows a therapeutic effect, scientists are interested in isolating and identifying the compounds that cause the effect to see if they can be used as new drugs.

In many cases, scientists repeatedly screen crude plant medicines in lab experiments to see if any compounds show a particular effect in cells grown in a dish or in cell-free assays. If a compound shows a positive effect in cells or test tubes, it could potentially be used as a drug, and the scientists go on to test it in animals. However, this process is a lot of work and doesn't account for changes that can happen to drugs when they enter the body - enzymes in the blood and liver can metabolize drugs into various forms called metabolites. In addition, some areas of the body, such as the brain, are difficult to access for many drugs, and only certain drugs or their metabolites will enter these tissues.

"The candidate compounds identified in traditional benchtop drug screens of plant medicines are not always true active compounds, because these assays ignore bio-metabolism and tissue distribution," explains Chihiro Tohda, senior author on the recent study published in Frontiers in Pharmacology. "So, we aimed to develop more efficient methods to identify authentic active compounds that take these factors into account."

The scientists were interested in finding active compounds for Alzheimer's disease in Drynaria Rhizome, a traditional plant medicine. They used mice with a genetic mutation as a model for Alzheimer's disease. This mutation gives the mice some characteristics of Alzheimer's disease, including reduced memory and a buildup of specific proteins in the brain, called amyloid and tau proteins. This means that the mice are a useful tool to test potential Alzheimer's disease treatments.

Initially, the researchers mashed the plant up and treated the mice orally using this crude plant extract. They found that the plant treatment reduced memory impairments and levels of amyloid and tau proteins in their brains. In a key step, the team then examined the mouse brain tissue, where the treatment is needed, 5 hours after they treated the mice with the extract. They found that three compounds from the plant had made it into the brain - these were a compound called naringenin and two naringenin metabolites.

The researchers then treated the mice with pure naringenin and noticed the same improvements in memory deficits and reductions in amyloid and tau proteins, meaning that naringenin and its metabolites were likely the active compounds in the plant. They found a protein called CRMP2 that naringenin binds to in neurons, which causes them to grow, suggesting that this could be the mechanism by which naringenin can improve Alzheimer's disease symptoms.

The team hope that the technique can be used to identify other treatments. "We are applying this method to discover new drugs for other diseases such as spinal cord injury, depression and sarcopenia," explains Tohda.

http://bit.ly/2sJiDfv

Older dads have 'geekier' sons

New King's College London research suggests that sons of older fathers are more intelligent, more focused on their interests and less concerned about fitting in, all characteristics typically seen in 'geeks'.

While previous research has shown that children of older fathers are at a higher risk of some adverse outcomes, including autism and schizophrenia, this new study published today in Translational Psychiatry suggests that children of older fathers may also have certain advantages over their peers in educational and career settings.

The researchers from King's College London and The Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai in the United States collected behavioural and cognitive

data from 15,000 UK-based twin pairs in the Twins Early Development Study (TEDS).

When the twins were 12 years old, they completed online tests that measured 'geek-like' traits, including non-verbal IQ, strong focus on the subject of interest and levels of social aloofness. Parents were also asked whether their child cares about how they are perceived by their peers and if they have any interests that take up substantial majority of their time. Using this information, the researchers computed a 'geek index' for every child in the study. Overall, higher geek index scores were reported in the sons of older fathers. This effect persisted after controlling for parent's social/economic status, qualifications and employment. In addition, they found that 'geekier' children do better in school exams, particularly in the STEM (science, technology, engineering and mathematics) subjects, several years after their geek index was measured.

Dr Magdalena Janecka from King's College London and The Seaver Autism Center at Mount Sinai, said: 'Our study suggests that there may be some benefits associated with having an older father. We have known for a while about the negative consequences of advanced paternal age, but now we have shown that these children may also go on to have better educational and career prospects.'

Although the study did not directly investigate the role of environmental factors, there are a number of potential reasons why older fathers may have 'geekier' sons. For example, older fathers are likely to have more established careers and a higher socioeconomic status than younger fathers, meaning that their children may be brought up in more enriched environments and have access to better schooling.

These results also have implications for understanding links between higher paternal age, autism and characteristics typically seen in 'geeks'. Although the researchers could not measure it directly, they hypothesise that some of the genes for geekiness and for autism are overlapping, and that those genes are more likely to be present in older fathers. Dr Janecka added: 'When the child is born only with some of those genes, they may be more likely to succeed in school. However, with a higher 'dose' of these genes, and when there are other contributing risk factors, they may end up with a higher predisposition for autism. This is supported by recent research showing that genes for autism are also linked with higher IQ.'

http://bit.ly/2t2JBRS

Gene variant protecting against Alzheimer's disease decreases plasma beta-amyloid levels

Gene variant protecting against Alzheimer's disease significantly decreases plasma beta-amyloid levels in a population cohort

New research from the University of Eastern Finland shows that the APP gene variant protecting against Alzheimer's disease significantly decreases plasma beta-amyloid levels in a population cohort. This is a very significant discovery, as many on-going drug trials in the field of Alzheimer's disease focus on decreasing beta-amyloid levels in the brain tissue. According to the study, a 30% life-long decrease in beta-amyloid levels is not associated with detrimental effects on lipid or glucose metabolism, or on any other metabolic factors.

The findings, drawing on the unique data of the METSIM (METabolic Syndrome In Men) study ongoing at the University of Eastern Finland, were published in Annals of Neurology.

Alzheimer's disease is a neurodegenerative disease strongly characterised by the accumulation of beta-amyloid in the brain tissue. Knowledge of the genetic background of Alzheimer's disease is crucial for finding new prevention measures and treatments, and for understanding the cellular level mechanisms of the disease. Uncovering the genetic pathogenesis of Alzheimer's disease has been a target of great interest over the past few years, and genome-wide mapping studies focusing on risk genes have led to significant advances in the field. These studies have identified not only several new risk genes for Alzheimer's disease, but also gene variants that protect against it.

Research groups focusing on Alzheimer's disease and diabetes at the University of Eastern Finland have now show that the APP A673T gene variant, which is a variant in the amyloid precursor protein gene protecting against Alzheimer's disease, leads to an average of 30 per cent decreased levels of the beta-amyloid subtypes 40 and 42. The effects of this previously discovered gene variant were analysed by utilising data from the unique and extensive METSIM study. Enjoying international recognition, the METSIM data comprises 10,000 men living in the eastern part of Finland.

Approximately 0.3% of the population are carriers of the APP A673T gene variant. Although the variant itself is rare, the observed association with decreased plasma beta-amyloid levels is important from the viewpoint of Alzheimer's drug trials. Several on-going drug trials for Alzheimer's disease focus on decreasing beta-amyloid levels in the brain tissue. The findings from the population cohort in eastern Finland show that a life-long decrease in beta-amyloid levels is not associated with detrimental effects on lipid or glucose metabolism, or on any other metabolically relevant events.

Furthermore, the findings also provide support for the amyloid cascade hypothesis, a hypothesis which is key in Alzheimer's research and which has recently been heavily questioned due to failed beta-amyloid based drug trials and treatment experiments. According to the hypothesis, the accumulation of beta-amyloid in the brain plays a key role in Alzheimer's disease.

The findings on the role of the APP A673T gene variant in Alzheimer's disease facilitate the planning of future research. This insight, in turn, will enable the identification of new drug targets, increasingly good predictive biomarkers and the development of personalised medical applications.

Henna Martiskainen, Sanna-Kaisa Herukka, Alena Stancáková, Jussi Paananen, Hilkka Soininen, Johanna Kuusisto, Markku Laakso, Mikko Hiltunen. Decreased plasma β-amyloid in the Alzheimer's disease APP A673T variant carriers. Annals of Neurology, published online 26.5.2017. DOI: 10.1002/ana.24969

http://www.bbc.com/news/health-40346539

Don't be scared to let animals on wards, say nurses

Hospitals should let more dogs and other animals on to wards and even into operating theatres to help patients, the Royal College of Nursing says.

The call comes after the RCN collected scores of anecdotes of therapy-animals, and sometimes pets, helping recovery.

Some young patients found having trained dogs accompany them to the anaesthetic room reduced their anxiety before and after surgery.

The RCN is working on national advice to encourage more animal visitors.

'Myths and dangers'

In a recent RCN survey of 750 nursing staff, 82% said animals could help patients be more physically active and 60% said they believed animals improved physical recovery.

But many nurses said animals were not allowed where they worked.

The main reasons behind this, according to Amanda Cheesley, who is putting together nationwide guidelines on animals in hospitals, are concerns that furry companions spread infections and other "myths around the dangers" of allowing animals on wards.

But she says she knows of examples where hospitals allowed dogs and other animals on wards safely, making a "remarkable difference."

