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Study suggests statins associated with lower rates of breast cancer and mortality

Suggests that statins are associated with lower rates of breast cancer and subsequent mortality

Barcelona, Spain - A 14 year study in more than one million people has found that women with high cholesterol have significantly lower rates of breast cancer and improved mortality. The research, presented today at ESC Congress, suggests that statins are associated with lower rates of breast cancer and subsequent mortality.

"This is the most conclusive and direct evidence as yet to confirm the link between high cholesterol and breast cancer, a topic that has been fascinating researchers for the past few years," said Dr Rahul Potluri, senior author and founder of the ACALM Study Unit at Aston Medical School, Aston University, Birmingham, UK.

"We previously found an association between having high cholesterol and developing breast cancer so we designed this study to follow up patients longitudinally and address the relationship more robustly," he continued. "Showing that patients with high cholesterol have a lower risk of developing breast cancer and subsequent mortality in a longitudinal study like this provides the strongest evidence for a protective effect, which is likely related to statins."

The current study followed-up women aged 40 or more with, and without, a diagnosis of high cholesterol and compared the development of breast cancer and subsequent mortality rates in the two groups. Patients admitted to UK hospitals with high cholesterol between 1 January 2000 and 31 March 2013 were recruited from the Algorithm for Comorbidities, Associations, Length of stay and Mortality (ACALM) clinical database. They were followed-up until 2013 for a new diagnosis of breast cancer and subsequent mortality obtained from the Office for National Statistics. Analyses were performed to adjust for demographic and clinical characteristics between the groups.

Out of a total of 1 220 024 patients in the ACALM study, there were 16 043 women with high cholesterol aged 40 or over who were compared to an equivalently sized and age-matched group of patients without high cholesterol.

The researchers found that those with high cholesterol were 45% less likely to develop breast cancer than those without high cholesterol. After adjusting for factors which might influence mortality, including age, sex, ethnicity, and the ten most common causes of death in the UK, the researchers found that patients who developed breast cancer were 40% less likely to die if they had high cholesterol than if they did not.

Dr Potluri said: "Compared to those without high cholesterol, patients with high cholesterol had a 45% reduced risk of breast cancer, and if they did develop breast cancer, a 40% reduced chance of death. If a diagnosis of high cholesterol leads to lower breast cancer rates this must either relate to something inherent in the condition or affected patients, or more likely, to treatment with widely used cholesterol lowering interventions such as statins."

Dr Paul Carter, lead author of this study and researcher at the ACALM Study Unit, said: "Our research confirms that women with a diagnosis of high cholesterol have strikingly lower rates of breast cancer with improved death rates and survival. Building on previous research by us and other groups, including animal studies in which statins reduced the risk of breast cancer, this gives a strong indication that statins produce this protective effect in breast cancer."

"Statins have some of the best mortality evidence amongst all cardiovascular medications and their use in patients with a diagnosis of high cholesterol is likely the reason this diagnosis appears to be protective against the development of breast cancer and subsequent mortality," continued Dr Carter.

He added: "The results of this study provide the strongest justification to date for a clinical trial evaluating the protective effect of statins in patients with breast cancer, and this is what we intend to do."

Dr Carter concluded: "Patients with breast cancer who have high cholesterol, people at high risk of cardiovascular disease, and those with established cardiovascular disease should be given statins according to current guidelines. I don't think at the moment we can give statins to prevent or reduce mortality from breast cancer per se. But a positive result in a clinical trial could change this and it is an exciting and rapidly progressing field."

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Anti-inflammatory drug 'cuts heart attack risk'

Anti-inflammatory drugs could cut the risk of heart attacks and strokes, a study of 10,000 patients suggests.

A trial of the drug canakinumab could represent the biggest breakthrough in treatment since the advent of statins to lower cholesterol, its authors say. The study reported a 15% reduction in the risk of a repeat heart attack among patients - but others questioned the drug's efficacy, side-effects and cost. Recipients of the drug had an increased risk of potentially fatal infections. However, the British Heart Foundation (BHF) said the "exciting and long-awaited trial" could still help save lives.

Arthritis drug

Heart attack patients are routinely given cholesterol-lowering statins and blood-thinning drugs to help reduce the risk of repeat attacks.

In this study, 10,000 patients who had previously had a heart attack were treated with the anti-inflammatory drug once every three months. The trial, held in almost 40 countries, monitored the individuals for up to four years. It found what researchers said were reductions in risk "above and beyond" those seen in patients who only took statins.

However, it also found a "significantly higher incidence" of potentially fatal infection and sepsis among those treated with the drug, according to the study. The results were presented at the European Society of Cardiology meeting, held in Barcelona, Spain.

Canakinumab was initially developed by pharmaceutical firm Novartis - which paid for the trial - to treat rheumatoid arthritis.

A heart attack is a serious medical emergency in which the supply of blood to the heart is suddenly blocked.

Experts have previously spoken about its possible link with inflammation of certain blood vessels. However, authors say such a link has never been proven before in humans.

The study's lead author Dr Paul Ridker, of Brigham and Women's Hospital, part of Harvard Medical School, said the study represented "a milestone in a long journey". "For the first time, we've been able to definitively show that lowering inflammation independent of cholesterol reduces cardiovascular risk," he said. "This has far-reaching implications."

Dr Ridker continued: "In my lifetime, I've gotten to see three broad eras of preventative cardiology. "In the first, we recognised the importance of diet, exercise and smoking cessation. In the second, we saw the tremendous value of lipid-lowering drugs such as statins. Now, we're cracking the door open on the third era. This is very exciting."

Dr Ridker said the findings also indicated "the possibility of slowing the progression of certain cancers", but further research was required.

'Safety trade-offs'

Dr Robert Harrington, chair of the Stanford University School of Medicine, sounded a note of caution in an editorial in the New England Journal of Medicine. He said the effects of anti-inflammatories could be "modest", and the absolute clinical benefit of canakinumab "cannot justify" its routine use "until we understand more about the efficacy and safety trade-offs, and unless a price restructuring and formal cost-effectiveness evaluation supports it."

Others, though, say the treatment could help those at risk of repeat heart attacks for whom statins are not enough.

Prof Jeremy Pearson, associate medical director at the BHF, said: "The findings suggest that existing anti-inflammatory drugs, such as canakinumab, could be given along with cholesterol-lowering drugs to treat survivors and further reduce their risk of another heart attack."

Gary Gibbons, director of the National Heart, Lung, and Blood Institute, said the findings provided "compelling evidence".

He called for further research into the findings.

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Study corrects the record on the relative risk of Alzheimer's between men and women

Women genetically predisposed to Alzheimer's are more susceptible than men between ages 65 and 75, researchers discover

White women whose genetic makeup puts them at higher risk for Alzheimer's disease are more likely than white men to develop the disease during a critical 10-year span in their lives, according to a study headed by Keck School of Medicine of USC researchers.

The findings from one of the world's largest big-data studies on Alzheimer's counter long-held beliefs about who is at greatest risk for the disease and when, suggesting new avenues for clinical trials.

Study results show genetically vulnerable 55- to 85-year-old white men and women have the same odds of developing the memory-erasing disease. One exception: From their mid-60s to mid-70s, these women still face significantly higher risk. That may provide clues to disease causes and potential interventions among these women.

"Our discovery is important because it highlights how clinical trials could be weighted toward women -- a susceptible part of the population -- to help scientists more rapidly identify effective drug interventions to slow or cure Alzheimer's," said Arthur Toga, director of the USC Stevens Neuroimaging and Informatics Institute at the Keck School of Medicine -- among the nation's leaders in innovative scientific discovery.

The study was published Aug. 28 in the Journal of the American Medical Association Neurology. It included data from 57,979 North Americans and Europeans in the Global Alzheimer's Association Interactive Network (GAAIN). This big-data project provides scientists around the world with shared data and sophisticated analysis tools to address a disease that makes up about 65 percent of the 47 million cases of dementia worldwide.

Times -- and data -- have changed

The results contradict a seminal 20-year-old study that found women with one copy of ApoE4, a gene variant linked to Alzheimer's, were diagnosed with the disease 50 percent more often than men with the same genetic profile.

The findings presented in the USC-led study expand the number of participant data by ninefold and indicate the critical decade falls between 65 and 75, more than 10 years after the start of menopause. Previous studies in animals and humans have reported a relationship between ApoE4, menopause and cognitive decline.

"So much work has been dependent on one 1997 finding, but with tools like GAAIN, we now have the ability to reinvestigate with increased statistical power," Toga said.

The new findings are significant because almost two-thirds of the more than 5 million Americans now living with Alzheimer's disease are women, according to the Alzheimer's Association.

Many attribute the imbalance in disease risk to the fact that women, on average, live longer than men. However, a growing body of evidence suggests other reasons also contribute to the difference. For instance, men have higher rates of heart disease and stroke. So, men who live longer may be healthier than women of the same age and may face less risk of developing Alzheimer's, according to the USC-led study.

In the future, doctors who want to prevent Alzheimer's may intervene at different ages for men and women, said Judy Pa, co-author of the study and an assistant professor of neurology at the USC Stevens Neuroimaging and Informatics Institute.

"Menopause and plummeting estrogen levels, which on average begins at 51, may account for the difference," Pa said. "However, scientists still don't know what is responsible. Researchers need to study women 10, 15 or even 20 years before their most vulnerable

period to see if there are any detectable signals to suggest increased risk for Alzheimer's in 15 years."

Worry less, work out more

Only some women are at increased risk of developing Alzheimer's in their mid-60s to mid-70s compared to men. To find out, women could have their DNA analyzed. However, Pa cautions that genetic testing for the ApoE4 variant is no crystal ball.

"There is controversy in terms of whether people should know their ApoE status because it is just a risk factor," Pa said. "It doesn't mean you're going to get Alzheimer's disease. Even if you carry two copies of ApoE4, your chances are greatly increased, but you could still live a long life and never have symptoms."

Even if some women discover they are at heightened risk, they can improve their odds by making life changes.

"Get more exercise. Work out your mind, especially in old age," Pa said. "Pick up hobbies that are cognitively or physically challenging. Reduce processed sugar intake because it's linked to obesity, which is associated with many chronic diseases."

More minorities please

Alzheimer's disease is the fifth-leading cause of death for Americans 65 and older, but it may one day outpace the nation's top two killers -- heart disease and cancer. Alzheimer's-related deaths increased by nearly 39 percent between 2000 and 2010 while heart disease-related deaths declined 31 percent and cancer deaths fell 32 percent, according to the Centers for Disease Control and Prevention.

Because Alzheimer's disease has a huge impact on lifelong health, USC has more than 70 researchers dedicated to the prevention, treatment and potential cure of the memory-erasing disease. Big data projects like this require experts across disciplines -- computer science, biology, pathophysiology, imaging and genetics -- to coordinate.

For this study, the researchers examined data from 27 different studies that assessed participants' ApoE gene variation, as well as characteristics such as sex, race, ethnicity, diagnosis (normal, mild cognitive impairment or Alzheimer's disease) and age at diagnosis.

The records of nearly 58,000 people were scrutinized. Meta-analyses were performed on 31,340 whites who received clinical diagnoses sometime between ages 55 and 85.

The proportion of minorities was so small that analysts could not draw statistically significant conclusions about their disease risk. Because of this, the study focused on whites only.

"Most of the archives around the world have insufficient numbers of underrepresented groups," Toga said. "One of the take-home messages from our study is people of all races and ethnicities need to be involved in Alzheimer's clinical trials because this disease is a problem that affects all of us."

The current findings need to be confirmed in more diverse study populations.

USC is working to build more diverse population studies related to Alzheimer's. Established in 1984, the Alzheimer Disease Research Center at the Keck School of Medicine reaches out to communities in the greater Los Angeles area to educate the city's diverse population about Alzheimer's and the clinical trials they might be interested in joining. Previous studies, for example, have focused on Latinos.

It's 2017: Time to focus on women

Historically, women have not been adequately represented in clinical trials, especially in studies on heart disease. Women need to be represented equally to men -- or even overrepresented, Pa said.

"The bottom line is women are not little men," Pa said. "A lot more research needs to target women because gender-specific variations can be so subtle that scientists often miss them when they control for gender or use models to rule out gender differences. Most research today is ignoring a big part of the equation."

The particulars

The study was made possible because of lead author Scott Neu, a leader in the development of a federated approach to analyzing

metadata and assistant professor of research at the Laboratory of Neuro Imaging at the Keck School of Medicine.

"GAAIN -- the free resource we created in conjunction with the Alzheimer's Association -- allows anyone to explore data sets around the world and conduct preliminary analyses to test scientific hypotheses," Neu said. "Our goal is to connect scientists with those who have collected data to create new collaborations to further research and understanding of Alzheimer's disease."

Analysts excluded people with a history of stroke, cerebrovascular disease, abnormal proteins that contribute to Parkinson's disease and dementia, gene mutations leading to higher levels of toxic amyloid brain plaques and any known neurological diseases.

Scientists did not adjust for known Alzheimer's risk factors such as education, family history of Alzheimer's or dementia because that information was not provided in all data sets. They also were unable to adjust for sex-dependent differences such as cigarette smoking, hormonal changes with age and alcohol usage.