She mentioned one young cancer patient who was too scared to have a life-saving procedure in theatre. The patient finally had the treatment she needed after a therapy dog accompanied her to the anaesthetic room and stayed with her afterwards.

Ms Cheesley said: "The dog calmed her down, making it so much less traumatic for her and her parents. Ultimately it allowed the staff to do a life-saving job." Another example involved a man who had had a brain injury that left him with difficulty walking.

After he was discharged, he found going for a walk with his pet donkey helped with his balance and, over time, he was able to walk more easily.

Ms Cheesley says more trained animals could help with mobility and physiotherapy - for example, by asking patients to walk towards a dog at the end of a walkway and gradually increasing the distance.

Dogs could also help divert a patient's attention - for example, if a child is scared of needles, a therapy dog could act as a distraction.

'Pet protocol'

To collect more evidence on the benefits and challenges of bringing animals on to wards, dog handler Lyndsey Uglow who has worked with therapy-animals in hospitals for five years, has started a research project at Southampton Children's Hospital.

Together with Ms Uglow, the Humanimal Trust, infection control specialists and hospital managers, the RCN aims to put together simple rules that could work across wards, clinics and hospices.

Concerns that pets might pass on infections for example, could be addressed by making sure animals do not wander from room to room or patient to patient, but are instead booked for a specific patient at a specific time.

Owners would also have to ensure the animal's vaccinations were up-to-date. And handlers could clean paws with hospital-grade wipes.

http://bit.ly/2rLI0fs

Temple study: Extra-virgin olive oil preserves memory & protects brain against Alzheimer's

Extra-virgin olive oil recognized as specific ingredient that protects against cognitive decline

Philadelphia, PA - The Mediterranean diet, rich in plant-based foods, is associated with a variety of health benefits, including a lower incidence of dementia. Now, researchers at the Lewis Katz School of Medicine at Temple University (LKSOM) have identified a specific ingredient that protects against cognitive decline: extra-virgin olive oil, a major component of the Mediterranean diet.

In a study published online June 21 in the Annals of Clinical and Translational Neurology, the researchers show that the consumption of extra-virgin olive oil protects memory and learning ability and reduces the formation of amyloid-beta plaques and neurofibrillary tangles in the brain -- classic markers of Alzheimer's disease.

The Temple team also identified the mechanisms underlying the protective effects of extra-virgin olive oil. "We found that olive oil reduces brain inflammation but most importantly activates a process known as autophagy," explained senior investigator Domenico Praticò, MD, Professor in the Departments of Pharmacology and Microbiology and the Center for Translational Medicine at LKSOM. Autophagy is the process by which cells break down and clear out intracellular debris and toxins, such as amyloid plaques and tau tangles.

"Brain cells from mice fed diets enriched with extra-virgin olive oil had higher levels of autophagy and reduced levels of amyloid plaques and phosphorylated tau," Dr. Praticò said. The latter substance, phosphorylated tau, is responsible for neurofibrillary tangles, which are suspected of contributing to the nerve cell dysfunction in the brain that is responsible for Alzheimer's memory symptoms.

Previous studies have suggested that the widespread use of extra-virgin olive oil in the diets of people living in the Mediterranean areas is largely responsible for the many health benefits linked to the Mediterranean diet.

"The thinking is that extra-virgin olive oil is better than fruits and vegetables alone, and as a monounsaturated vegetable fat it is healthier than saturated animal fats," according to Dr. Praticò.

In order to investigate the relationship between extra-virgin olive oil and dementia, Dr. Praticò and colleagues used a well-established Alzheimer's disease mouse model. Known as a triple transgenic model, the animals develop three key characteristics of the disease: memory impairment, amyloid plagues, and neurofibrillary tangles.

The researchers divided the animals into two groups, one that received a chow diet enriched with extra-virgin olive oil and one that received the regular chow diet without it. The olive oil was introduced into the diet when the mice were six months old, before symptoms of Alzheimer's disease begin to emerge in the animal model.

In overall appearance, there was no difference between the two groups of animals. However, at age 9 months and 12 months, mice on the extra virgin olive oil-enriched diet performed significantly better on tests designed to evaluate working memory, spatial memory, and learning abilities.

Studies of brain tissue from both groups of mice revealed dramatic differences in nerve cell appearance and function.

"One thing that stood out immediately was synaptic integrity," Dr. Praticò said. The integrity of the connections between neurons, known as synapses, were preserved in animals on the extra-virgin olive oil diet. In addition, compared to mice on a regular diet, brain cells from animals in the olive oil group showed a dramatic increase in nerve cell autophagy activation, which was ultimately responsible for the reduction in levels of amyloid plaques and phosphorylated tau.

"This is an exciting finding for us," explained Dr. Praticò. "Thanks to the autophagy activation, memory and synaptic integrity were preserved, and the pathological effects in animals otherwise destined to develop Alzheimer's disease were significantly reduced. This is a very important discovery, since we suspect that a reduction in autophagy marks the beginning of Alzheimer's disease."

Dr. Praticò and colleagues plan next to investigate the effects of introducing extra-virgin olive oil into the diet of the same mice at 12 months of age, when they have already developed plaques and tangles. "Usually when a patient sees a doctor for suspected symptoms of dementia, the disease is already present," Dr. Praticò added. "We want to know whether olive oil added at a later time point in the diet can stop or reverse the disease."

Other investigators contributing to the new study include Elisabetta Lauretti, a graduate student in Dr. Pratico's laboratory at LKSOM; and Luigi Iuliano, a Professor of Medicine in the Department of Medical Sciences and Biotechnology, Sapienza University of Roma, Italy.

The research was funded in part by a grant from the Wanda Simone Endowment for Neuroscience.

http://bit.ly/2tFsMdh

Underused cancer test could improve treatment for thousands

Simple blood test could improve treatment for more than 1 in 6 stage 2 colon cancer patients

ROCHESTER, Minn. -- A simple blood test could improve treatment for more than 1 in 6 stage 2 colon cancer patients, suggests new Mayo Clinic research. The researchers also discovered that many patients who could benefit from the test likely aren't receiving it. The findings were published in the Journal of Gastrointestinal Surgery.

Using data from the National Cancer Database for 40,844 patients, Mayo Clinic physicians and scientists teamed up to look at benefits of a blood test that measures the protein called carcinoembryonic antigen, or CEA, in stage 2 colon cancer. Carcinoembryonic antigen can be found in higher levels in people with certain cancers, especially colon cancer.

The researchers found that knowing these blood test results prior to treatment could have changed the classification for 17 percent of stage 2 colon cancer patients from average risk to high risk. That change could have altered treatment options, including whether to use chemotherapy.

"The decision to give a patient chemotherapy after surgery is not a light one, and physicians must weigh the risks and benefits," says senior author Kellie Mathis, M.D., a Mayo Clinic colon and rectal surgeon. "We are currently using the blood test to help make these difficult decisions, and we suggest other physicians do the same."

The blood test has been around for decades but is not broadly used across the country.

It was recorded in 54 percent of cases meeting other relevant criteria for the study. While in some cases the test may not have been entered in the database, many other patients may not be getting it.

"There is no good reason for a physician to omit this blood test, and more work needs to be done to ensure that all patients receive it," Dr. Mathis says.

When patients get the blood test, the authors point out it is often done after surgery to monitor the cancer's development. Greater, and earlier, consideration of protein level may be warranted, the researchers say.

Colorectal cancer is the fourth most common cancer in the U.S. and the second deadliest.

There are four primary stages of colon cancer. Generally, with stage 2, the cancer hasn't spread to nearby lymph nodes or distant organs but has grown into or through the wall of the colon. Some stage 2 patients fare worse than some stage 3 patients, who usually benefit most from chemotherapy. But the research team believes this blood test can help determine which stage 2 patients are at a higher risk and therefore could benefit from therapy.

The researchers also discovered that, for stage 2 patients who had surgery but not chemotherapy, the five-year survival rate was 66 percent for those with elevated protein levels and 76 percent for those without elevated levels. And for patients with elevated protein levels, those who had chemotherapy and surgery fared better than those who only had surgery.

"If a patient with a new diagnosis of stage 2 colon cancer has an elevated carcinoembryonic antigen level, physicians should consider chemotherapy in addition to surgery," says Dr. Mathis.

To perform the patient-centered research, physicians in the Mayo Clinic Division of Colon and Rectal Surgery collaborated with scientists in the Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery.

The lead author is Blake Spindler, M.D., a resident in the Mayo Clinic School of Graduate Medical Education. The other authors are John Bergquist, M.D., and Cornelius Thiels, D.O., both residents in the Mayo Clinic School of Graduate Medical Education, and Elizabeth Habermann, Ph.D., Scott Kelley, M.D., and David W. Larson, M.D., all from Mayo Clinic.

The study was funded by the Mayo Clinic Department of Surgery, the Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery and the Mayo Clinic Clinician-Investigator Training Program.

http://bit.ly/2tG5GmQ

More frequent sexual activity can boost brain power in older adults, according to study

More frequent sexual activity has been linked to improved brain function in older adults, according to a study by the universities of Coventry and Oxford.

Researchers found that people who engaged in more regular sexual activity scored higher on tests that measured their verbal fluency and their ability to visually perceive objects and the spaces between them.

The study, published today in the Journals of Gerontology, Series B: Psychological and Social Sciences, involved 73 people aged between 50 and 83.

Participants filled in a questionnaire on how often, on average, they had engaged in sexual activity over the past 12 months - whether that was never, monthly or weekly - as well as answering questions about their general health and lifestyle.

The 28 men and 45 women also took part in a standardised test, which is typically used to measure different patterns of brain function in older adults, focussing on attention, memory, fluency, language and visuospatial ability.

This included verbal fluency tests in which participants had 60 seconds to name as many animals as possible, and then to say as many words beginning with F as they could - tests which reflect higher cognitive abilities.

They also took part in tests to determine their visuospatial ability which included copying a complex design and drawing a clock face from memory.

It was these two sets of tests where participants who engaged in weekly sexual activity scored the most highly, with the verbal fluency tests showing the strongest effect.

The results suggested that frequency of sexual activity was not linked to attention, memory or language. In these tests, the participants

performed just as well regardless of whether they reported weekly, monthly or no sexual activity.

This study expanded on previous research from 2016, which found that older adults who were sexually active scored higher on cognitive tests than those who were not sexually active.

But this time the research looked more specifically at the impact of the frequency of sexual activity (i.e. does it make a difference how often you engage in sexual activity) and also used a broader range of tests to investigate different areas of cognitive function.

The academics say further research could look at how biological elements, such as dopamine and oxytocin, could influence the relationship between sexual activity and brain function to give a fuller explanation of their findings.

Lead researcher Dr Hayley Wright, from Coventry University's Centre for Research in Psychology, Behaviour and Achievement, said:

"We can only speculate whether this is driven by social or physical elements - but an area we would like to research further is the biological mechanisms that may influence this.

"Every time we do another piece of research we are getting a little bit closer to understanding why this association exists at all, what the underlying mechanisms are, and whether there is a 'cause and effect' relationship between sexual activity and cognitive function in older people.

"People don't like to think that older people have sex - but we need to challenge this conception at a societal level and look at what impact sexual activity can have on those aged 50 and over, beyond the known effects on sexual health and general wellbeing."

http://bit.ly/2t6bSXP

Marriage makes men fatter, shows new research

Being married makes men gain weight, and the early days of fatherhood add to the problem, finds new research from the University of Bath's School of Management.

The study shows that married men have a higher Body Mass Index (BMI) than their non-married counterparts, adding approximately three pounds or 1.4kg to the scales.

There's no effect on male BMI if their wife becomes pregnant, but in the early years after childbirth men gain weight. It takes the period just before and after divorce to register a dip in male BMI.

The findings clear up the confusion of competing theories put forward by social scientists linking BMI to marital status. It confirms the idea that people who are single but seeking marriage have more incentive to stay fit and make more effort than those who are married.

It also supports the theory that marriage leads to more social occasions involving richer foods, or more regular meals for men; while putting paid to the idea that married couples have better physical health because of increased social support.

The study of heterosexual couples in the United States, between 1999 and 2013, used data from the Panel Study of Income Dynamics and is published in the journal Social Science and Medicine.

Dr Joanna Syrda, Business Economist in the School of Management, said: "It's useful for individuals to understand which social factors may influence weight gain, especially common ones such as marriage and parenthood, so that they can make informed decisions about their health and well-being. For married men who want to avoid BMI increases that will mean being mindful of their own changing motivation, behaviour and eating habits.

"Given major public health concerns about obesity, understanding more about the social science factors that can cause weight fluctuation is important."

The impact of marriage and parenthood on male body mass index: Static and dynamic effects is published in Social Science & Medicine. DOI: 10.1016/j.socscimed.2017.05.033 http://www.sciencedirect.com/science/article/pii/S0277953617303349

Research by the School of Management was ranked 8th in the UK in the independently-assessed Research Excellence Framework. 89 per cent of their submitted case studies were deemed to have an outstanding or very considerable impact.

http://bit.ly/2s7jwgh

Yarraman flu or horse flu? Words and graphics influence willingness to vaccinate

Findings show that the way health information is communicated, matters

"Yarraman flu is a virus quickly infecting the U.S. ...." The mock announcement was enough to make readers worry. But when the name of the hypothetical illness was changed to "horse flu", the news elicited a different reaction.

Readers were not as concerned, and reported being less motivated to get a vaccine that would prevent them from contracting the illness.

Graphics, too, altered perceptions of risk.

Even though each of three graphics presented the same information, colorful heat maps in which the point of outbreak blazed red consistently triggered stronger reactions than dot maps that punctuate geographical distribution of the influenza, and bar-type graphs.

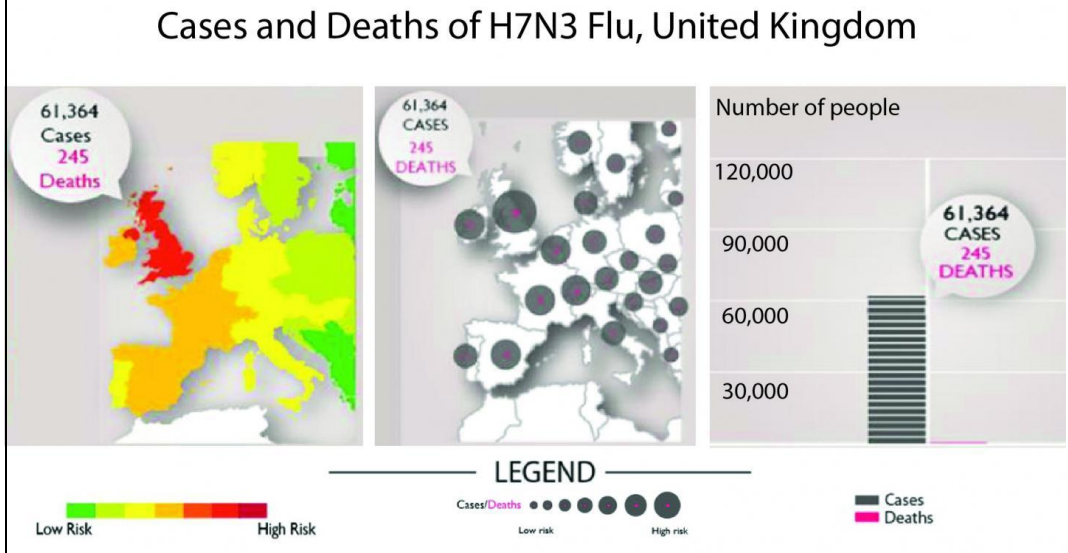
Based on a survey of 16,510 participants from 11 countries, the findings show that the way health information is communicated, matters.

A research collaboration between scientists at U of U Health University of Michigan, University of Iowa, and Radboud University in the Netherlands, was published as two studies: one recently in Vaccine and the second in Emerging Infectious Diseases on June 21.

"Our results highlight that choices for public communications about health issues cannot be made simply by convenience or without consideration," says Angie Fagerlin, Ph.D., chair of population health sciences at U of U Health. "If we can present information in ways that increase the public's understanding, it's a win for everybody."

Additional studies are needed to examine whether messaging can go beyond changing readers' intent to actually altering behavior, driving more people to get vaccinated during critical times.

Leading health and news organizations regularly publish reports on public health issues, including infectious disease outbreaks, bringing information to millions of people. Yet little research has been done to gauge how subtle differences in the ways in which the information is presented shapes public perception.



Three types of graphics -- heat maps, dot maps, and picto-trendlines -- show the prevalence of a hypothetical influenza, and number of related deaths. Even though the graphics depicted the same information, an international survey revealed that each type elicited different responses from participants. **Elastique**

To investigate, the research team distributed an opt-in online survey within nine European countries, the U.K., and the U.S.

Participants read a mock news article written in their primary language that described the spread of a pandemic flu within their country. They then completed a survey measuring their attitudes toward vaccination, knowledge about information in the article, and concern for contracting the flu.

Participants read the mock story with one of three random flu names and graphic visualizations. Inspired by actual disease names (ie. Spanish flu, H1N1 influenza, bird flu), the imaginary illnesses included the exotic sounding "Yarraman flu" (Yarraman is an Aboriginal word for "horse"), the scientific "H11N3 influenza", and "horse flu", named for the animal that transmits the virus.