The study was supported by the Alzheimer's Association through the Global Alzheimer's Association Interactive Network initiative (GAAIN-14-244631) via a $5 million grant and a portion of two National Institutes of Health grants: $12 million from Big Data to Knowledge (U54-EB020406) and $5 million from neuroimaging and genetics (P41-EB015922).

http://bit.ly/2vHbvkJ

A clockwork rover for venus

A good watch can take a beating and keep on ticking. With the right parts, can a rover do the same on a planet like Venus?

A concept inspired by clockwork computers and World War I tanks could one day help us find out. The design is being explored at NASA's Jet Propulsion Laboratory in Pasadena, California.

The Automaton Rover for Extreme Environments (AREE) is funded for study by the NASA Innovative Advanced Concepts program. The program offers small grants to develop early stage technology, allowing engineers to work out their ideas.

AREE was first proposed in 2015 by Jonathan Sauder, a mechatronics engineer at JPL. He was inspired by mechanical computers, which use levers and gears to make calculations rather than electronics.

AREE is a clockwork rover inspired by mechanical computers. A JPL team is studying how this kind of rover could explore extreme environments, like the surface of Venus. **NASA/JPL-Caltech**

By avoiding electronics, a rover might be able to better explore Venus. The planet's hellish atmosphere creates pressures that would crush most submarines. Its average surface temperature is 864 degrees Fahrenheit (462 degrees Celsius), high enough to melt lead.

Steampunk computing

Mechanical computers have been used throughout history, most often as mathematical tools like adding machines. The most famous might be Charles Babbage's Difference Engine, a 19th century invention for calculating algebraic equations. The oldest known is the Antikythera mechanism, a device used by ancient Greeks to predict astronomical phenomena like eclipses.

Mechanical computers were also developed as works of art. For hundreds of years, clockwork mechanisms were used to create automatons for wealthy patrons. In the 1770s, a Swiss watchmaker named Pierre Jaquet-Droz created "The Writer," an automaton that could be programmed to write any combination of letters.

Sauder said these analog technologies could help where electronics typically fail. In extreme environments like the surface of Venus, most electronics will melt in high temperatures or be corroded by sulfuric acid in the atmosphere.

"Venus is too inhospitable for kind of complex control systems you have on a Mars rover," Sauder said. "But with a fully mechanical rover, you might be able to survive as long as a year."

Wind turbines in the center of the rover would power these computers, allowing it to flip upside down and keep running. But the planet's environment would offer plenty of challenges.

The extreme planet

No spacecraft has survived the Venusian surface for more than a couple hours.

Venus' last visitors were the Soviet Venera and Vega landers. In the 1970s and 1980s, they sent back a handful of images that revealed a craggy, gas-choked world.

"When you think of something as extreme as Venus, you want to think really out there," said Evan Hilgemann, a JPL engineer working on high temperature designs for AREE. "It's an environment we don't know much about beyond what we've seen in Soviet-era images."

Sauder and Hilgemann are preparing to bake mechanical prototypes, allowing them to study how thermal expansion could affect their moving parts. Some components of the Soviet landers had actually been designed with this heat expansion in mind: their parts wouldn't work properly until they were heated to Venusian temperatures.

Tank treads for Venus

AREE includes a number of other innovative design choices.

Mobility is one challenge, considering there are so many unknowns about the Venusian surface. Sauder's original idea was inspired by the "Strandbeests" created by Dutch artist Theo Jansen. These spider-like structures have spindly legs that can carry their bulk across beaches, powered solely by wind. Ultimately, they seemed too unstable for rocky terrain. Sauder started looking at World War I tank treads as an alternative. These were built to roll over trenches and craters.

Another problem will be communications. Without electronics, how would you transmit science data? Current plans are inspired by another age-old technology: Morse code.

An orbiting spacecraft could ping the rover using radar. The rover would have a radar target, which if shaped correctly, would act like "stealth technology in reverse," Sauder said. Stealth planes have special shapes that disperse radar signals; Sauder is exploring how to shape these targets to brightly reflect signals instead. Adding a rotating shutter in front of the radar target would allow the rover to turn the bright, reflected spot on and off, communicating much like signal lamps on Navy ships.

Now in its second phase of NIAC development, the JPL team is selecting parts of the AREE concept to be refined and prototyped. Team members hope to flesh out a rover concept that will eventually be able to study the geology of Venus and perhaps drill a few samples.

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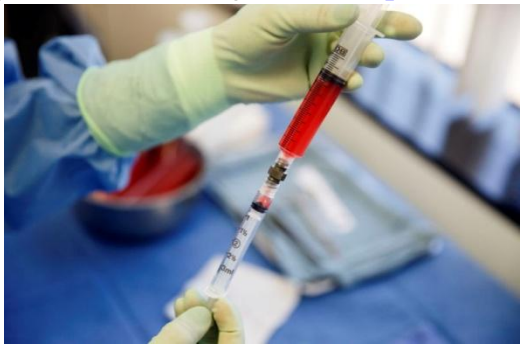
Dubious stem cell clinic got hold of smallpox vaccine. FDA just took it away

Agency warns of crackdown on "deceitful actors" and investigates the vaccine's origins.

Beth Mole - 8/29/2017, 8:40 AM

The Food and Drug Administration just put dubious stem cell clinics on notice. The agency announced plans on Monday for new policies and enforcement efforts to stamp out what it called "unscrupulous actors" peddling unproven, potentially dangerous, and often expensive stem cell therapies—including a bizarre and troubling instance involving smallpox vaccine.



A syringe of cells prepared for stem cell therapies **Getty | The Washington Post**

As an initial demonstration of its harder stance, the agency today posted information on two enforcement efforts. One was a warning letter to a Florida stem cell clinic that had posed as legitimate clinical research and ended up blinding three patients after injecting stem cells directly into their eyeballs. The other was a concerning announcement that the agency had seized five vials of smallpox vaccine from stem cell clinics in California.

The clinics, run by StemImmune Inc., were said to be mixing the dangerous vaccine with stem cells for an unproven, unapproved, and potentially harmful cancer treatment that was injected intravenously into patients or directly into their tumors. Though the injection of stem cells alone lacks safety and efficacy data, the vaccine is known to be dangerous. The vaccine contains a live poxvirus, similar but less harmful than smallpox. When it's injected into patients with weakened immune systems—such as many cancer patients—the vaccine can cause life-threatening side effects, such as swelling of the heart.

In today's announcement, the agency noted that the vaccine, Vaccinia Virus Vaccine (Live), is not commercially available. It is reserved for people at high risk of being infected by the otherwise eradicated virus, such as researchers or military personnel. "The FDA has serious concerns about how StemImmune obtained the product for use as part of an unapproved and potentially dangerous treatment," the agency said. The FDA added that it is actively investigating the vials' origins.

Disquieting dose

At least some of the vials came from the Centers for Disease Control and Prevention, according to CDC spokesperson Thomas Skinner. In an interview with Ars, Skinner explained that private and public institutions around the country can request the vaccine and that the agency has rules and regulations governing how it's dispensed. According to Skinner, StemImmune had told the CDC it needed the vaccine to protect some of its own researchers.

But in the FDA's announcement, the agency reported that it had confirmed that StemImmune was actually using the vaccine in cancer patients. The FDA said that, of the five vials it seized, four were intact and one was partially used. The agency is investigating where the other vials came from and how StemImmune got them.

In an e-mail to Ars, StemImmune did not respond to questions about the FDA's safety concerns or the origins of the vaccine vials. The company did offer this statement:

StemImmune, a biopharmaceutical company engaged in cutting-edge R&D of adult human stem cell-based therapies for the treatment of cancer, is fully cooperating with the FDA about the development of its stem cell-based investigational cancer therapy. We look forward to continuing our dialogue with the FDA as we seek to bring this important cancer therapy to cancer patients.

As for the Florida stem cell clinic, US Stem Cell, the FDA warned that it was marketing products without FDA approval. The clinic also had "significant deviations from current good manufacturing practice requirements, including some that could impact the sterility of their products, putting patients at risk," according to the FDA.

In a statement e-mailed to Ars, US Stem Cell responded:

The safety and health of our patients are our number-one priority, and the strict standards that we have in place follow the laws of the Food and Drug Administration. Since November 2014, we have offered the FDA unrestricted access to our facilities and our processes and will continue to work with them as it pertains to clinical and industry improvements. The FDA has stated that they will have specific stem cell guidelines by the 21st Century Cures Act deadline of December 13, 2017, and we intend to follow those standards as well.

Low-hanging fruit?

Questionable and harmful clinics like those run by StemImmune and US Stem Cell have proliferated in the US, according to researchers. A study last year found nearly 600 clinics had popped up across the country, claiming to treat everything from autism to Parkinson's disease, mild joint pain, mental health conditions, and cancers.

In today's announcement, FDA Commissioner Scott Gottlieb spoke firmly about cracking down on those clinics and their treatments:

Speaking as a cancer survivor, I know all too well the fear and anxiety the diagnosis of cancer can have on a patient and their loved ones and how tempting it can be to believe the audacious but ultimately hollow claims made by these kinds of unscrupulous clinics or others selling so-called cures... The FDA will not allow deceitful actors to take advantage of vulnerable patients by purporting to have treatments or cures for serious diseases without any proof that they actually work.

But Leigh Turner, a bioethicist at the University of Minnesota who has extensively researched these stem cell clinics (and published last year's study enumerating the clinics), is hesitant to say this is the beginning of the end for the harmful treatments. "In some respects, I feel encouraged by today's developments," he told Ars when reached by phone. The enforcement efforts and plans for new policies and working group are positive signs.

But, there have been "bold statements" before about crackdowns and nothing much happened afterward, he said. "And so, one question from me is—assuming [the FDA will] do something—are we going to see a more systemic, comprehensive, organized kind of approach to what looks like a serious problem in the market place? Or are we going to see a more 'low-hanging fruit' approach," in which the FDA goes after egregious cases following lots of complaints, media investigations, reports of harms, or lawsuits, etc.

"It's good to see the FDA do something," Turner said, but not when it's "on the backside of people being badly injured."

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Drug breakthrough for mosquito virus outbreaks

Scientists have discovered a way that could help treat severe inflammation from an infectious mosquito-borne disease during outbreaks.

A team of researchers led by Professor Suresh Mahalingam at Griffith University's Institute for Glycomics on the Gold Coast are developing ways to treat debilitating diseases caused by alphaviruses such as Chikungunya and Ross River virus. Their study is published this week in the journal Nature Microbiology.

Some mosquito-borne viruses cause severe joint and muscle inflammation, and there are no vaccines or specific drugs to treat the disease caused by these viruses. Chikungunya virus (CHIKV), a re-emerging alphavirus responsible for several outbreaks worldwide in the past decade, causes debilitating joint inflammation and severe pain.

During acute infection with Chikungunya virus, scientists found that a molecular complex, known as the inflammasome, became activated in patients suffering acute signs of the disease.

"When we infected mice with Chikungunya, we found that a type of inflammasome known as NLRP3 was activated, which triggered an inflammatory cascade, leading to severe joint inflammation and bone damage," said Dr Ali Zaid, a lead author of the study. "So we used a molecule which specifically inhibits the activation of NLRP3, and we found that it helped reduce Chikungunya inflammation in mice, and also helped reduce bone loss and muscle inflammation.

"We found the same in mice infected with Ross River virus. Targeting the inflammasome using this kind of drug could be an efficient way to treat patients suffering from acute Chikungunya or Ross River virus disease during outbreaks."

Collaborator Professor Matt Cooper from the Institute of Molecular Bioscience at the University of Queensland added, "By precisely modulating how our immune system responds to infection, we hope to develop new therapies that can be used to treat people with these serious diseases"

Chikungunya virus (CHIKV) has been responsible for millions of cases over the past decade, with locally confined epidemics striking the Indian Ocean island of La Réunion in 2006, India in 2008 and the Caribbean in 2015.

Ross River virus (RRV), an arthritogenic alphavirus endemic to Australia and the South Pacific, which causes similar manifestations, affects about 5000 people annually.

Professor Mahalingam said the findings were important as inflammasome NLRP3 was prominently expressed in CHIKV patients with severe disease. "The NLRP3 inhibitor drug, MCC950, provided significant amelioration of inflammation and disease in CHIKV-infected mice. The drug provided these therapeutic benefits without compromising antiviral immunity."

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Altered bacterial communities in the gut could be an indicator for Parkinson's disease

In search of a biomarker

Parkinson's disease is an insidious disease: by the time it manifests as the typical motor dysfunctions such as tremors or muscle rigidity, portions of the brain have already been irreversibly destroyed. By this stage, the disease will have often begun already decades earlier. In search of an early portent of the disease, researchers led by Prof. Paul Wilmes, head of the Eco-Systems Biology Group at the Luxembourg Centre for Systems Biomedicine (LCSB) of the University of Luxembourg, may now have found one in the gut: they have shown that the bacterial community in the gut of Parkinson's patients differs from that of healthy people even at a very early stage of the disease. The researchers present their results in the scientific journal Movement Disorders.

Experts have long been discussing the notion that Parkinson's disease originates far outside the brain. According to the "dual hit" hypothesis, a hitherto unknown pathogen intrudes into the body through two ports of entry: the nose or the gastrointestinal tract. Once there, it sets a pathological process in motion, above all the misfolding of the protein alpha-synuclein. This is a protein whose exact function remains unknown. Among other things, it is presumed to be involved in the excretion of messengers such as dopamine. The misfolding of this protein could propagate through the nerve pathways, where - decades later - it produces the typical clumping in the dopaminergic cells, known as Lewy bodies, that are characteristic of Parkinson's. Ultimately, nerve cells start to die off and the typical symptoms of Parkinson's disease appear.

The researchers led by Wilmes, together with physicians Prof. Brit Mollenhauer and Prof. Wolfgang Oertel and their teams in Göttingen, Kassel and Marburg, explored the question of whether the early events in the course of the disease also change the bacterial community, the microbiome, at the two possible ports of entry. They took samples from the nose and gut of 76 Parkinson's patients and 78 healthy control people who are taking part in a long-term study. They also examined the microbiome of 21 subjects diagnosed with iRBD, Idiopathic Rapid-Eye-Movement Sleep Behaviour Disorder. People with this sleep disorder have a greatly elevated risk of developing Parkinson's disease later in life.

It turned out that the bacterial community of the gut differed considerably between all three groups. "Parkinson's patients could be differentiated from healthy controls by their respective gut bacteria," explains the first author Dr. Anna Heintz-Buschart from the Eco-Systems Biology Group. And the majority of the differential bacteria showed similar trends in the iRBD group. For example, certain germs were more prevalent in one group while the count was lower in others. In the samples from the subjects' nasal cavities, however, the researchers found no such differences. The study also revealed that certain gut microbes are associated with non-motor Parkinson's symptoms, for example depression.

"We hope that, by comparing the groups, we will learn to better understand the role of the microbiome in the process of the disease and to find out what changes occur and when," Paul Wilmes explains. "This might deliver new starting points for early treatment of the disease. It would also be essential knowledge for one day being able to use the absence or presence of certain bacteria as a biomarker for early detection of the disease."

Apart from the LCSB researchers, scientists from the Paracelsus-Elena-Klinik in Kassel, the Department of Neurology of Philipps Universität in Marburg, and the Departments of Neurology and Neuropathology of the University Medical Center Göttingen were involved in the study. The work was supported by the Luxembourg Rotary Club under its "Espoir en tête" programme, by the Luxembourg National Research Fund (FNR) and the German Research Foundation (DFG).

http://bit.ly/2xAoqGg

Tears in tiny bone cells called osteocytes appear an important step to better bones

The force gravity and physical activity put on our bones causes tiny tears in the membranes of the tiny cells that enable us to make or break down bone, scientists say

AUGUSTA, Ga. - The force gravity and physical activity put on our bones causes tiny tears in the membranes of the tiny cells that enable us to make or break down bone, scientists say.

While that may sound bad, it's actually a key piece of how the force we put on our bones helps keep them strong, they report in the Journal of Orthopaedic Research.

"The bone has to constantly adapt and make sure that is has the right design to withstand the loads you are going to put it through," says Dr. Meghan E. McGee-Lawrence, biomedical engineer in the Department of Cellular Biology and Anatomy at the Medical College of Georgia at Augusta University.

Osteocytes manage the osteoblasts that make bone as well as the osteoclasts that break bone down and were known to sense mechanical loading, but just how they sensed load was unknown.

McGee-Lawrence and MCG cell biologist Dr. Paul McNeil are the first to find the small tears in response to force exacted by walking up the stairs or lifting weights.

Not only do the cells experience membrane tears but it's the highest number McNeil, an expert in cell membrane repair, has seen in a variety of cell types. "It's remarkable," says the study coauthor. And, the heavier the mechanical load, the more tears; for example the mice walking on a treadmill versus just moving about in their cage.

Better understanding the specific mechanism by which these cells sense then respond to mechanical load should enable identification of logical targets for improving the strength and health of aging bones as well as bones challenged by diseases like diabetes, says McGee-Lawrence the study's corresponding author.

Osteocytes are plentiful in bone and each has hundreds of tiny processes reaching out in every direction that help secure them to the bone matrix. McGee-Lawrence likens their look to a sweetgum ball. She and McNeil have early evidence the diminutive cells and their projections are both very vulnerable to tearing and that vulnerability appears to make them a natural for responding to mechanical load.

Once tears happen to cell membranes, more calcium rushes inside the cells. This mineral closely associated with bone health and present outside the cell at concentrations 10,000 times higher than inside the cell, was known to be an initiating signal, McNeil says. His work has shown how in many cell types including now osteocytes, the load causes the tears which allows calcium to rush in to both rapidly heal tears and to set in motion inside a host of actions that, in this case, remodels bone.

In cell cultures, they watched as increased calcium levels inside osteocytes triggered an increase in the production of the protein c-fos. The protein also is well-studied and known to be involved in the signaling pathways that lead to stronger bones in response to exercise, but c-fos' connection with membrane tearing was another unknown.

Osteocytes use their micron-thin tentacles to communicate with each other and the scientists also learned that when one osteocyte gets tears, it appears to communicate its load to neighboring osteocytes so the calcium level goes up in those as well even without a tear. The message the torn osteocyte shares it to tell osteoblasts to make the bones stronger and the osteoclasts to quit breaking bone down.

The idea of further shoring up bone is likely to be better prepared for whatever mechanical load comes next, McGee-Lawrence says.

Conversely, the lack of loading and subsequent tearing may be why astronauts' bone and muscle weaken in zero gravity, McNeil says.

McGee-Lawrence is principal investigator on a new $450,000 National Science Foundation grant that will help them further parse this important puzzle and the potential for enabling better bone health with age and disease.

"We are wondering if bone loss with aging is due to osteocytes becoming more fragile or less able to repair as we age," say McNeil, co-investigator on the ongoing studies. "If they do, you would lose them over time and, in fact, we know you do lose them."

Part of what they are doing with the new grant includes looking at mice with a genetic deficiency in cell membrane repair. They want to see if the 50-year-old drug poloxamer 188, which was designed to reduce the thickness of blood, is found in products like toothpaste and has been shown to repair other cell membranes, might help osteocytes remain proficient at responding to mechanical load. Like many of our senses that dull with age, aging osteocytes don't sense critical mechanical loads as well.

"It's a way you can influence membrane repair rates so if we speed up how fast that tear repairs, is that going to influence the osteocytes?" McGee-Lawrence says. They'll also look at the impact of slowing repair down.

No drug on the market for osteoporosis is known to enhance osteocyte sensitivity.

"We are starting to understand why calcium signaling gets initiated in wounded cells and then that gives us a mechanism we can target to try to influence how well bone detects mechanical loading," McGee-Lawrence says.

Disease may also complicate the common action of cell membrane tear and repair. For example, McNeil has shown diabetes, which is associated with bone loss, can lead to problems with membrane repair of other cell types. Now the MCG scientists are looking at whether it similarly affects osteocytes.

Bone and muscle health are inextricably connected and McNeil has done pioneering work that shows one way we keep our muscles strong and even increase their size is through this process of tear and repair in the membrane of muscle cells.

"If you go to the gym and exercise your muscles, they are going to get bigger and stronger and at the same time if you sit around all day your muscles are going to get weaker," McGee-Lawrence says. "Bone does the same thing." McNeil notes the difference between the right and left hands and arms of a right-handed tennis player.

"This bone is full of cells. Some are building new bone, some are breaking down bone and it is constantly being remodeled," McNeil adds, holding up a large muskox bone.

People hit their peak bone mass in the late 20s or early 30s. After that, the percentage of osteoblasts to osteoclasts starts to shift so that you are slowly losing rather than building bones. Active youth, they note, tend to build a better bone mass that should comfortably see them into old age, particularly if they remain active.

Failure of rapid membrane repair is associated with weaker muscles even muscle disease, they note, and the scientists expect the same also holds true in bone. Future studies include exploring whether repair failure contributes to common problems like osteoporosis.

http://bit.ly/2vIsbrS

Sense of smell is key factor in bird navigation

How do birds navigate over long distances? This complex question has been the subject of debate and controversy among scientists for decades, with Earth's magnetic field and the bird's own sense of smell among the factors said to play a part.

Now, researchers from the universities of Oxford, Barcelona and Pisa have shown in a new experiment that olfaction – or sense of smell – is almost certainly a key factor in long-distance oceanic navigation, eliminating previous misgivings about this hypothesis.

The research is published in the journal Scientific Reports.

Study leader Oliver Padget, a doctoral candidate in Oxford University's Department of Zoology, said: 'Navigation over the ocean is probably the extreme challenge for birds, given the long distances covered, the changing environment, and the lack of stable landmarks. Previous experiments have focused on the physical displacement of birds, combined with some form of sensory manipulation such as magnetic or olfactory deprivation. Evidence from these experiments

has suggested that removing a bird's sense of smell impairs homing, whereas disruption of the magnetic sense has yielded inconclusive results.

'However, critics have questioned whether birds would behave in the same way had they not been artificially displaced, as well as arguing that rather than affecting a bird's ability to navigate, sensory deprivation may in fact impair a related function, such as its motivation to return home or its ability to forage.

'Our new study eliminates these objections, meaning it will be very difficult in future to argue that olfaction is not involved in long-distance oceanic navigation in birds.'

In this new experiment, the researchers closely followed the movements and behaviour of 32 free-ranging Scopoli's shearwaters off the coast of Menorca. The birds were split into three groups: one made temporarily anosmic (unable to smell) through nasal irrigation with zinc sulphate; another carrying small magnets; and a control group. Miniature GPS loggers were attached to the birds as they nested and incubated eggs in crevices and caves on the rocky Menorcan coast. But rather than being displaced, they were then tracked as they engaged in natural foraging trips.

All birds went out on foraging trips as normal, gained weight through successful foraging, and returned to exchange incubation periods with their partners. Thus, removing a bird's sense of smell does not appear to impair either its motivation to return home or its ability to forage effectively.

However, although the anosmic birds made successful trips to the Catalan coast and other distant foraging grounds, they showed significantly different orientation behaviour from the controls during the at-sea stage of their return journeys. Instead of being well-oriented towards home when they were out of sight of land, they embarked on curiously straight but poorly oriented flights across the ocean, as if following a compass bearing away from the foraging grounds without being able to update their position.

Their orientation then improved when approaching land, suggesting that birds must consult an olfactory map when out of sight of land but are subsequently able to find home using familiar landscape features.

Senior author Tim Guilford, Professor of Animal Behaviour and leader of the Oxford Navigation Group in Oxford's Department of Zoology, said: 'To the best of our knowledge, this is the first study that follows free-ranging foraging trips in sensorily manipulated birds. The displacement experiment has – rightly – been at the heart of bird navigation studies and has produced powerful findings on what birds are able to do in the absence of information collected on their outward journey.

'But by its nature, the displacement experiment cannot tell us what birds would do if they had the option of using outward-journey information, as they did in our study. This heralds a whole new era of work in which careful track analysis of free-ranging movements, with and without experimental interventions, can provide inferences about the underlying behavioural mechanisms of navigation. Precision on-board tracking technology and new analytical methods, too computationally heavy to have been possible in the past, have made this feasible.'

O. Padget et al. Anosmia impairs homing orientation but not foraging behaviour in free-ranging shearwaters, Scientific Reports (2017). DOI: 10.1038/s41598-017-09738-5

http://bit.ly/2grqT8w

Senegalese 'miracle grain' could see Sahel prosper: TED

Fonio is a type of millet, a seeded grass which is a key staple in Africa

August 29, 2017 by Fran Blandy

A Senegalese chef is one step closer to turning an ancient grain found in his country—gluten-free and bursting with nutrients and amino acids—into the next trendy superfood.

Pierre Thiam, one of Africa's best-known chefs, told the TEDGlobal conference in Tanzania on Monday night of his dream to see "fonio" turn around the fortunes of the arid Sahel region which stretches just south of the Sahara

The grain is a nutty-tasting cross between couscous and quinoa which has been cultivated on the continent for some 5,000 years.

Thiam said he stumbled across it several years ago in south-eastern Senegal while doing research for a cookbook.

He discovered it was once so popular it was found in Egyptian tombs, accompanying people to the afterlife, and that Mali's ethnic Dogon people believe the entire universe sprung from a grain of fonio.

Now however, it is only produced in the western part of the Sahel in places like Kedougou, one of the poorest regions of Senegal.

"Desertification and lack of job prospects means much of the youth have left, they choose the deadly path of migration in search of better opportunities," said Thiam

"This is the reality of Kedougou and much of the Sahel today. A scary future, scarce food and no opportunities to change their situation."

Thrives in harsh environment

Fonio cultivation is "great for the environment", says Thiam.

"It tolerates poor soil and needs very little water. It thrives where nothing else will grow." And with the developed world's multi-billion-dollar gluten-free industry and its obsession with superfoods and healthy eating, Thiam wonders if "bringing fonio to the rest of the world could be the answer".

Last year he secured a commitment from US health food giant Whole Foods to carry the grain, with fonio appearing on New York shelves in July. However fonio is extremely laborious to husk, pound and turn into food, and having the grain readily available at a consistent quality for commercial users remains a challenge. Thiam said he would like to see a special African-owned and operated mill on the continent to streamline the process.