Alternatively, the article included one of three types of graphics, each showing a rise in the prevalence of influenza, and number of related deaths, over three months.

Participants who read about "horse flu" were significantly less motivated to get vaccinated compared to those who read about "Yarraman flu" or "H11N3 influenza".

That same trend echoed across each of the 11 countries surveyed. Out of a 7-point scale, with the highest number meaning "definitely would get a vaccination" and the lowest indicating "definitely would not get a vaccination", the sentiment dropped from 4.66 to 4.54 ($p = 0.002$).

"In public health, relatively small effects can have relatively large impacts on a population level," explains first author of the flu label study, Aaron Scherer, Ph.D., from the University of Iowa.

For visuals, readers indicated they preferred heat maps, and those who used them to interpret the hypothetical outbreak said they were more likely to vaccinate than those who saw bar-type graphs (4.67 vs. 4.56, $p = 0.01$).

Heat map viewers also thought they were more likely to get the flu, had a better grasp of the facts about the outbreak, and a greater interest in learning more.

More than that, the findings suggest that some tactics work better than others to inform health decisions.

"It is incredibly important that we communicate effectively, as it has the potential to improve public health," says co-author and pulmonologist Thomas Valley, M.D., M.Sc. from the University of Michigan.

This work was supported by the European Union's Seventh Framework Programme for research, technological development and demonstration.

In addition to Fagerlin, Scherer and Valley, co-authors of both studies included Megan Knaus, Brian J. Zikmund-Fisher, and Enny Das.

"Communicating infectious disease prevalence through graphics: results from an international survey" was published in Vaccine.

"Effect of Influenza Label on Worry and Behavioral Intentions: A Multi-Country Web-Based Experiment" was published in Emerging Infectious Diseases.

http://bit.ly/2t6wCiG

Forgetting can make you smarter

For most people having a good memory means being able to remember more information clearly for long periods of time.

For neuroscientists too, the inability to remember was long believed to represent a failure of the brain's mechanisms for storing and retrieving information.

But according to a new review paper from Paul Frankland, a senior fellow in CIFAR's Child & Brain Development program, and Blake Richards, an associate fellow in the Learning in Machines & Brains program, our brains are actively working to forget. In fact, the two University of Toronto researchers propose that the goal of memory is not to transmit the most accurate information over time, but to guide and optimize intelligent decision making by only holding on to valuable information.

"It's important that the brain forgets irrelevant details and instead focuses on the stuff that's going to help make decisions in the real world," says Richards.

The review paper, published this week in the journal Neuron, looks at the literature on remembering, known as persistence, and the newer body of research on forgetting, or transience. The recent increase in research into the brain mechanisms that promote forgetting is revealing that forgetting is just as important a component of our memory system as remembering.

"We find plenty of evidence from recent research that there are mechanisms that promote memory loss, and that these are distinct from those involved in storing information," says Frankland.

One of these mechanisms is the weakening or elimination of synaptic connections between neurons in which memories are encoded. Another mechanism, supported by evidence from Frankland's own lab, is the generation of new neurons from stem cells. As new neurons integrate into the hippocampus, the new connections remodel hippocampal circuits and overwrite memories stored in those circuits,

making them harder to access. This may explain why children, whose hippocampi are producing more new neurons, forget so much information.

It may seem counterintuitive that the brain would expend so much energy creating new neurons at the detriment of memory. Richards, whose research applies artificial intelligence (AI) theories to understanding the brain, looked to principles of learning from AI for answers. Using these principles, Frankland and Richards frame an argument that the interaction between remembering and forgetting in the human brain allows us to make more intelligent memory-based decisions.

It does so in two ways. First, forgetting allows us to adapt to new situations by letting go of outdated and potentially misleading information that can no longer help us maneuver changing environments.

"If you're trying to navigate the world and your brain is constantly bringing up multiple conflicting memories, that makes it harder for you to make an informed decision," says Richards.

The second way forgetting facilitates decision making is by allowing us to generalize past events to new ones. In artificial intelligence this principle is called regularization and it works by creating simple computer models that prioritize core information but eliminate specific details, allowing for wider application.

Memories in the brain work in a similar way. When we only remember the gist of an encounter as opposed to every detail, this controlled forgetting of insignificant details creates simple memories which are more effective at predicting new experiences.

Ultimately, these mechanisms are cued by the environment we are in. A constantly changing environment may require that we remember less. For example, a cashier who meets many new people every day will only remember the names of her customers for a short period of time, whereas a designer that meets with her clients regularly will retain that information longer.

"One of the things that distinguishes an environment where you're going to want to remember stuff versus an environment where you want to forget stuff is this question of how consistent the environment is and how likely things are to come back into your life, " says Richards.

Similarly, research shows that episodic memories of things that happen to us are forgotten more quickly than general knowledge that we access on a daily basis, supporting the old adage that if you don't use it, you lose it. But in the context of making better memory-based decisions, you may be better off for it.

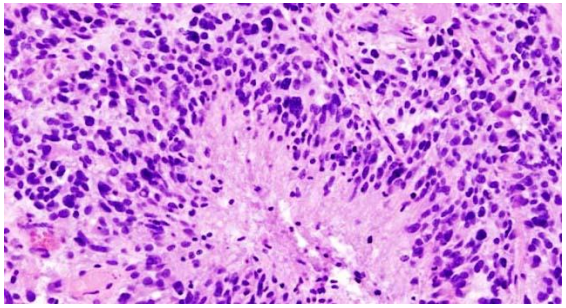
After the article publishes, it will be available at: http://www.cell.com/neuron/fulltext/S0896-6273(17)30365-3.

http://bit.ly/2tI9L9Z

Immune Cells Deliver Cancer Drugs to the Brain

Neutrophils loaded with the chemotherapy drug paclitaxel traverse the blood-brain barrier and kill residual cancer cells after tumor-resection surgery in mice.

By Diana Kwon



Glioblastomas, highly aggressive malignant brain tumors, have a high propensity for recurrence and are associated with low survival rates. Even when surgeons remove these tumors, deeply infiltrated cancer cells often remain and contribute to relapse.

Cerebral glioblastomaWIKIMEDIA, KGH

By harnessing neutrophils, a critical player in the innate immune response, scientists have devised a way to deliver drugs to kill these residual cells, according to a mouse study published today (June 19) in *Nature Nanotechnology*.

Neutrophils, the most common type of white blood cell, home in to areas of injury and inflammation to fight infections. Prior studies in both animals and humans have reported that neutrophils can cross the

blood-brain barrier, and although these cells are not typically attracted to glioblastomas, they are recruited at sites of tumor removal in response to post-operative inflammation.

To take advantage of the characteristics of these innate immune cells, researchers at China Pharmaceutical University encased paclitaxel, a traditional chemotherapy drug, with lipids. These liposome capsules were loaded into neutrophils and injected in the blood of three mouse models of glioblastoma. When the treatment was applied following surgical removal of the main tumor mass, the neutrophil-carrying drugs were able to cross the blood-brain barrier, destroy residual cancer cells, and slow the growth of new tumors. Overall, mice receiving treatment lived significantly longer than controls.

The treatment was unable to completely prevent tumor recurrence, however. "The surviving mice were not fully cured during the studied monitoring period, and several islands of tumor cells were still detected in the normal brain parenchyma," study coauthor Ran Mo, a professor of pharmaceutics at China Pharmaceutical University, writes in an email.

"Glioblastoma is a very aggressive tumor and the prognosis of patients is very poor. Despite all our great progress in medicine, we still haven't made as big of a dent as we'd like to in terms of improving outcomes for [these] patients," Michael Lim, a neurosurgery professor at Johns Hopkins University who was not involved in the study, tells *The Scientist*. "We need to think out of the box, and I applaud the authors for that."

"The strength [of this method] is that neutrophils are the most abundant white blood cells, so it's possible to collect them from a patient's blood in significant amounts," says Erwin Van Meir, a neuro-oncology researcher at Emory University who also did not participate in the work. However, he adds, in their animal models the authors used approximately ten times the number of neutrophils found in normal mouse circulation, meaning the amount of blood needed for this type of procedure in humans could be quite substantial.

Van Meir also points out that a limitation of this study is that "the brain tumor models they used are all flawed." He explains that two of the models are disliked within the neuro-oncology community because they elicit an immune rejection response, and the third model is based on a human glioblastoma cell line that a 2016 study discovered was different from the original tumor source. "So it's not clear at this stage how applicable this can be to humans," he says.

Although additional studies are necessary to further validate this method, this strategy of using neutrophils to deliver drugs across the blood-brain barrier could also be applied to neurodegenerative diseases and other inflammation-mediated disorders. "Any disease that naturally attracts neutrophils could be targeted [with this method]," Van Meir says.