Tiny grain, big answers

And he rapped the "colonial mentality" that had made the Senegalese believe their own products were inferior—enjoying rice imported from China and baguettes and croissants from France while believing their home-grown grain was for "country people". "There is untapped agricultural capacity in the Sahel, all it takes is changing market conditions to activate that capacity," he said. "In a drought and famine-prone region, fonio grows freely. This tiny grain may provide big answers."

The TEDGlobal conference, which brings together speakers with innovative ideas, is taking place in Africa for the first time in a decade.

"Africa has a chance to lead the world by creating a new path to modernity. The biggest challenges facing the world over the next 20 years are already playing out in Africa," said conference curator Emeka Okafor.

These range from food security to creating millions of jobs in an increasingly automated world, redesigning cities, water scarcity and the fight against climate change.

http://bit.ly/2vwtNsL

Scientists map genomic atlas of your inner fish gut

Scientists have discovered a network of genes and genetic regulatory elements in the lining of the intestines that has stayed remarkably the same from fishes to humans.

Many of these genes are linked to human illnesses, such as inflammatory bowel diseases, diabetes and obesity.

The findings, which appear in the journal PLOS Biology, establish the fish as an experimental platform for studying how this ancient genetic information—distilled over 420 million years of evolution—controls the development and dysfunction of the intestine.

"Our research has uncovered aspects of intestinal biology that have been well-conserved during vertebrate evolution, suggesting they are of central importance to intestinal health," said John F. Rawls, Ph.D., senior author of the study and associate professor of molecular genetics and microbiology at Duke University School of Medicine. "By doing so, we have built a foundation for mechanistic studies of intestinal biology in non-human model systems like fish and mice that would be impossible to perform in humans alone."

The intestine serves a variety of important functions that are common to all vertebrates. It takes up nutrients, stimulates the immune system, processes toxins and drugs, and provides a critical barrier to microorganisms. Defects in the intestinal epithelial cells lining the intestine have been implicated in a growing number of ailments, including inflammatory bowel diseases, colorectal cancer, food allergy, diabetes, obesity, malnutrition and infectious diarrheas.

For decades, scientists have relied on animal models to gather information on intestinal epithelial cells that could help combat human diseases. But it wasn't clear just how alike these cells were across multiple species.

In this study, Rawls and his team used a comparative biology approach to tackle that question. Research associate Colin R. Lickwar, Ph.D., and colleagues generated genome-wide data from intestinal epithelial cells in four evolutionarily distant species: zebrafish, stickleback fish, mouse and human. Lickwar then created maps for each of the species depicting not only the activity level of all of the genes, but also the location of specific genetic sequences or regulatory elements that flipped those genes on and off.

Lickwar was surprised to find a striking amount of similarity between the different vertebrate species. He identified a common set of genes—an intestinal epithelial cell signature—some of which had shared patterns of activity in specific regions along the length of the intestine. What's more, many of the genes included in this conserved signature had previously been implicated in a variety of human diseases. Lickwar and Rawls wondered if this conserved genetic signature was controlled by regulatory elements that might also be shared between species.

To test if this was the case, they took various regulatory elements from fish, mice and humans and stuck them into the zebrafish. Because zebrafish are transparent organisms, the researchers could look under the microscope for patterns of color to tell whether a green fluorescent protein or red fluorescent protein, which they had inserted along with the regulatory element, had been flipped on in the intestine. They found that the regulatory switches transplanted from the other species worked in zebrafish, indicating a remarkable level of conservation.

"Our findings suggest that intestinal epithelial cells use an ancient core program to do their job in the body of most vertebrates," said Lickwar, who is lead author of the study. "Now that we have identified this core program, we can more easily translate results back and forth between humans and zebrafish."

"Genomic Dissection of Conserved Transcriptional Regulation in Intestinal Epithelial Cells," PLOS Biology (2017). DOI: 10.1371/journal.pbio.2002054

http://bbc.in/2qtdE0v

New meningitis test 'could save lives'

A hospital A&E department in Northern Ireland is to start using a new, rapid test for meningitis that should speed up diagnosis and save lives.

Meningitis can kill in hours yet the current way to positively identify the infection takes about two days.

UK researchers say the new test that the Royal Belfast Hospital for Sick Children will use gives results in under 60 minutes. This should let doctors treat fast and accurately, rather than "just in case".

Speedy treatment is vital because the infection can quickly overwhelm the body, and symptoms may not be obvious until it is dangerously advanced.

At the moment, doctors rely on clinical judgement to decide whether antibiotics are urgently needed.

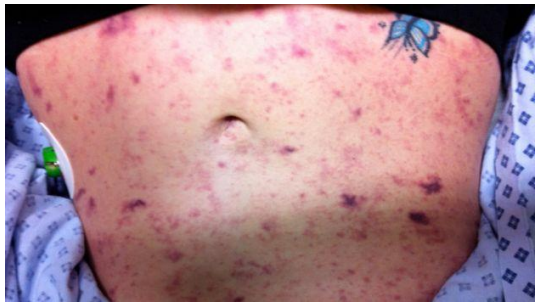
They err on the side of caution, which means some patients are given treatment they don't need.

However, on rare occasions cases can be missed, which is where a rapid "Lamp" (Loop Mediated Isothermal Amplification) test on blood, spinal fluid or nasal swab samples could help.

Anyone can get meningitis, but it is more common in babies, children and teenagers or young adults.

Amy's story

Amy Davis was 18 when she became severely ill with meningitis. Initially, she thought she just had a simple case of flu. Hours later, her body was covered head-to-toe in the alarming blotchy purple rash which is a classic - although not always present - sign of meningitis.



Amy's whole body was covered with the characteristic rash **Meningitis Research Foundation**

Amy, now 25, recalls: "My mum, being an ex-nurse, knew what it was straightaway and called an ambulance. "It was really scary. I remember looking at my dad and he looked absolutely terrified so I knew something was seriously wrong." Amy developed a serious complication called septicaemia or blood poisoning. The damage that this caused meant she needed her left leg amputated below the knee.

Meningitis facts

- ***Meningitis is an infection of the protective membranes surrounding the brain and spinal cord and caused by a number of different pathogens***
- ***Viral meningitis is the most common and least serious type. Bacterial meningitis is rare but can be very serious if not treated***
- ***If you are worried that someone is seriously ill with meningitis, trust your instincts and seek urgent medical help. Don't wait for a "tell-tale" rash***
- ***There are vaccines that can protect against some forms of meningitis***

Treating potential bacterial cases with antibiotics is still the safest approach and doctors at the Royal Belfast Hospital will continue to do this during the two-year pilot. But they will also use the rapid Lamp test to quickly see if their clinical hunches are right.

Researcher Dr Tom Waterfield from Queen's University, Belfast, said it could also spot less obvious cases that might otherwise slip through the net. "With the best will in the world you can still miss cases if a child looks quite well and you think it is viral rather than bacterial. "The test could also provide reassurance earlier to anxious parents that their sick child is getting the right treatment. Two days is a long time to wait for a confirmed diagnosis."

Rob Dawson, from the Meningitis Research Foundation, said a simple, rapid diagnostic was long overdue. "There is an urgent need for developments in this area and we look forward to seeing how this test could work in a hospital or healthcare settings."

The work is funded by the Health and Social Care NI Public Health Agency and by the Royal College of Emergency Medicine and is being done in collaboration with Queen's University Belfast, the Paediatric Emergency Research UK & Ireland Network and The Belfast Trust. Private company Hibergene have patented the Lamp testing equipment that is on loan to the hospital for the study.

http://bit.ly/2eJOM0V

Some women with history of pre-eclampsia have significantly lower risk for breast cancer

Buck Institute scientists use tissue samples from the California Teachers Study to confirm that the protection comes via a common genetic variant, goal is to develop new breast cancer prevention strategies for all women

Researchers have demonstrated that women with a history of preeclampsia, a pregnancy complication characterized by high blood pressure, have as much as a 90% decrease in breast cancer risk if they carry a specific common gene variant. Further studies are now underway to determine the mechanism of this protection in an effort to develop new breast cancer prevention strategies for all women. The study is now online in Cancer Causes & Control, and can be found here.

The research, directed by lead author Mark Powell, MD, MPH, and Buck Institute professor Christopher Benz, MD, was carried out in the large California Teachers Study. Women with preeclampsia were found to have a 74% lower risk of the most common type of breast cancer (hormone receptor positive) if they carried two T alleles of a

variant of the insulin-like growth factor receptor gene when compared to women carrying no T alleles. This decrease in risk increased to 90% if the pregnancy with preeclampsia occurred before the age of 30.

"We are thrilled to work with researchers from our Scientific Advisory Board on this exciting project with the potential for developing a new approach to prevention. This very much fits with our goal of reducing the risk of breast cancer," said Rose Barlow, Executive Director of Zero Breast Cancer, which administered the study with funding from the Avon Foundation for Women.

"This research could contribute to understanding the key impact of pregnancy on breast cancer risk, and may help explain why some women are protected while others are not," said Powell, who is a visiting scientist at the Buck Institute and is Director of the Breast Cancer Prevention Project.

Powell said women who develop high blood pressure in pregnancy have many associated changes in levels of hormones and growth factors, resulting in permanent protective breast tissue changes in women who carry the specific common gene variant. Powell and Benz are now working on a major collaborative effort to identify the mechanism of this protective effect with the goal of developing badly needed new prevention strategies. "Fellow researchers have demonstrated enormous interest in working with us," said Benz, who is also a practicing oncologist at the University of California San Francisco (UCSF). "This collective endeavor includes breast cancer investigators from UCSF, the Mayo Clinic, and many other leading research institutions." Working with the Komen Tissue Bank, Powell and Benz have obtained breast tissue from women identified as having high levels of protection, and are now analyzing this tissue in an effort to apply this naturally occurring process to all women.

"These study results may have a more immediate application in risk assessment," Powell added. "Research has shown this decrease in risk applies to women with gestational hypertension who carry the protective gene variant as well as those with preeclampsia. It is estimated that there are 9 million women in the U.S. whose risk could now be more accurately assessed, resulting in enhanced individualized breast cancer screening protocols."

Powell says the study results confirm and expand upon earlier findings from the Marin Women's Study, which consists of 13,344 Marin women whose contribution to this research cannot be overstated. Results were compelling enough to warrant validation in the larger California Teachers Study (CTS), which is a major long-term research study initiated in 1995 by the Cancer Prevention Institute of California (CPIC), and is comprised of 133,479 active and retired female public school teachers and administrators. This study was completed in collaboration with CPIC Senior Research Scientist Peggy Reynolds, PhD, MPH.

Citation: Functional IGF1R variant predicts breast cancer risk in women with preeclampsia in California Teachers Study DOI: 10.1007/s100552-017-0942-7

http://bit.ly/2etUqat

Inherited herpesvirus study finds links to ancient humans

Research into inherited human herpesvirus 6 identifies origins in a small number of people thousands of years ago and highlights the potential to 'reactivate'

An international study of integrated HHV-6 has discovered that a small number of human ancestors, one from about 24,000 years ago, have been responsible for transmitting ancient strains of the virus to individuals today - affecting about a million people in the UK alone.

Research led by the University of Leicester collected DNA samples from unrelated people who were carriers of the human herpesvirus 6, mostly from the UK and Europe but also from Japan, China and Pakistan. The researchers found that some of the inherited HHV-6 genomes are very similar to each other and are also ***located in the same chromosome in people having no known family relationship***. This showed that the HHV-6 genomes, which the scientists sequenced, originated in a small number of ancestors thousands of years ago.

The researchers also found that most of the ***inherited HHV-6 genomes are intact and therefore may be able to reactivate as viruses.***

The study makes an important contribution towards understanding the possible impact of inherited HHV-6 on the 1-2% of the UK population who carry it.

Dr Nicola Royle of the Department of Genetics and Genome Biology at the University of Leicester, who headed the study, said: "There are two types of HHV-6 (HHV-6A and HHV-6B) that have different biological, immunological, pathological and molecular properties.

"Initial infection by HHV-6 usually occurs in early childhood. Then, like most herpesviruses, HHV-6 enters a state of latency and persists for life in a small number of cells. Reactivation of latent HHV-6 can have severe consequences and often occurs in patients with a compromised immune system, for example in patients undergoing chemotherapy or haematopoietic stem cell (HSC) therapy, in particular when the stem cells are from cord blood.

"Unexpectedly, about 1-2% of the UK population ***(650,000 -1.3 million people)*** have inherited a copy of the human herpesvirus 6 genome as if it is part of their own human genome. The inherited HHV-6 genome is large, containing at least 86 viral genes, and is carried in a telomere. Telomeres are the essential capping structure at the ends of chromosomes that stablise the human genome and play important roles in cancer and ageing. Carriers of integrated HHV-6 bear one copy of the viral genome per cell and therefore have a high load of viral DNA. There has been very little research into the consequences for people who have inherited HHV-6, although a recent Canadian study has shown they have an increased risk of suffering from angina pectoris.

"We used molecular dating methods to compare, for example, the inherited HHV-6B genomes in five individuals from Sardinia, Orkney and England, and estimated that the most recent common ancestor with the inherited HHV-6B existed 24,500 ±10,600 years ago. Despite the antiquity of this inherited HHV-6B genome, it is intact and therefore potentially functional in all five carriers.

"We want to find out whether integrated HHV-6 carriers have an increased risk of disease or other adverse effects, and, if so, how this might be manifested. We think that there are three ways in which the inherited HHV-6 genome could have a deleterious effect:

The presence of the HHV-6 genome could compromise the function of the telomere in which it is integrated or affect the expression of nearby human genes

HHV-6 genes could be expressed from time to time over the carrier's lifetime and elicit an adverse immune response

the inherited HHV-6 genome could potentially reactivate and generate viable viruses.

"Our new research makes an important contribution towards understanding the possible impact of inherited HHV-6 on people that carry it. We now know that in Europe, and most likely in other populations as well, most inherited HHV-6 genomes have been inherited from a small number of ancestors thousands of years ago and still appear to have the potential to reactivate."

Stratification of carriers of inherited HHV-6 in modern populations due to common ancestry is an important consideration for genome-wide association studies that aim to identify disease risks for carriers. In addition the discoveries represent potentially important considerations for immune-compromised patients, in particular in the setting of organ transplantation and in stem cell therapy.

The work, published in the Journal of Virology, was carried out by staff and students in the Telomere Group, headed by Dr Nicola Royle in the Department of Genetics at the University of Leicester in collaboration with Prof. Andrew Davison and Prof. Ruth Jarrett and their teams in the MRC-University of Glasgow Centre for Virus Research.

The funders included the Medical Research Council and the Wellcome Trust Institutional Strategic Support Fund to the University of Leicester. Generation Scotland, funded by the Scottish Government Health Directorates and the Scottish Funding Council was a source for some of the samples used in the study.

The article appears here: JVI Accepts /
http://jvi.asm.org/content/early/2017/08/17/JVI.01137-17.abstract

http://bit.ly/2wnqkvw

Fetal membranes may help transform regenerative medicine

A new review looks at the potential of fetal membranes, which make up the amniotic sac surrounding the fetus during pregnancy, for regenerative medicine.

Fetal membranes have been used as biological bandages for skin grafts as well as for serious burns. They may also have numerous other applications because they contain a variety of stem cells, which might be used to treat cardiovascular and neurological diseases, diabetes, and other medical conditions.

"The fetal membranes have been used successfully in medical applications for over a century, but we continue to discover new properties of these membranes," said Dr. Rebecca Lim, author of the STEM CELLS Translational Medicine review. "The stem cell populations arising from the fetal membranes are plentiful and diverse, while the membrane itself serves as a unique biocompatible scaffold for bioengineering applications."

Concise Review: Fetal Membranes in Regenerative Medicine: New Tricks from an Old Dog?

- **Rebecca Lim**

Abstract

The clinical application of the fetal membranes dates back to nearly a century. Their use has ranged from superficial skin dressings to surgical wound closure. The applications of the fetal membranes are constantly evolving, and key to this is the uncovering of multiple populations of stem and stem-like cells, each with unique properties that can be exploited for regenerative medicine. In addition to pro-angiogenic and immunomodulatory properties of the stem and stem-like cells arising from the fetal membranes, the dehydrated and/or decellularized forms of the fetal membranes have been used to support the growth and function of other cells and tissues, including adipose-derived mesenchymal stem cells. This concise review explores the biological origin of the fetal membranes, a history of their use in medicine, and recent developments in the use of fetal membranes and their derived stem and stem-like cells in regenerative medicine. Stem Cells Translational Medicine *2017;6:1767–1776*

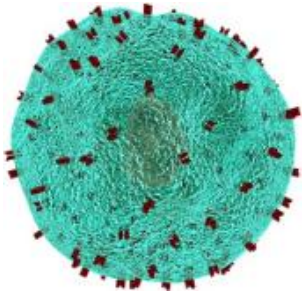
http://bit.ly/2woABaA

First CAR T-Cell Therapy Approved in U.S.

The genetically modified blood cells will be used for patients with a type of acute lymphoblastic leukemia, when other treatments fail.

By Shawna Williams | August 30, 2017

The US Food and Drug Administration (FDA) announced today (August 30) that it has approved the first therapy involving chimeric antigen receptor (CAR) T cells for clinical use. Each dose of Novartis's drug, Kymriah, will consist of a patient's own white blood cells, harvested from the body and genetically programmed to seek an antigen on the surface of leukemia cells.



Each patient's T-cells will be harvested from the body and genetically programmed to target leukemia cells. ALLINONEMOVIE, PIXABAY

"We're entering a new frontier in medical innovation with the ability to reprogram a patient's own cells to attack a deadly cancer," says FDA Commissioner Scott Gottlieb in a statement. "New technologies such as gene and cell therapies hold out the potential to transform medicine and create an inflection point in our ability to treat and even cure many intractable illnesses."

Kymriah is approved for patients 25 years old and younger who have B-cell acute lymphoblastic leukemia, and whose disease has relapsed at least twice or is still detectable after other treatment. In a clinical trial, the therapy left 83 percent of such patients cancer-free after three months. *STAT* notes that only a few hundred patients per year may be eligible for the cell therapy. Priced at $475,000, it will be offered at just 32 sites around the country. ***See "The CAR T-Cell Race"***

Despite the limited use of Kymriah, the approval ushers in "a new approach to the treatment of cancer and other serious and life-threatening diseases," FDA says. *Business Insider* reports that at an FDA meeting last month, oncologist Tim Cripe of Nationwide

Children's Hospital called Kymriah "the most exciting thing I've seen in my lifetime."

http://bbc.in/2goXEZN

Cyber-flaw affects 745,000 pacemakers

A total of 745,000 pacemakers have been confirmed as having cyber-security issues that could let them be hacked.

The Food and Drug Administration revealed that 465,000 pacemakers in the US were affected, in an advisory note about a fix to the problem. The pacemaker's manufacturer, Abbott, told the BBC there were a further 280,000 devices elsewhere. The flaws could theoretically be used to cause the devices to pace too quickly or run down their batteries.

However, Abbott said it was not aware of any cases of this happening, adding that it would require a "highly complex set of circumstances".

The Department of Homeland Security has said that an attacker would need "high skill" to exploit the vulnerabilities.

Three-minute fix

The affected pacemakers are branded as having been made by St Jude Medical, which was acquired by Abbott earlier this year.

Patients are being advised to ask their doctors about an available firmware update at their next scheduled appointment.

The pacemakers can receive the revised code by being placed close to a radio wave-emitting wand in a process that lasts about three minutes.

Pacemakers manufactured after 28 August will come with the new firmware pre-installed. "As with any firmware update, there is a very low risk of an update malfunction," the FDA said.

The regulator noted a very small number of St Jude devices had lost all functionality after a firmware update in the past.

Abbott said some patients might opt to continue with the old firmware as a consequence. "In some cases, doctors and patients will decide that the risks that could be associated with performing the new pacemaker firmware update for some patients may outweigh the benefits," it said in a note to pacemaker users. "If you do not receive the update, your pacemaker will continue to function as intended, and you can receive the update at any future time."

Legal battle

The benefit of allowing the pacemakers to send and receive data wirelessly is that patients can pair them with a transmitter at home that monitors the devices as they sleep and can potentially alert them to medical problems.

Abbott has already issued a firmware fix to its home transmitter system **Abbott**

A hedge fund, Muddy Waters Research, first warned the media in August 2016 that the cardiac equipment had security flaws and claimed they could be exploited by "low-level hackers". The investment company also revealed it had bet St Jude's shares would drop after it had been told of the issues by security company MedSec.

"[St Jude's] apparent lack of device security is egregious, and in our view, likely a product of years of neglect," Muddy Waters said at the time. St Jude responded by saying it stood behind the security and safety of its equipment and sued its accuser for defamation.

However, shortly after Abbott bought St Jude in January, the FDA confirmed there were vulnerabilities in the company's wireless home monitor system, which were subsequently addressed.

Then, in April, the watchdog said Abbott had failed to properly investigate wider cyber-security concerns. Even so, the medical company's legal action against Muddy Waters continues.

http://bit.ly/2eL8UzC

Study finds pallid bat is unfazed by venom of Arizona bark scorpion

The Arizona bark scorpion is the most venomous scorpion in North America.

It possesses venom that causes serious pain in humans and can kill a child if anti-venom is not administered quickly.

The pallid bat, a species that lives in a region ranging from southern British Columbia to central Mexico, is believed to be resistant to scorpion venom, but no laboratory studies have been performed to confirm this.

Pallid bat about to strike a giant desert hairy scorpion, which is larger than the Arizona bark scorpion used in the UC Riverside study. **I. Pittalwala, UC Riverside**

Researchers at the University of California, Riverside now report in a paper published online in PLOS ONE that the pallid bat hunts the Arizona bark scorpion but is unaffected by its venom even after it is stung multiple times during the hunt.

The study presents the first evidence that pallid bats are resistant to Arizona bark scorpion venom at concentrations that cause significant pain and death in mice.

"Even direct injection of venom in this bat in known doses has little effect on its behavior," said Khaleel A. Razak, Ph.D., an associate professor of psychology, who led the research project. "This suggests the evolution of mechanisms to modulate venom-induced pain in this bat species."

The pallid bat eats a variety of prey items: crickets, scorpions, centipedes, ground beetles, grasshoppers, cicadas, praying mantises, and long-horned beetles. They are also known to eat lizards and rodents. The species is a gleaning bat (meaning it plucks prey from leaves or the ground) and uses passive listening of prey-generated noise to localize and hunt terrestrial prey. This bat uses echolocation only for general orientation and obstacle avoidance.

Razak and his team had two main reasons for conducting the study on venom resistance: First, they wanted to identify mechanisms of pain modulation in the pallid bat. Second, they wanted to perform a comparison across animal species to understand different mechanisms of venom resistance. For example, the grasshopper mouse also has a mechanism of Arizona bark scorpion venom resistance.

The researchers used high-speed video in the lab to determine that the Arizona bark scorpion does indeed sting the pallid bat. Next, they injected a known concentration of the scorpion's venom directly into the pallid bat. They found the bat was resistant to the venom.

Razak and his team then performed an analysis of the dorsal root ganglia - clusters of nerve cell bodies in the dorsal root of spinal nerves - of the pallid bat and focused on "voltage gated sodium ion channels" which are present in pain receptors (or nociceptors). Pain signals are transduced into action potentials by pain receptors using these ion channels. Scorpion venom typically targets these ion channels.

The researchers identified amino acid substitutions in the voltage gated sodium ion channels in the dorsal root ganglia that may confer resistance to the venom. Specifically, they identified a few mutations in the channels that transduce pain signals.

"These mutations are novel in the pallid bat, suggesting an unknown mechanism of pain modulation in the pallid bat that involves altered ion channel function," said Bradley H. Hopp, a graduate student in Razak's lab and the first author of the research paper. He got interested in this research after identifying scorpion pieces in known pallid bat roosts. "Our work sets the stage to not only identify potentially novel mechanisms of pain modulation with application to human pain management but also increase our understanding of adaptive modifications of ion channel function that modulate the excitability of neurons."

The research team plans to test the function of mutations they found to help explain the mechanism by which pallid bats are immune to Arizona bark scorpion venom.

"We know that voltage gated sodium ion channels are important in generating the neural signals that we perceive as pain," Razak said. "We hope to identify the ways that the pallid bat has altered these channels to reduce pain, and to see if that process can be mimicked pharmacologically. We also want to study gleaning behavior from an evolutionary perspective. About 30 of the ~1200 species of bats use gleaning as their foraging strategy. But they come from different families of bats, which means gleaning—and potentially scorpion venom resistance in other bats—must have evolved in a convergent manner."

Razak, who began his career as an engineer in India, worked for a company that built ultrasound scanners to detect pregnancies. This got him interested in sonar, radar, and hearing. At the University of Wyoming, where he got his doctoral degree, he took an interest in biosonar, also known as echolocation—the production, reception, and analysis of sound waves for the purpose of locating objects. At UC Riverside, his lab mostly focuses on research questions relevant to the sense of hearing, including hearing in bats.

http://bit.ly/2vx6LCh

Study negates concerns regarding radioactivity in migratory seafood

New research shows negligible risk from consumption of meat from migratory marine predators following Fukushima nuclear disaster

When the Fukushima power plant released large quantities of radioactive materials into nearby coastal waters following Japan's massive 2011 earthquake and tsunami, it raised concerns as to whether eating contaminated seafood might impair human health—not just locally but across the Pacific.

A new study by an international research team shows that those concerns can now be laid to rest, at least for consumption of meat from migratory marine predators such as tuna, swordfish, and sharks.

The team focused on cesium, a silvery metal with a large number of radioactive isotopes. Two of these, 134Cs and 137Cs, form when uranium fuel breaks down in nuclear reactors. The cesium isotopes are of particular concern because they were discharged in large quantities following the disaster, exhibit relatively long half-lives (2.1 and 30 years respectively), and tend to accumulate in the muscle tissues that people like to eat.