According to Mo, the team is currently preparing to launch preclinical tests of their neutrophil-mediated drug delivery system. "We expect our treatment strategy will give [glioblastoma patients] some hope of a better life," says Mo. "But [there] is still a long way to go."

J. Xue et al., "Neutrophil-mediated anticancer drug delivery for suppression of postoperative malignant glioma recurrence," **Nature Nanotechnology**, *doi:10.1038/NNANO.2017.54, 2017.*

http://bbc.in/2u23mpK

Century-old Parkinson's question answered

Scientists say they have found the first direct evidence that the immune system does attack the brain in Parkinson's disease.

By James Gallagher Health and science reporter, BBC News website

The role of "autoimmunity" was first suggested nearly a century ago, but had not been confirmed. The discovery, in the journal Nature, suggests that drugs to calm the immune system could help manage the disease.

In Parkinson's the brain is progressively damaged leading to a tremor and difficulty moving. And at the same time very high levels of the protein alpha-synuclein accumulate in the brain.

Scientists - at Columbia University Medical Center and the La Jolla Institute for Allergy and Immunology - analysed the blood of 67

patients with the disease to see if they could find evidence of autoimmunity. The team discovered that T-cells, a part of your immune system, were launching an assault on the alpha-synuclein.

It means the immune system is recognising alpha-synuclein as a foreign invader such as a bacterium or virus.

It is likely the immune system tries to purge the body of alpha-synuclein and kills brain cells where the alpha-synuclein accumulates.

Prof David Sulzer, one of the researchers from Columbia University, said: "The idea that a malfunctioning immune system contributes to Parkinson's dates back almost 100 years. "But until now, no one has been able to connect the dots."

Radical

He believes that the study ties in with an another emerging theme in Parkinson's - that the disease may start in the gut. Prof Sulzer told the BBC News website: "We imagine that T-cells may first identify alpha-synuclein out in periphery, particularly in the nervous system of gut which is not a problem until the T-cells enter the brain."

Dr Alessandro Sette, from La Jolla, said: "Our findings raise the possibility that an immunotherapy approach could be used to increase the immune system's tolerance for alpha-synuclein, which could help to ameliorate or prevent worsening symptoms in Parkinson's disease patients."

David Dexter, from the charity Parkinson's UK, said: "This research lends weight to the radical idea that the condition may involve the immune system becoming confused and damaging our own cells.

"We still need to understand more about how the immune system may be involved in the complex chain of events that contribute to Parkinson's. "Ultimately this presents an exciting new avenue to explore to help develop new treatments that may be able to slow or stop the condition in its tracks."

http://bit.ly/2rPahSf

Biofilms -- the eradication has begun

Canadian scientists take a step forward in the fight against microbial armour?

Montreal - Have you ever heard of biofilms? They are slimy, glue-like membranes that are produced by microbes, like bacteria and fungi, in order to colonize surfaces. They can grow on animal and plant tissues, and even inside the human body on medical devices such as catheters, heart valves, or artificial hips. Biofilms protect microbes from the body's immune system and increase their resistance to antibiotics. They represent one of the biggest threats to patients in hospital settings. But there is good news - a research team led by the Research Institute of the McGill University Health Centre (RI-MUHC) and The Hospital for Sick Children (SickKids) has developed a novel enzyme technology that prevents the formation of biofilms and can also break them down.

This finding, recently published in Proceedings of the National Academy of Sciences (PNAS), creates a promising avenue for the development of innovative strategies to treat a wide variety of diseases and hospital-acquired infections like pneumonia, bloodstream and urinary tract infection. Biofilm-associated infections are responsible for thousands of deaths across North America every year. They are hard to eradicate because they secrete a matrix made of sugar molecules which form a kind of armour that acts as a physical and chemical barrier, preventing antibiotics from reaching their target sites within microbes.

"We were able to use the microbe's own tools against them to attack and destroy the sugar molecules that hold the biofilm together," says the study's co-principal investigator, Dr. Don Sheppard, director of the Division of Infectious Diseases at the MUHC and scientist from the Infectious Diseases and Immunity in Global Health Program at the RI-MUHC. "Rather than trying to develop new individual 'bullets' that target single microbes we are attacking the biofilm that protects those

microbes by literally tearing down the walls to expose the microbes living behind them. It's a completely new and novel strategy to tackle this issue."

This work is the result of a four-year successful collaboration between Dr. Sheppard's team and scientists in the laboratory of Dr. P. Lynne Howell, senior scientist in the Molecular Medicine program at SickKids. They have been working to combat biofilms for several years, focusing on two of the most common organisms responsible for lung infections: a bacterium called Pseudomonas aeruginosa and a fungus called Aspergillus fumigatus. Infections with these organisms in patients with chronic lung diseases like cystic fibrosis represent an enormous challenge in medical therapy.

While studying machinery that these organisms use to make their biofilms, the scientists discovered enzymes that cut up the sugar molecules, which glue biofilms together. "Microbes use these enzymes to move sugar molecules around and cut them into pieces in order to build and remodel the biofilm matrix," says Dr. Sheppard, who is also a professor in the departments of Medicine and Microbiology and Immunology at McGill University. The researchers found a way to use these enzymes to degrade the sugar armour, exposing the microbe to antibiotics and host defenses.

"We made these enzymes into a biofilm destroying machine that we can use outside the microbe where the sugar molecules are found," explains co-first study author Brendan Snarr, a PhD student in Dr. Sheppard's laboratory. "These enzymes chew away all of the sugar molecules in their path and don't stop until the matrix is destroyed."

"Previous attempts to deal with biofilms have had only limited success, mostly in preventing biofilm formation. These enzymes are the first strategy that has ever been effective in eradicating mature biofilms, and that work in mouse models of infection," adds Dr. Sheppard.

"When we took the enzymes from bacteria and applied them to the fungi, we found that they worked in the same way on the fungi biofilm; which was surprising," says the study's co-principal investigator, Dr. P. Lynne Howell, who is also a professor in the Department of Biochemistry at the University of Toronto. "What's key is that this approach could be a universal way of being able to leverage the microbes' own systems for degrading biofilms. This has bigger implications across many microbes, diseases and infections."

"Over 70 percent of hospital-acquired infections are actually associated with biofilms and we simply lack tools to treat them!" states Dr. Sheppard. According to both lead scientists, the potential of this novel therapy is enormous and they hope to commercialize it in the coming years.

About the study

This study was funded by the Canadian Institutes of Health Research (CIHR), Cystic Fibrosis Canada, the Natural Sciences and Engineering Research Council of Canada, Canada Research Chairs Program, the Fonds de recherche Quebec santé (FRQS) and SickKids Foundation.

Dr. Howell and Dr. Sheppard are also Network Investigators with the Canadian Glycomics Network (GlycoNet), part of the Networks of Centres of Excellence of Canada that has provided financial support for this work.

For additional information, we invite you to read the study. DOI: https://doi.org/10.1101/113696

http://bit.ly/2sEhdVd

Paracetamol during pregnancy can inhibit masculinity

Paracetamol during pregnancy can inhibit the development of 'male behavior' in mice; new research from the University of Copenhagen shows that it can reduce sex drive and aggressive behavior

University of Copenhagen The Faculty of Health and Medical Sciences

Paracetamol is popular for relieving pain. But if you are pregnant, you should think twice before popping these pills according to the researchers in a new study. In an animal model, Paracetamol, which is the pain-relieving substance found in the pills, actually damages the development of male behaviours.

Previous studies have shown the paracetamol can inhibit the development of the male sex hormone testosterone in male foetuses, thus increasing the risk of malformation of the testicles in infants. But

a reduced level of testosterone at the foetal stage is also significant for the behaviours of adult males, says Ph.D. David Møbjerg Kristensen, a researcher employed during the studies at the Department of Biomedical Sciences and the Novo Nordisk Foundation Center for Protein Research at the Faculty of Health and Medical Sciences.

"We have demonstrated that a reduced level of testosterone means that male characteristics do not develop as they should. This also affects sex drive. In a trial, mice exposed to paracetamol at the foetal stage were simply unable to copulate in the same way as our control animals. Male programming had not been properly established during their foetal development and this could be seen long afterwards in their adult life. It is very worrying," says David Møbjerg Kristensen.

The dosage administered to the mice was very close to the recommended dosage for pregnant women. Because the trials are restricted to mice, the results cannot be transferred directly to humans. However, the researchers' certainty about the harmful effects of paracetamol means it would be improper to undertake the same trials on humans, explains David Møbjerg Kristensen.

Markedly reduced male behaviour

Testosterone is the primary male sex hormone that helps develop the male body and male programming of the brain. The masculine behaviours in mice observed by the researchers involved aggressiveness to other male mice, ability to copulate and the need for territorial marking. The mice reacted significantly more passively than normal for all three parameters. They did not attack other males, they were unable to copulate and behaved more like female mice when it come to urinary territorial marking.