However, the team's sampling of tissues from predatory fishes and other large vertebrates collected across the northern Pacific between 2012 and 2015 revealed no detectable levels of 134Cs, and 137Cs concentrations that were generally consistent with background levels from aboveground nuclear testing during the 1940s and 50s. They collected the animals from waters near Japan, Hawaii, and California.

Lead author Daniel Madigan of Harvard University says, "Our measurements and associated calculations of how much radioactive cesium a person would ingest by eating this seafood shows that impacts to human health are likely to be negligible. For marketed fish to be restricted from trade, the cesium levels would have to be more than 1,600 times higher than in any samples we measured."

Co-author Kevin Weng, an assistant professor at William & Mary's Virginia Institute of Marine Science, participated in the study by collecting fish samples in waters around Oahu and a remote seamount. He says, "Go ahead and eat some sushi! Our work shows that radioactivity from the Fukushima disaster is very low in open-ocean vertebrates."

Also contributing to the study were Zofia Baumann and Nicholas Fisher of Stony Brook University; Owyn Snodgrass, Heidi Dewar, and Peter Dutton of NOAA's Southwest Fisheries Science Center; Michelle Berman-Kowalewski of the Channel Islands Cetacean Research Unit; and Jun Nishikawa of Tokai University.

The researchers undertook their analysis partly in response to earlier studies by Madigan and colleagues showing elevated levels of radioactive cesium in bluefin and albacore tuna caught off the California coast shortly after the Fukushima disaster—evidence that these fishes had swum almost 6,000 miles in less than two months. (It

took ocean currents more than two years to deliver much-diluted cesium from Fukushima to those same waters.)

Although this early work focused on the utility of cesium isotopes as a happenchance tool that could help scientists characterize migratory patterns among a group of heavily exploited commercial fishes, public attention focused on perceived risks to human health.

"The earlier studies showed extremely low risks from cesium to anyone eating these migratory species, but public concern persisted," says Weng. That concern also expanded to include not only the species of tuna in which cesium had been measured, but to other fishes, marine mammals, and sharks.

"People were very concerned about North Pacific salmon, halibut and scallops off British Columbia, and sea lions in Southern California," says Madigan. "There was even information on the Internet that 'the Pacific is dead'."

"One goal of our study," he says, "was to put these perceived risks in context by surveying a broad range of vertebrate species across the entire North Pacific for the presence or absence of Fukushima-derived radiocesium. Our results, which show very low or undetectable levels in these animals, are important both for public perception of seafood safety and for scientific understanding of radionuclide transfer."

The authors suggest that scientists and funding agencies should look for at least one silver lining in any future nuclear or industrial accidents.

"We can and should use future point sources of contamination, radioactive or otherwise, to shed new light on migratory dynamics of pelagic species that are poorly understood, heavily exploited, or of high conservation concern," says Madigan. "But we would need to act quickly, within that narrow opportunistic timespan."

More information: Daniel J. Madigan et al, Assessing Fukushima-Derived Radiocesium in Migratory Pacific Predators, Environmental Science & Technology (2017). DOI: 10.1021/acs.est.7b00680

http://bit.ly/2eLk5bN

Apes' abilities misunderstood by decades of poor science

Apes' intelligence may be entirely misunderstood, because research has so far failed to measure it fairly and accurately, according to scientists.

Hundreds of scientific studies over two decades have told us that apes are clever - just not as clever as us.

A new analysis argues that what we think we know about apes' social intelligence is based on wishful thinking and flawed science.

Dr David Leavens, of the University of Sussex, with Professor Kim Bard, University of Portsmouth, and Professor Bill Hopkins, Georgia State University, published their analysis in the journal Animal Cognition.

Dr Leavens said: "The fault underlying decades of research and our understanding of apes' abilities is due to such a strongly-held belief in our own superiority, that scientists have come to believe that human babies are more socially capable than ape adults. As humans, we see ourselves as top of the evolutionary tree. This had led to a systematic exaltation of the reasoning abilities of human infants, on the one hand, and biased research designs that discriminate against apes, on the other hand.

"Even when apes clearly outperform young human children, researchers tend to interpret the apes' superior performance to be a consequence of inferior cognitive abilities.

"There is not one scientifically sound report of an essential species difference between apes and humans in their abilities to use and understand clues from gestures, for example. Not one.

"This is not to say such a difference won't be found in future, but much of the existing scientific research is deeply flawed."

This isn't the first time science has seen such a pervasive collapse of rigor - 100 years ago scientists were sure that northern Europeans were the most intelligent in our species. Such bias is now seen as antiquated, but comparative psychology is applying the same bias to

cross-species comparisons between humans and apes, the researchers say.

Professor Bard said: "In examining the literature, we found a chasm between evidence and belief. This suggests a deep commitment to the idea that humans alone possess sophisticated social intelligence, a bias that is often not supported by the evidence."

The starting point in comparative psychology research is that if an ape makes a pointing gesture, say a point to a distant object, the meaning is ambiguous, but if a human does it, a double standard of interpretation is applied, concluding that humans have a degree of sophistication, a product of evolution, which other species can't possibly share.

In the absence of rigorous scientific research, Professor Bard said, "it is reasonable to ask if current comparative or developmental psychology has anything useful to contribute to our understanding of the 'cognitive foundations' of communication development.

"For researchers interested in the origins of language, focusing on behaviours without considering the animal's specific learning experiences will easily and inaccurately load results in favour of humans."

Examples of this bias include in one large set of studies, the children were raised in Western households, steeped in the cultural conventions of nonverbal signalling, whereas the apes were raised without that cultural exposure. When both were tested on their understanding of Western conventions of non-verbal communication, of course the children out-performed the apes on some tasks, but it remains ambiguous whether this is due to their evolutionary histories or their specific learning experiences with respect to non-verbal communication.

In another study, children aged 12 months were compared to apes aged, on average, 18-19 years old. The study found that humans alone have evolved to be able to point towards an absent object, taking no account of the differences in the humans' and apes' age, life history, or environment. More recent studies have amply demonstrated that, like human children, adult apes do communicate about absent objects.

The researchers cite four possible remedies for what they describe as the pervasive superiority complex in comparative psychology research:

Cross fostering - where apes are 'adopted' by humans, gives the clearest available comparison between the two species. The method has a long history and raises many ethical issues, so this is a theoretically strong remedy but one that is often not ideal in practice. Cross fostering has shown that apes brought up alongside humans cannot produce many spoken words, but they can communicate in ways other apes do not.

Radical operationalisation - where scientific explanations for comparisons between apes and humans are grounded in variables which can be objectively measured. Dr. Leavens and colleagues say many explanations for skills in comparative psychology research can't be observed or measured, and therefore can't be scientifically tested.

Training - if apes are to be compared to humans, they should first be given training and experience in the skills being tested. Science has for too long assumed human behaviour is spontaneous and not taken account of the training and experience a human child has, for example, in seeing others point and coming to learn and understand the gesture. Specifying the amount and types of training necessary for a naïve individual to learn a skill, would advance the field.

Sampling - almost all studies comparing humans with apes have compared humans from a small group - Western, educated, industrialised, rich and democratic - with apes who have been orphaned and/or raised in sterile institutions. In 2014, Professor Bard and Dr Leavens proposed, in the Annual Review of Anthropology, that more than a single group of humans should be compared to more than a single group of apes to determine the influence of environment on communicative outcomes, for example.

More information: David A. Leavens et al. The mismeasure of ape social cognition, Animal Cognition (2017). DOI: 10.1007/s10071-017-1119-1

http://bit.ly/2x0mRo3

Mouth clicks used in human echolocation captured in unprecedented detail

Findings could aid efforts to use synthetic mouth clicks to better understand human echolocation

Like some bats and marine mammals, people can develop expert echolocation skills, in which they produce a clicking sound with their mouths and listen to the reflected sound waves to "see" their surroundings. A new study published in PLOS Computational Biology provides the first in-depth analysis of the mouth clicks used in human echolocation.

The research, performed by Lore Thaler of Durham University, U.K., Galen Reich and Michael Antoniou of Birmingham University, U.K., and colleagues, focuses on three blind adults who have been expertly trained in echolocation. Since the age of 15 or younger, all three have used echolocation in their daily lives. They use the technique for such activities as hiking, visiting unfamiliar cities, and riding bicycles.

While the existence of human echolocation is well documented, the details of the underlying acoustic mechanisms have been unclear. In the new study, the researchers set out to provide physical descriptions of the mouth clicks used by each of the three participants during echolocation. They recorded and analyzed the acoustic properties of several thousand clicks, including the spatial path the sound waves took in an acoustically controlled room.

Analysis of the recordings revealed that the clicks made by the participants had a distinct acoustic pattern that was more focused in its direction than that of human speech. The clicks were brief--around three milliseconds long--and their strongest frequencies were between two to four kilohertz, with some additional strength around 10 kilohertz.

The researchers also used the recordings to propose a mathematical model that could be used to synthesize mouth clicks made during human echolocation. They plan to use synthetic human clicks to investigate how these sounds can reveal the physical features of objects; the number of measurements required for such studies would be impractical to ask from human volunteers.

"The results allow us to create virtual human echolocators," Thaler says. "This allows us to embark on an exciting new journey in human echolocation research."

Citation: PLOS Computational Biology: Thaler L, Reich GM, Zhang X, Wang D, Smith GE, Tao Z, et al. (2017) Mouth-clicks used by blind expert human echolocators - signal description and model based signal synthesis. PLoS Comput Biol 13(8): e1005670. https://doi.org/10.1371/journal.pcbi.1005670

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http://bit.ly/2x0yz29

PolyU discovers a newly emerged superbug

A newly emerged superbug, hyper-resistant and hypervirulent Klebsiella pneumoniae

The Partner State Key Laboratory of Chirosciences at the Department of Applied Biology and Chemical Technology (ABCT) of The Hong Kong Polytechnic University (PolyU) discovered a newly emerged superbug, hyper-resistant and hypervirulent Klebsiella pneumoniae, which may cause untreatable and fatal infections in relatively healthy individuals and will pose enormous threat to human health.

Prof. Chen Sheng, Professor of ABCT, collaborating with Prof. Rong Zhang from the Second Affiliated Hospital of Zhejiang University, conducted an investigation into a fatal outbreak of pneumonia in the Second Affiliated Hospital of Zhejiang University in China in February 2016. The study involved five patients who underwent surgical operation for multiple-trauma. All of them were later infected in the intensive care unit (ICU) and developed severe pneumonia, and eventually died of septicaemia and multiple organ failure. The causative agent of these five patients was found to be a carbapenem-

resistant K. pneumoniae (CRKP) strain, a type of previously-defined superbug. Furthermore, these CRKP strains are also hypervirulent and belong to ST11 type of CRKP, the most prevalent and transmissible CRKP strains in Asia. As these strains simultaneously exhibit the features of hyper-resistance, hypervirulence and high transmissibility, they can be considered a real superbug known as ST11 CR-HvKP (ST11 carbapenem-resistant hypervirulent K. pneumoniae).

ST11 K. pneumoniae strains proliferate in the gastrointestinal tract (GI tract) of human and animals and may cause opportunistic infections such as pneumonia in clinical settings. These strains, after acquiring plasmid encoding a carbapenemase gene, become resistant to the carbapenem antibiotics and caused untreatable or hard-to-be treated infections, therefore defined as superbug. These superbug strains could further evolve to become ST11 CR-HvKP through acquisition of the hypervirulence plasmids. The ST11 CR-HvKP strains do not only infect lungs and cause pneumonia, but also invade the bloodstream and other internal organs. Due to its hypervirulence and phenotypic resistance to commonly used antibiotics, ST11 CR-HvKP strains may cause untreatable and fatal infections in relatively healthy individuals with normal immunity.

ST11 CR-HvKP strains possess a mucoid outer layer, which enables them to stick to various materials, such as the surface of medical devices and tubing as well as other surfaces in the ICU. The transmission route is not clear yet, but our data suggest that medical equipment such as ventilator and different catheters might be transmitting these new superbug strains. Human-to-human transmission may also be possible, mainly in hospital settings. Improved infection prevention and control policy in hospital seems to be effective to control further transmission of this superbug in the ICU. Novel strategies must be devised to prevent ST11 CR-HvKP from proliferating extensively in the human intestinal tract where they were detected. ST11 CR-HvKP can easily be detectable by the Polymerase chain reaction (PCR) method, targeting specific resistance and virulence genes. The study showed that the use of colistin (the last resort drug for carbapenem-resistant enterobacteriaceae infections) alone or in combination with other drugs were not very effective in treating infections caused by ST11 CR-HvKP. Ceftazidime/avibactam may be the effective antibiotic, but ST11 CR-HvKP may develop resistance to this antibiotic very quickly based on the clinical data from the USA.

Prevalence of ST11 CR-HvKP strains in Hong Kong is currently unknown. Two studies conducted in Hong Kong have shown that mortality rate due to K. pneumoniae-mediated bloodstream infections was high, reaching 20% and 32% respectively. We plan to collaborate with clinicians in local hospitals to investigate the proportion of clinical K. pneumoniae isolates that belong to HvKP or CR-HvKP, and characterize their genetic features.

This study is recently published in the prestigious academic journal The Lancet Infectious Diseases. The full article can be accessed via the link: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30489-9/fulltext.

http://bit.ly/2wspyqI

Fossil footprints challenge established theories of human evolution

Newly discovered human-like footprints from Crete may put the established narrative of early human evolution to the test.

The footprints are approximately 5.7 million years old and were made at a time when previous research puts our ancestors in Africa - with ape-like feet.

Ever since the discovery of fossils of Australopithecus in South and East Africa during the middle years of the 20th century, the origin of the human lineage has been thought to lie in Africa. More recent fossil discoveries in the same region, including the iconic 3.7 million year old Laetoli footprints from Tanzania which show human-like feet and upright locomotion, have cemented the idea that hominins (early members of the human lineage) not only originated in Africa but

remained isolated there for several million years before dispersing to Europe and Asia. The discovery of approximately 5.7 million year old human-like footprints from Crete, published online this week by an international team of researchers, overthrows this simple picture and suggests a more complex reality.

Human feet have a very distinctive shape, different from all other land animals. The combination of a long sole, five short forward-pointing toes without claws, and a hallux ("big toe") that is larger than the other toes, is unique. The feet of our closest relatives, the great apes, look more like a human hand with a thumb-like hallux that sticks out to the side. The Laetoli footprints, thought to have been made by Australopithecus, are quite similar to those of modern humans except that the heel is narrower and the sole lacks a proper arch. By contrast, the 4.4 million year old Ardipithecus ramidus from Ethiopia, the oldest hominin known from reasonably complete fossils, has an ape-like foot. The researchers who described Ardipithecus argued that it is a direct ancestor of later hominins, implying that a human-like foot had not yet evolved at that time.

The new footprints, from Trachilos in western Crete, have an unmistakably human-like form. This is especially true of the toes. The big toe is similar to our own in shape, size and position; it is also associated with a distinct 'ball' on the sole, which is never present in apes. The sole of the foot is proportionately shorter than in the Laetoli prints, but it has the same general form. In short, the shape of the Trachilos prints indicates unambiguously that they belong to an early hominin, somewhat more primitive than the Laetoli trackmaker. They were made on a sandy seashore, possibly a small river delta, whereas the Laetoli tracks were made in volcanic ash.

'What makes this controversial is the age and location of the prints,' says Professor Per Ahlberg at Uppsala University, last author of the study.

At approximately 5.7 million years, they are younger than the oldest known fossil hominin, Sahelanthropus from Chad, and contemporary with Orrorin from Kenya, but more than a million years older than Ardipithecus ramidus with its ape-like feet. This conflicts with the hypothesis that Ardipithecus is a direct ancestor of later hominins. Furthermore, until this year, all fossil hominins older than 1.8 million years (the age of early Homo fossils from Georgia) came from Africa, leading most researchers to conclude that this was where the group evolved. However, the Trachilos footprints are securely dated using a combination of foraminifera (marine microfossils) from over- and underlying beds, plus the fact that they lie just below a very distinctive sedimentary rock formed when the Mediterranean sea briefly dried out, 5.6 million years ago. By curious coincidence, earlier this year, another group of researchers reinterpreted the fragmentary 7.2 million year old primate Graecopithecus from Greece and Bulgaria as a hominin. Graecopithecus is only known from teeth and jaws.

During the time when the Trachilos footprints were made, a period known as the late Miocene, the Sahara Desert did not exist; savannah-like environments extended from North Africa up around the eastern Mediterranean. Furthermore, Crete had not yet detached from the Greek mainland. It is thus not difficult to see how early hominins could have ranged across south-east Europe and well as Africa, and left their footprints on a Mediterranean shore that would one day form part of the island of Crete.

'This discovery challenges the established narrative of early human evolution head-on and is likely to generate a lot of debate. Whether the human origins research community will accept fossil footprints as conclusive evidence of the presence of hominins in the Miocene of Crete remains to be seen,' says Per Ahlberg.

http://bit.ly/2qsomAA

Asthma medicine halves risk of Parkinson's

Using data gathered from 100 million Norwegian prescriptions, researchers at the University of Bergen have found that asthma medicine can halve a patient's risk of developing Parkinson's disease

Parkinson´s disease is a chronic disease with unknown causes. The disease destroys the brain cells that control body movements. Shivering, stiff arms and legs and poor coordination are typical symptoms of Parkinson´s. The symptoms may develop slowly, and it sometimes takes time to make a correct diagnosis.

Researchers at the Department of Global Public Health and Primary Care (IGS) at the University of Bergen (UiB) have completed a large study that included data from the Norwegian Prescription Database, in cooperation with researchers at Harvard University.

"Our analysis of data from the whole Norwegian population has been decisive for the conclusion in this study," says Professor Trond Riise at IGS. He leads the registery study in Norway.

100 million prescriptions

Together with colleagues Anders Engeland and Kjetil Bjørnevik, Riise has analysed more than 100 million Norwegian prescriptions registered since 2004.

In the study, the treatment of Parkinson´s was linked to prescriptions of asthma medicine and the medicine for high blood pressure. It enabled the researchers to see the connection between medicine use and illness.

The UiB-researchers were able to make these comparisons by using the prescription database. The Norwegian analysis was done after researchers at Harvard University found these effects of the medicines in animal tests and in experiments with brain cells in the lab. Their results showed that these different medicines had opposite effects on the risk of Parkinson´s.

Possible new treatment

To find out if these medicines had the same effect on humans, the researchers at Harvard University started to collaborate with the Norwegian research team, and their unique resource of having access to the unique and large Norwegian database, where all Norwegian prescriptions are registered.

"We analysed the whole Norwegian population and found the same results as in the animal testing at Harvard University. These medicines have never been studied in relation to Parkinson's disease," says Riise.

Trond Riise underlines the fact that "Our discoveries may be the start of a totally new possible treatment for this serious disease. We expect that clinical studies will follow these discoveries."

http://bit.ly/2xFSpqj

Baby's Lead Poisoning Caused by 'Homeopathic Magnetic' Bracelet

The "spacer beads" in the baby's bracelet had extremely high levels of lead.

By Sara G. Miller, Staff Writer | August 31, 2017 01:00pm ET

An infant girl in Connecticut developed lead poisoning after wearing - and chewing on - a bracelet made with lead beads, according to a new report of the child's case.

Doctors discovered that the 9-month-old had abnormally high blood lead levels during a routine checkup. Her blood lead level was 41 micrograms per deciliter (ug/dL); anything over 5 ug/dL is considered abnormal, according to the report, published today (Aug. 31) by the Centers for Disease Control and Prevention (CDC).

The "spacer beads" in the baby's bracelet had extremely high levels of lead.
CDC/MMWR

Health investigators visited the infant's home, and found two windows with peeling lead-based paint. However, the infant wouldn't have been able to reach these areas, according to the report. In addition, the girl's three siblings, who were between ages 3 and 5, had blood lead levels of less than 3 ug/dL, suggesting that the peeling paint wasn't the source of the lead poisoning.

Instead, investigators focused on a handmade bracelet the parents had given the infant. The bracelet was a "homeopathic magnetic hematite healing bracelet" that the parents purchased from an artisan at a local fair. The parents had given the infant the bracelet for "teething-related discomfort," the report said. Sometimes the infant chewed on the bracelet, the report added. (Despite a lack of scientific evidence, some people purport that magnets have healing properties if placed close to the body.)

When investigators tested the beads on the bracelet, they found that some of the beads had extremely high levels of lead: 17,000 parts per million (ppm). The amount of lead that's considered safe for children's products is 90 ppm or 100 ppm, depending on the type of product, according to the U.S. Consumer Product Safety Commission (CPSC).

In general, the most common way children get lead poisoning is by ingesting something that contains lead. In 2003 and 2006, for example, there were several cases of severe lead poisoning and death linked to lead-containing jewelry and charms marketed to children, the report said. After these instances, the CPSC set limits on the amount of lead allowed in products marketed to kids, and each year, there are recalls of children's jewelry that exceed those limits. However, the limits do not apply to products that aren't intended for use by children, the report noted.

Investigators were unable to track down the manufacturer of the beads or the bracelet maker, according to the report.

There's no safe amount of lead exposure for children, according to the CDC, and the toxic heavy metal can affect nearly every part of the body. In many cases, lead exposure can occur with no obvious symptoms. Symptoms of severe lead poisoning can include confusion, seizures, coma and death.

This is not the first time that homeopathic teething products have been found to put children at risk. In October 2016, the U.S. Food and Drug Administration announced an investigation into homeopathic teething products that were linked to reports of seizures in infants and children. The products in that instance weren't being investigated for lead levels, however; instead, the FDA was concerned that the products contained purportedly "natural" substances that weren't regulated by the agency. Homeopathy is an alternative medicine practice based on the idea that "like cures like." In homeopathy, extremely minute concentrations of toxic substances are used in the idea that they could cure the symptoms that they would cause at higher doses.

http://bit.ly/2wsHiIR

How Neanderthals made the very first glue

The world's oldest known glue was made by Neanderthals. But how did they make it 200,000 years ago?

Leiden archaeologists have discovered three possible ways. The study is published in Scientific Reports.

A Neanderthal spear is predominantly made up of two parts, a piece of flint for the point, and a stick for the shaft. But one aspect is often overlooked, and has recently been puzzling archaeologists: the glue that fixes the point to the shaft. For this, Neanderthals used tar from birch bark, a material that researchers often assumed was complex and difficult to make.

Credit: Leiden University

Leiden archaeologists have now shown that this assumption was unfounded. Led by Paul Kozowyk and Geeske Langejans, the researchers discovered no fewer than three different ways to extract tar from birch bark. For the simplest method, all that is needed is a roll of bark and an open fire. This enabled Neanderthals to produce the first glue as early as 200,000 years ago.

The researchers made this surprising discovery by setting to work with only the tools and materials that Neanderthals possessed. They used experimental archaeology because the preservation of ancient adhesives is incredibly rare and there is no direct archaeological evidence about how tar was made during the Palaeolithic. In situations

like this, experimental archaeology provides a window into the past that would not otherwise exist.

'In earlier experimental attempts, researchers only managed to extract small quantities of tar from birch bark, or they didn't get anything at all,' says Kozowyk. 'It was believed that this was because the fire needed to be controlled to within a narrow temperature range. However, we discovered that there are more ways to produce tar, and that some work even with a significant temperature variation. So, precisely controlling the temperature of the fire is not as important as was initially thought.'

Kozowyk and his colleagues show that Neanderthals discovered tar production by combining existing knowledge and materials. Neandertals may have started with a simple method that required only fire and birch bark, and later adopted a more complex method to obtain higher yields of tar.

More information: P. R. B. Kozowyk et al. Experimental methods for the Palaeolithic dry distillation of birch bark: implications for the origin and development of Neandertal adhesive technology, Scientific Reports (2017). DOI: 10.1038/s41598-017-08106-7

http://bit.ly/2x1Gkon

Parasites inside your body could be protecting you from disease

Some E. Coli protect humans from more harmful strains.
Shutterstock

Ben Ashby Research fellow, University of Bath

It's fair to say parasites are generally bad for their hosts. Many cause disease and death so, like most species, we humans usually try to avoid infection at all costs. But it turns out that some parasites, although potentially harmful in isolation, can in fact help hosts to cope with more deadly infections.

Understanding when parasitism is beneficial has important implications for how we manage infectious diseases, but we currently know very little about this phenomenon. Our new study, published in Evolution Letters, tells us that parasites can readily evolve different mechanisms to defend their hosts from other infections, which suggests that host protection should be common in nature.

***Friends, for now.* U.S. Signal Corps**

The idea that "the enemy of my enemy is my friend" has been around in human society for a long time but it is far from unique to human conflict. The natural world is full of examples where parasites are harmful under some conditions and helpful under others.

Bacteria that live in our gut can occasionally cause problems, but they also prevent colonisation by more harmful microbes such as *Salmonella enterica*, which causes food poisoning. Similarly, bacteria that commonly infect insects are usually costly but can provide protection against more deadly infections. And the larvae of monarch butterflies are more likely to survive infection by a parasitic fly when they are also infected by a protozoan (single-celled organism).

Parasites can also help their hosts in other ways, for example by causing more serious disease in other species. This is one of the main reasons why grey squirrels have rapidly displaced red squirrels from most of the UK. Grey squirrels are carriers of squirrel pox virus, which is usually fatal to red squirrels but is rarely harmful to greys. Likewise, some species of bacteria engage in a form of primitive biological warfare by carrying viruses to which competing bacteria are not immune.

These examples reveal that being infected is not necessarily a bad thing and in fact can sometimes be beneficial. But what they don't tell us is how and when parasites evolve to be useful to their hosts.

Recent lab experiments have shown that mildly harmful bacteria living inside microscopic worms can evolve in just a few days to protect their hosts from a lethal infection. This striking result indicates

that bacteria can rapidly evolve host protection against other infectious diseases.

Still, very little is known about how and when such evolution occurs in nature. And if a parasite evolves to protect its host from a more deadly infection, has the enemy now become a friend?