After observing the changed behavioural patterns, Prof. Anders Hay-Schmidt, who was employed at the then Department of Neuroscience and Pharmacology during his studies at the University of Copenhagen, investigated the specific effects of a lack of testosterone on the brain. The results showed up clearly here, too.

"The area of the brain that controls sex drive - the sexual dimorphic nucleus - had half as many neurons in the mice that had received paracetamol as the control mice. The inhibition of testosterone also led to a halving of the activity in an area of the brain that is significant for male characteristics," he explains.

Also affects female fertility

This study focused on the effect of paracetamol on masculine characteristics but paracetamol during pregnancy also has the potential to influence the subsequent lives of female mice. In 2016, the researchers published a study showing that female mice had fewer eggs in their ovaries if their mothers had had paracetamol during pregnancy. This led to the mice becoming infertile more quickly. But even if paracetamol is harmful, that does not mean it should never be taken, even when pregnant.

"I personally think that people should think carefully before taking medicine. These days it has become so common to take paracetamol that we forget it is a medicine And all medicine has side effects. If you are ill, you should naturally take the medicine you need. After all, having a sick mother is more harmful for the foetus," says David Møbjerg Kristensen.

He emphasizes that pregnant women should continue to follow the guidelines given by their country's health authorities and recommends people to contact their GP if in doubt about the use of paracetamol.

The study, "Prenatal exposures to paracetamol/acetaminophen and precursor aniline impair masculinisation of male brain and behaviour," has just been published in the scientific journal Reproduction.

http://bit.ly/2tI1OSs

Popular prostate drug linked to serious side effects

Treatment of benign prostatic hyperplasia with Avodart may put men at an increased risk for serious side effects

Boston - Treatment of benign prostatic hyperplasia (BPH) with the commonly prescribed Avodart (Dutsteride) may put men at an increased risk for diabetes, elevated cholesterol levels, non-alcoholic fatty liver disease (NAFLD) and worsening erectile dysfunction.

Physicians should be fully aware of these new findings according to the researchers, and to discuss with their patients the potential adverse side effects of Avodart on metabolic and sexual function before prescribing it. The study appears in the journal Hormones Molecular Biology and Clinical Investigations.

As men age, their prostate enlarges. This condition often results in urinary retention or other lower urinary tract symptoms, such as reduced urinary flow which results in waking up several times at night to urinate. To help improve symptoms, men are often prescribed an alpha blocker, such as Tamsulosin (Flomax) which relaxes the prostate smooth muscle and improves urination or other drugs such as Proscar (Finasteride) or Avodart (Dutsteride) which work by reducing prostate volume thus, improving urinary function.

"We believe our findings suggest that Avodart has a negative impact on men's overall health since it increases blood sugar and A1C and also increases blood lipids. The increase in blood glucose and A1C may predispose men to diabetes and the increase in lipids may predispose them to NAFLD. Most importantly, this agent worsens sexual function and reduces quality of life," explained corresponding author Abdulmaged M. Traish, MBA, PhD, professor of biochemistry and urology at Boston University School of Medicine (BUSM).

This retrospective study included one group of men with BPH who were prescribed Avodart and a second group who were prescribed Tamsulosin (an alpha blocker). Both groups were followed for 36-42 months. Data on blood glucose, hemoglobin A1C, total cholesterol, LDL cholesterol (bad cholesterol), HDL cholesterol (good cholesterol), liver function enzymes were determined at each visit over the entire follow up period. Participants also completed questionnaires to evaluate quality of life and the international index of erectile function to assess their sexual activity. The data for the men in Avodart group was then compared with the men prescribed Tamsulosin.

The BUSM researchers believe the data from this study and those reported by others in animal models as well in clinical studies strongly suggest that Avodart may have serious adverse side effects that were not obvious several years ago. "In order to reduce the negative impact on overall health and quality of life, physicians need to discuss with their patients the potential adverse side effects of taking Avodart," said Traish.

http://bit.ly/2u2Aq0P

A surprisingly simple explanation for the shape of bird eggs

Scientists have a convincing explanation for this stunning diversity: The shape of a bird's egg depends on how much its species flies

By Elizabeth Pennisi

A sandpiper's egg is shaped like a teardrop, an owl's like a golf ball, and a hummingbird's like a jelly bean. Now, for the first time, scientists have a convincing explanation for this stunning diversity: The shape of a bird's egg depends on how much its species flies.

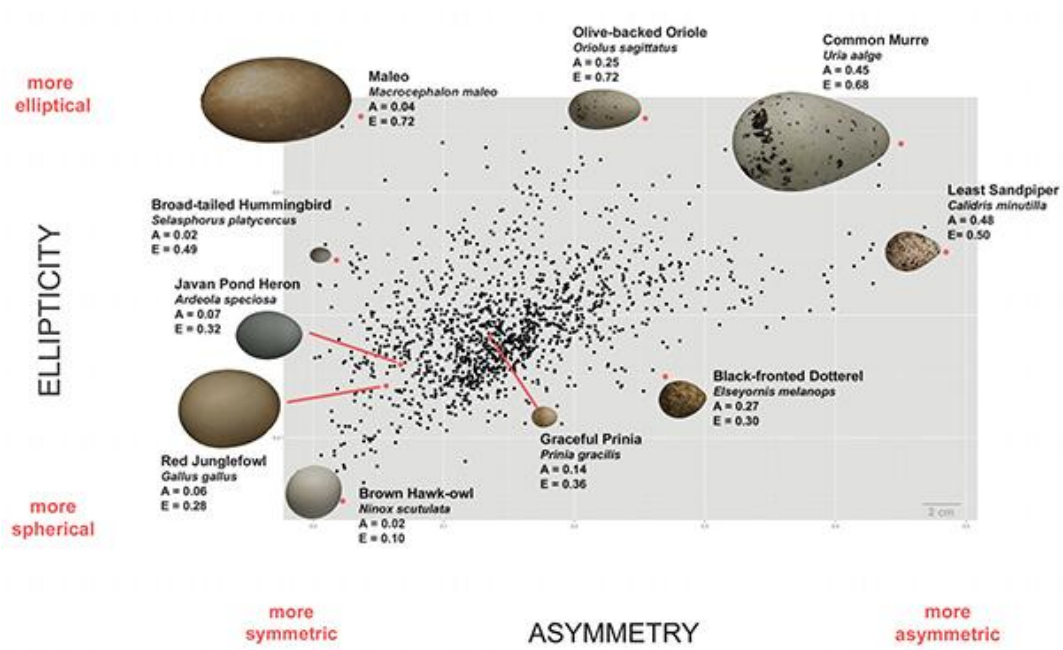
"It's nice to see a complete story of egg shape," says Mark Hauber, a behavioral ecologist at Hunter College in New York City who was not involved in the work. "[It's] an instant classic article."

Princeton University evolutionary biologist Mary Stoddard has long been fascinated that eggs are so diverse, even though they all basically do one thing—nourish and protect the developing chick. Fortunately, over the past century, the Museum of Vertebrate Zoology in Berkeley, California, has amassed thousands of egg shells from 1400 species and put digital photos of them online.

Stoddard and her colleagues wrote a computer program, Eggxtractor, that picks out the egg in any image and measures its length, width, and shape. The team used those measurements to determine how far from perfectly spherical each of nearly 50,000 eggs was—that is, how pointy or elongated it was. Some eggs are both pointy and elongated, some are one but not the other, and some are neither. But no eggs are short and pointy—approximately the shape of a hot air balloon.

Knowing that an egg's shape is determined not by the shell itself but by the membrane inside, Stoddard worked with Harvard University

physicist L. Mahadevan and his student Ee Hou Yong to come up with a mathematical representation based on the membrane's properties and how much pressure it received—from the developing chick on the inside. They then used their model to create scores of egg shapes by altering the membrane's stiffness and changing the pressure.



These are average egg shapes for each of 1400 species (black dots), illustrating variation in asymmetry and ellipticity. **L. Mahadevan/Museum of Vertebrate Zoology, Berkeley**

"Adjusting these [features], allows us to generate the entire diversity of egg shapes that we observe in nature," Stoddard says. The only one a real bird couldn't easily generate: an egg shaped like a hot air balloon.

This alone impresses experts in the field. "What's cool is you have the [overall] formula for egg shape," says Martin Sander, a paleontologist at Bonn University in Germany.

When Stoddard and her colleagues made a family tree of 1000 bird species, they realized that each group of birds tended to have a characteristic egg shape. But there seemed to be little correlation between that shape and nest type, nest location, or the number of young in a clutch—all previous proposed explanations for the shape of eggs.

As part of the work, the team also evaluated whether a proxy for flying ability—the ratio of a bird's wing length to its width—had an effect. "There was an obscure hypothesis that egg shape could be related to flight ability that no one had paid any attention to," Stoddard says. To her team's surprise, flying ability matters, they report today in Science. Good flyers like sandpipers and murres tend to lay eggs that are more elongated and more asymmetrical—a bit like the shape of a Zeppelin—likely because lots of time in the air requires lightweight, compact bodies. Meanwhile, birds that spend little or no time in the air, like tropical pittas and trogons, have more spherical eggs.

The reason, Stoddard speculates, is that round eggs require a wider pelvis than ones that are more elongated. Thus, just as birds that spend most of their time airborne have evolved more streamlined bodies and lighter, small skeletons, they have also evolved streamlined egg shapes to fit through the pelvis, she says.

"I'm surprised, but I'm also convinced," Sander says. "Based on this data set, they are making a very good case." He and Hauber are pleased that now they can guess how good a flyer a species is just by the shape of its eggs. "You can take this study and look at the egg and vey immediately get some general information," Sander says.

The work is significant on two levels, Stoddard says. For one, understanding egg shape and the role the membrane plays "could be of value to the egg industry," she says, perhaps by helping it create more durable eggs. But for her, just solving the puzzle of egg diversity is reward in itself. "Eggs aren't just a favorite breakfast food," she explains. A specialized egg, like that of modern birds, made it possible for developing young to survive on land, she notes, and thus allowed our land vertebrate ancestors to leave the seas about 360 million years ago. "They kick-started a revolution."

http://bit.ly/2tItLt9

High fat diet reduces gut bacteria, Crohn's disease symptoms

Results could lead to new anti-inflammatory probiotics

Researchers at Case Western Reserve University School of Medicine have shown a high fat diet may lead to specific changes in gut bacteria that could fight harmful inflammation--a major discovery for patients suffering from Crohn's disease. Crohn's disease, a type of inflammatory bowel syndrome, causes debilitating intestinal swelling, cramping, and diarrhea. The disease affects half a million people in the United States, but its cause is yet unclear.

In the new study, a diet of plant-derived "good" fats, including coconut oil or cocoa butter, drastically reduced bacterial diversity in mice with Crohn's-like disease. Mice fed beneficial fatty diets had up to thirty percent fewer kinds of gut bacteria as those fed a normal diet, collectively resulting in a very different gut microbial composition. Some of the species changes showed up in feces, while others were different in cecum, a portion of the intestine commonly inflamed in Crohn's disease. Mice fed even low concentrations of coconut oil or cocoa butter also had less severe small intestine inflammation.

"The finding is remarkable because it means that a Crohn's patient could also have a beneficial effect on their gut bacteria and inflammation by only switching the type of fat in their diet," said Alexander Rodriguez-Palacios, DVM, DVSc, PhD, first author on the study and Assistant Professor of Medicine at Case Western Reserve University. "Patients would only need to replace a 'bad' fat with a 'good' fat, and eat normal amounts."

The study is one of the first to identify specific changes in gut bacteria--our microbiome--associated with Crohn's disease. It is also the first to show how high fat diets can alter gut bacteria to combat inflammation. Rodriguez-Palacios presented his results at the annual Digestive Disease Week® conference in Chicago, Illinois earlier this month. The study was one of six accepted for presentation at the conference out of the laboratory of Fabio Cominelli, MD, PhD, Professor of Medicine and Pathology at Case Western Reserve University, and Division Chief of Gastroenterology at University Hospitals Cleveland Medical Center.

Results from the study could help doctors identify bacteria to use in probiotics to treat patients suffering from inflammatory bowel syndromes. "Ongoing studies are now helping us to understand which component of the 'good' and 'bad' fats make the difference in the gut microbes and make mice healthier," Rodriguez-Palacios said. "Ultimately, we aim to identify the 'good' fat-loving microbes for testing as probiotics."

The researchers anticipate their findings may have varying effects for patients. "Not all 'good' fats might be good in all patients," Rodriguez-Palacios cautioned. "Mice indicate that each person could respond differently. But diet is something we are very hopeful could help at least some patients without the side-effects and risks carried by drugs. The trick now is to really discover what makes a fat 'good' or 'bad' for Crohn's disease."

This research was supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (awards P30DK097948 which supports the Silvio O. Conte Cleveland Digestive Diseases Research Core Center and R01DK055812). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

http://bit.ly/2sPa7f5

Proton pump inhibitors do not contribute to dementia or Alzheimer's disease

Recent safety questions about PPIs answered in new study

Proton pump inhibitors (PPIs) are medications used to treat digestive problems such as ulcers and reflux disease by reducing the body's production of the acid that helps us digest food. Ulcers are sores that develop on the lining of our digestive system; when they develop in the upper part of the small intestine they are called "duodenal ulcers." Reflux disease is a condition in which stomach acid or other fluids in

the digestive system irritate our food pipe, also known as the esophagus.

Recently, safety questions about these medications have been raised in several studies. These studies suggested that PPIs increased the risk for dementia and Alzheimer's disease in people 75-years-old or older.

Noting that the prescription of PPIs is on the rise among middle-aged and older adults, a team of researchers designed a new study to examine PPIs and the risk of dementia, mild cognitive impairment, and Alzheimer's disease. They published their study in the Journal of the American Geriatrics Society. The researchers also examined whether people with mild cognitive impairment who took PPIs were at higher risk for developing dementia or Alzheimer's disease.

The researchers examined information from the National Alzheimer's Coordinating Center (NACC) database for 2005 through 2015. Data came from people who were 50-years-old or older and had either normal brain function (their scores on cognitive tests were normal and they could perform everyday activities) or mild cognitive impairment (their cognitive test scores were lower than normal but they could still perform everyday activities). The researchers monitored whether the participants took PPIs, how often they took them, and which PPIs they used.

Of the 10,486 participants:

More than 8 percent said they always used PPIs.

More than 18 percent used them occasionally.

More than 73 percent never used PPIs.

The people who always or occasionally used PPIs were significantly older than those who didn't. What's more, compared to the non-PPI users, a significantly higher percentage of those who took PPIs regularly or occasionally had heart disease, diabetes, hypertension, stroke or transient ischemic attack (TIA, a brief stroke-like attack that generally ends quickly but still requires immediate medical attention), and depression.

A higher percentage of people who took PPIs regularly or occasionally also took a higher percentage of anticholinergic medications, which are often used to treat incontinence, depression, and sleep disorders. These medications have been linked to cognitive impairment, too.

There was a decreased risk of cognitive decline among the people who used PPIs regularly, as well as among people who used them occasionally, said the researchers. The researchers cautioned that clinical trials would be needed to confirm whether PPIs were linked to a greater risk of cognitive decline.

This summary is from "Proton Pump Inhibitors and Risk for Mild Cognitive Impairment and Dementia." It appears online ahead of print in the May 2017 issue of the Journal of the American Geriatrics Society. The study authors are Felicia C. Goldstein, PhD; Kyle Steenland, PhD; Liping Zhao, MSPH; Whitney Wharton, PhD; Allan I. Levey, MD, PhD; and Ihab Hajjar, MD, MS.

http://bit.ly/2t4YORZ

More breast cancers were diagnosed at early stage after Affordable Care Act took effect

African Americans and Latinas saw largest increases in Stage 1 diagnoses

MAYWOOD, IL - A Loyola University Chicago study published this month has found an increase in the percentage of breast cancer patients who were diagnosed in early Stage 1, after the Affordable Care Act took effect. The increases in Stage 1 diagnoses were higher among African American and Latina breast cancer patients, compared to white patients.

The study by Abigail Silva, PhD, MPH, and colleagues is published in the journal Cancer Epidemiology. Silva is an assistant professor in the Department of Public Health Sciences of Loyola University Chicago Stritch School of Medicine.

The Affordable Care Act eliminated copayments and other out-of-pocket costs for 45 preventive care services, including mammograms. This made mammograms more affordable, potentially leading to earlier diagnoses.

The earlier cancer is detected, the more effectively it can be treated. Diagnosing breast cancer when it is still in Stage 1 could improve the prognosis for thousands of women and reduce the need for invasive treatments such as chemotherapy for a substantial number of women, Silva and colleagues wrote.

Breast cancer is the most common cancer among women in the United States. The American Cancer Society estimates nearly 253,000 women will be diagnosed this year. Compared to white women, Latinas are less likely to receive mammograms overall and African Americans are less likely to receive mammograms at recommended intervals. Out-of-pocket payments have been identified as a potential barrier to getting screening mammograms.

The retrospective study included 470,465 breast cancer patients between the ages of 50 and 74 who were covered by private insurance or Medicare and were newly diagnosed with Stage 1-4 cancer. Researchers examined two time periods: 2007-2009 (before the Affordable Care Act took effect) and 2011-2013 (after the act took effect). Researchers obtained data from the National Cancer Database, which includes approximately 70 percent of all newly diagnosed cancers in the United States from about 1,500 hospitals.

Overall, the percentage of breast cancers that were diagnosed at Stage 1 increased 3.6 percentage points, from 54.4 percent to 58.0 percent. There was a corresponding decrease in Stage 2 and Stage 3 diagnoses, while the proportion of Stage 4 cancers did not change. The shift toward Stage 1 breast cancer diagnoses increased by 3.2 percentage points among whites, 4.0 percentage points among African Americans and 4.1 percentage points among Latinas.

Compared to African Americans and Latinas, a higher percentage of white breast cancer patients are diagnosed at Stage 1. This disparity decreased following the Affordable Care Act, as minorities saw modestly higher improvements in Stage 1 diagnoses.

Researchers concluded that further studies to evaluate the impact of the Affordable Care Act on cancer outcomes and disparities "should be supported as they will help inform future policy recommendations."

The study was supported by grants from the National Institutes of Health and the Avon Foundation.

The study is titled "Potential impact of the Affordable Care Act's preventive services provision on breast cancer stage: A preliminary assessment."

In addition to Silva, other co-authors are Talar Markossian, PhD, MPH, of Loyola's Department of Public Health Sciences; Yamile Molina, PhD, of the University of Illinois School of Public Health, and Nazia Saiyed, MPH, of the Sinai Urban Health Institute.

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Existing drugs could benefit patients with bone cancer, genetic study suggests

A subset of bone cancer patients may respond to IGF1R inhibitors based on their genetic profile

A subgroup of patients with osteosarcoma - a form of bone cancer - could be helped by an existing drug, suggest scientists from the Wellcome Trust Sanger Institute and their collaborators at University College London Cancer Institute and the Royal National Orthopaedic Hospital NHS Trust. In the largest genetic sequencing study of osteosarcoma to date, scientists discovered that 10 per cent of patients with a genetic mutation in particular growth factor signalling genes may benefit from existing drugs, known as IGF1R inhibitors.

The results, published today (23 June) in Nature Communications suggest a re-trial of IGF1R inhibitors for the subset of patients with osteosarcoma who are likely to respond based on their genetic profile.

Osteosarcoma is the most common form of primary bone cancer in children and young adults, usually affecting people aged 10 to 24 years*. 160 new patients are diagnosed with osteosarcoma in the UK each year, of which around one third cannot be cured.

The current treatment for osteosarcoma is chemotherapy followed by surgery, where the bone tumours are removed. There has not been a new treatment for osteosarcoma in almost 40 years, in spite of extensive research.

In the study, scientists analysed the genome of 112 childhood and adult tumours - double the number of tumours studied previously. In

10 per cent of cases, the team discovered cancer-driving mutations in insulin-like growth factor (IGF) signalling genes.

IGF signalling plays a major role in bone growth and development during puberty. Researchers believe that IGF signalling is also implicated in the uncontrollable growth of bone that is characteristic of osteosarcoma.

IGF signalling genes are the target of existing drugs, known as IGF1R inhibitors. Past clinical trials of IGF1R inhibitors as a treatment for osteosarcoma yielded mixed results although occasional patients responded to the treatment. In spite of this, IGF1R inhibitors have not been further tested in osteosarcoma, as it had been unclear who would benefit from the treatment.

Dr Sam Behjati, first author from the Wellcome Trust Sanger Institute and University of Cambridge, said: "Osteosarcoma is difficult to treat. Despite extensive research over the past 40 years, no new treatment options have been found. In this study we reveal a clear biological target for osteosarcoma that can be reached with existing drugs."

In the study, scientists looked for mutations in the tumours to understand the mechanism of osteosarcoma development. The genetic information revealed a specific process for rearranging the chromosomes that results in several cancer-driving mutations at once.

Professor Adrienne Flanagan, senior author from the Royal National Orthopaedic Hospital NHS Trust and University College London Cancer Institute, said: "By sequencing the whole genome of the tumours, we have unpicked the mechanism behind osteosarcoma for the first time. We discovered a new process -- chromothripsis amplification - in which the chromosome is shattered, multiplied and rejigged to generate multiple cancer-driving mutations at the same time. We believe this is why we see very similar osteosarcoma tumours in children and adults, which are not the result of ageing."

Dr Peter Campbell, lead author from the Wellcome Trust Sanger Institute, said: "Currently, there are no new osteosarcoma treatments on the horizon. Genomic sequencing has provided the evidence needed to revisit clinical trials of IGF1R inhibitors for the subset of patients that responded in the past. The mutations of patients' tumours may enable clinicians to predict who will, and will not respond to these drugs, resulting in more efficient clinical trials. The drugs could be effective for 10 per cent of osteosarcoma patients."

Notes to Editors

About Osteosarcoma

Almost all -- 94 per cent -- of osteosarcomas start in the long bones of the arms and legs, including the lower thigh bone (distal femur), upper shin bone (proximal tibia) and upper arm bone (proximal humerus). It is an aggressive cancer that can spread in the bloodstream to the lungs, where it forms bony nodules that must be detected and cut out by hand.

http://bit.ly/2sOZFV0

Immunotherapy kinder than chemotherapy for patients with head and neck cancer

Nivolumab is kinder than chemotherapy for people with advanced head and neck cancer

The immunotherapy nivolumab is kinder than chemotherapy for people with advanced head and neck cancer - easing many of the negative effects of the disease on patients' quality of life.

Both head and neck cancer and the treatment for it can have a huge impact on patients - affecting their speech, breathing, eating and drinking, facial appearance, and general wellbeing.

All of this can cause substantial psychological, as well as physical, distress.

But patients taking part in a major phase III clinical trial reported that nivolumab helped them maintain a better quality of life for longer.

By contrast, the study -- led by researchers at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust -- found that people treated with standard chemotherapies docetaxel, methotrexate or cetuximab reported a decline in quality of life from the start of treatment.

Last year, the clinical trial of 361 patients found that nivolumab -- which sparks the immune system into action against cancers -- greatly increased survival for people with recurrent or metastatic head and

neck cancer. But the drug was initially rejected by NICE in April this year and is currently under consultation before a final decision is due.

The new results add to the growing body of evidence that immunotherapy can be a smarter, kinder treatment for people with cancer.

In the latest study, 129 patients on the trial filled in questionnaires about their quality of life - covering physical symptoms, mental health and general wellbeing. The research is published in the journal The Lancet Oncology today (Friday) and was funded by Bristol-Myers Squibb, with support from the NIHR Biomedical Research Centre at The Royal Marsden and The Institute of Cancer Research (ICR).

While patients on chemotherapy judged their quality of life to be lower at nine and 15 weeks into the trial, patients on nivolumab gave consistently better ratings throughout.

After nine weeks, patients given nivolumab reported that they were doing better than their counterparts on other treatments for a range of symptoms, including pain, sensory problems, appetite loss, tiredness and breathing problems. After 15 weeks, the list of beneficial effects was even longer, with patients taking nivolumab being less badly affected by nausea, insomnia and weight loss.

Professor Kevin Harrington, Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust, said:

"Head and neck cancer is an extremely debilitating disease, and if it spreads or patients relapse then it's extremely difficult to treat.

"But our research has found that nivolumab really is a game-changing treatment for patients with head and neck cancer. Not only does it extend survival -- we have now shown that patients feel much better in the extra time that the drug grants them.

"When immunotherapies first hit the clinic, there were concerns over side-effects and the fact that they didn't work for everyone. But in only two or three years we have become very good at managing the side-effects they cause, and we are better able to select patients in whom these treatments are most likely to be effective.

"We now need to test if we can move away from resorting to traditional chemotherapies, which come with far too much collateral damage, and see these smarter, kinder therapies used as a first-line treatment to replace chemotherapy altogether."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said: "Creating cancer treatments that can not only extend life but also minimise the impact of the disease on patients' lives is a major aim of researchers worldwide.

"So it's great news that this trial has found that as nivolumab greatly extends life among these patients it also gives marked improvements in quality of life compared with current treatment options.

"I hope that this drug will be now approved very soon for use on the NHS so that this group of patients, who badly need new treatment options, can see the benefit."

Professor David Cunningham, Director of Clinical Research at The Royal Marsden NHS Foundation Trust and Director of the NIHR Biomedical Research Centre at The Royal Marsden and The Institute of Cancer Research, London, said:

"Using the body's own immune system to attack cancer continues to find wider application across the spectrum of cancers we have to treat in the clinic. Head and neck cancer is a particularly challenging disease and these results are an important step in improving outcomes for our patients."

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