From foe to friend

Using mathematical modelling, we explored the evolution of two forms of host protection: resistance and tolerance. Parasites that protect by conferring resistance to their hosts reduce the likelihood that a second species will be able to infect them, such as when bacteria in the gut prevent colonisation by other microbes. In contrast, parasites that confer tolerance to their hosts reduce the harm caused by another species after it infects them, as appears to be the case with the protozoa that protect monarch butterfly larvae from parasitic flies.

We discovered that both forms of host protection evolve under a wide range of conditions even though the protective parasite may have to divert resources from its own growth or reproduction to defend the host. Protection still evolves because this cost is more than offset by the increased survival of the host (and hence the protective parasite).

Monarch butterfly larvae are protected from one parasite by another. **Shutterstock**

But there are some notable differences between the two forms of protection. For instance, resistance usually increases the population size of the host, but tolerance can have a negative effect because it increases the overall prevalence of disease. These differences indicate that the mechanism of protection is crucial for determining whether a protective parasite is truly beneficial.

We can now combine mathematical modelling with lab experiments of evolving microbes to answer intriguing questions about how other species evolve in response to host protection. Does the host evolve to harbour the protective parasite, and is this how we developed a symbiotic relationship with some of our gut bacteria? Can more harmful parasites evolve to overcome host protection? Answering questions like these can help us find new ways to treat infectious diseases.

The results of our research shed light on a fascinating biological phenomenon about which we still know very little.

Yet taken together with the growing number of examples of host protection, it is clear – at least if you're hosting a parasite – that the enemy of your enemy can indeed be your friend.

Disclosure statement: Ben Ashby receives funding from the Natural Environment Research Council (NERC). He is affiliated with Sense About Science.

http://bit.ly/2quy6dN

Equatorial jet in Venusian atmosphere discovered by Akatsuki

Observations by Japan's Venus climate orbiter Akatsuki have revealed an equatorial jet in the lower to middle cloud layer of the planet's atmosphere, a finding that could be pivotal to unraveling a phenomenon called superrotation.

Venus rotates westward with a very low angular speed; it takes 243 Earth days to rotate once. The planet's atmosphere rotates in the same direction but at much higher angular speeds, which is called "superrotation." The planet is covered by thick clouds that extend from an altitude of about 45 kilometers to 70 kilometers. The superrotation reaches its maximum near the top of this cloud, where the rotational speed is about 60 times that of the planet itself.

The cause of this phenomenon, however, is shrouded iVen mystery.

Akatsuki was launched in 2010 by the Japan Aerospace Exploration Agency to unravel the atmospheric mysteries of Venus.

Although lower-altitude clouds cannot be seen through with visible light, Akatsuki's near-infrared camera IR2 successfully tracked the clouds - in particular, thicker clouds between 45 kilometers to 60

kilometers in altitude. This was made possible by observing the silhouettes of clouds that appear when infrared light from thermal radiation originating in the lower atmosphere filter through clouds.

Similar observations were previously made by the Venus Express orbiter of the European Space Agency and Galileo spacecraft of the U.S. National Aeronautics and Space Administration, but they provided only limited data of the planet's low-latitude zones. From these observations, scientists speculated that wind speeds at lower-to-middle cloud altitudes are horizontally uniform and have few temporal variations.

In the study published in Nature Geoscience, the team of researchers including Hokkaido University Associate Professor Takeshi Horinouchi analyzed the data collected by Akatsuki between March and August 2016. The team employed a cloud-tracking method they recently developed to deduce horizontal distributions of winds based on data from Akatsuki.

They discovered an equatorial jet in the wind velocities based on image data from July 2016 and that the jet existed at least two months after that. In March that year, the wind velocities in the same latitude zones were rather slow - thus there was no jet.

The findings showed for the first time that wind velocities can be markedly high forming a jet near the equator, which have never been found not only in the scantily observed lower to middle cloud layers but also in the more-extensively studied high layers.

"Our study uncovered that wind velocities in the lower-to-middle cloud layer have temporal and spatial variabilities much greater than previously thought," says Takeshi Horinouchi. "Although it remains unclear why such an equatorial jet appears, the mechanisms that could cause it are limited and related to various theories about superrotation. So, further study of the Akatsuki data should help glean useful knowledge not only about local jets but also would help address superrotation theories."

http://bit.ly/2eA28jc

Immune system changes during pregnancy are precisely timed

Scientists at the Stanford University School of Medicine have completed the first-ever characterization of the meticulously timed immune system changes in women that occur during pregnancy.

The findings, which will be published Sept. 1 in Science Immunology, reveal that there is an immune clock of pregnancy and suggest it may help doctors predict preterm birth.

"Pregnancy is a unique immunological state. We found that the timing of immune system changes follows a precise and predictable pattern in normal pregnancy," said the study's senior author, Brice Gaudilliere, MD, PhD, assistant professor of anesthesiology, perioperative and pain medicine.

Although physicians have long known that the expectant mother's immune system adjusts to prevent her body from rejecting the fetus, no one had investigated the full scope of these changes, nor asked if their timing was tightly controlled. "Ultimately, we want to be able to ask, 'Does your immune clock of pregnancy run too slow or too fast?'" said Gaudilliere.

The new research comes from the March of Dimes Prematurity Research Center at Stanford University, which aims to understand why preterm births happen and how they could be prevented. Nearly 10 percent of U.S. infants are born prematurely, arriving three or more weeks early, but physicians lack a reliable way to predict premature deliveries.

"It's really exciting that an immunological clock of pregnancy exists," said the study's lead author, Nima Aghaeepour, PhD, instructor in anesthesiology, perioperative and pain medicine. "Now that we have a reference for normal development of the immune system throughout pregnancy, we can use that as a baseline for future studies to understand when someone's immune system is not adapting to pregnancy the way we would expect."

Prior research at Stanford and elsewhere suggested that inflammatory immune responses may help trigger early labor. If scientists identify an immune signature of impending preterm birth, they should be able to design a blood test to detect it.

The study used blood samples collected from 18 women who had full-term pregnancies. Each woman gave four blood samples -- one during each of the three trimesters of pregnancy and one six weeks after delivery. Samples from an additional group of 10 women with full-term pregnancies were used to validate the findings.

How each immune cell experiences pregnancy

The researchers used mass cytometry, a technique developed at Stanford, to simultaneously measure up to 50 properties of each immune cell in the blood samples. They counted the types of immune cells, assessed what signaling pathways were most active in each cell, and determined how the cells reacted to being stimulated with compounds that mimic infection with viruses and bacteria.

With an advanced statistical modeling technique, introduced for the first time in this study, the scientists then described in detail how the immune system changes throughout pregnancy.

"This algorithm is telling us how specific immune cell types are experiencing pregnancy," Gaudilliere said.

Instead of grouping the women's blood samples by trimester for analysis, their model treated gestational age as a continuous variable, allowing the researchers to account for the exact time during pregnancy at which each sample was taken. The mathematical model also incorporated knowledge from the existing scientific literature of how immune cells behave in nonpregnant individuals to help determine which findings were most likely to be important. The model improved understanding of the immune system much as mapping software that knows which streets are one-way gives better driving directions. "If there are several models that are statistically equivalent, we are interested in the model that is most consistent with our existing knowledge of immunology," said Aghaeepour.

Hopes of finding 'sweet spot'

The study confirmed immune features of pregnancy that were already known. For instance, the scientists saw that natural killer cells and neutrophils have enhanced action during pregnancy. The researchers also uncovered several previously unappreciated features of how the immune system changes, such as the finding that activity of the STAT5 signaling pathway in CD4+T cells progressively increases throughout pregnancy on a precise schedule, ultimately reaching levels much higher than in nonpregnant individuals. The STAT5 pathway is involved in helping another group of immune cells, regulatory T cells, to differentiate. Interestingly, prior research in animals has indicated that regulatory T cells are important for maintaining pregnancy.

The next step will be to conduct similar research using blood samples from women who deliver their babies prematurely to see where their trajectories of immune function differ from normal.

"We're especially interested in understanding more precisely what is happening very early and very late in pregnancy," Gaudilliere said. "We'd like to see if there is really a switch we can catch, a sweet spot where deviation from the norm would be maximal with pathology."

"The immune system does not act in isolation, and we're now very interested in profiling its interplay with other aspects of mothers' biology, such as their genetics, metabolism and the body's microbial communities to come up with a holistic biological clock of pregnancy," Aghaeepour added.

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Other Stanford authors of the study are basic life science research associate Edward Ganio; postdoctoral scholars David McIlwain, PhD, and Mohammad Ghameni, PhD; life sciences researcher Amy Tsai; research nurses Martha Tingle and Robin Okada; Dyani Gaudilliere, DMD, clinical assistant professor of surgery; clinical fellow Quentin Baca, MD, PhD; clinical research coordinator Leslie McNeil; David Furman, PhD, adjunct professor at Stanford's Institute for Immunity, Transplantation and Infection; Ronald Wong, PhD, senior research scientist; Virginia Winn, MD, associate professor of

obstetrics and gynecology; Maurice Druzin, MD, professor of obstetrics and gynecology; Yasser El-Sayed, MD, professor of obstetrics and gynecology; Cecele Quaintance, administrative director of the March of Dimes Prematurity Research Center at Stanford; Ronald Gibbs, MD, clinical professor of obstetrics and gynecology; Gary Darmstadt, MD, professor of neonatal and developmental pediatrics; Gary Shaw, DrPH, professor of pediatrics; David Stevenson, MD, professor of pediatrics and director of Stanford's March of Dimes center; Robert Tibshirani, PhD, professor of biomedical data science and of statistics; Garry Nolan, PhD, professor of microbiology and immunology; David Lewis, MD, professor of pediatrics; and Martin Angst, MD, professor of anesthesiology, perioperative and pain medicine. Brice Gaudilliere, Winn, El-Sayed, Shaw, Stevenson, Tibshirani, Nolan and Lewis are members of Stanford's Child Health Research Institute. Scientists from Ghent University in Belgium also contributed to this work.

The research was supported by the March of Dimes Prematurity Research Center at Stanford, the Bill and Melinda Gates Foundation, the Ovarian Cancer Research Fund, the Canadian Institute of Health Research, the International Society for Advancement of Cytometry, the National Institutes of Health (grants 1K23GM111657, 5R01AI10012104, U19AI057229 and 1U19AI100627), the Stanford Child Health Research Institute, the Mary L. Johnson Research Fund, the Christopher Hess Research Fund, and the Food and Drug Administration.

Nolan holds a patent on the mass cytometry technology, which is manufactured by Fluidigm. He also holds equity in Fluidigm.

Stanford's Department of Anesthesiology, Perioperative and Pain Medicine also supported the work.

http://bit.ly/2ezySt8

Did Squabble Over a Vaccine Cause a Rift in Ben Franklin's Marriage?

Why was Benjamin Franklin estranged from his wife for nearly two decades? A new theory argues that the founding father's marriage may have been strained by his son's health — and an argument about inoculation.

By Sara G. Miller, Staff Writer | September 1, 2017 03:35pm ET

The theory is detailed by author and historian Stephen Coss in the September 2017 issue of Smithsonian Magazine.

According to the article, people often attribute Franklin's long absence from his wife, Deborah Read, to his promiscuous nature. But analysis of Franklin's autobiography, along with letters and editorials that he published in his newspaper, the Pennsylvania Gazette, point to a possible dispute over a smallpox inoculation. [Tiny & Nasty: Images of Things That Make Us Sick]

Franklin first learned about smallpox inoculation in 1721, when there was an outbreak of the disease in Boston. The inoculation was a precursor to the modern-day vaccine: A doctor took fluid from a smallpox blister and then injected that fluid into a shallow cut in a healthy person's arm. During a smallpox outbreak in 1730 in Boston, the Pennsylvania Gazette reported that of the "several hundreds" of people inoculated against the virus, "about four" had died.

Despite Franklin's enthusiasm for the inoculation, he didn't inoculate his young son, Franky, who died from the disease in 1731 during an outbreak in Philadelphia.

In his autobiography, Franklin wrote, "I long regretted bitterly & still regret that I had not given it [smallpox] to him by inoculation." Coss said this suggests Franklin had a choice about whether to inoculate his son, but didn't because his wife disagreed with the decision. Indeed, in 1759, Franklin wrote that if "one parent or near relation is against [inoculation], the other does not chuse to inoculate a child without free consent of all parties, lest in case of a disastrous event, perpetual blame should follow."

http://bit.ly/2eS93Bq

Computer knows how much pain you are in by studying your face

Putting on a brave face won't fool this algorithm.

By Matt Reynolds

A new system that rates how much pain someone is in just by looking at their face could help doctors decide how to treat patients. By examining tiny facial expressions and calibrating the system to each person, it provides a level of objectivity in an area where that's normally hard to come by.

"These metrics might be useful in determining real pain from faked pain," says Jeffrey Cohn at the University of Pittsburgh in the US. The system could make the difference between prescribing potentially addictive painkillers and catching out a faker. Objectively measuring pain levels is a tricky task, says Dianbo Liu, who created the system

with his colleagues at the Massachusetts Institute of Technology. People experience and express pain differently, so a doctor's estimate of a patient's pain can often differ from a self-reported pain score.

In an attempt to introduce some objectivity, Liu and his team trained an algorithm on videos of people wincing and grimacing in pain. Each video consisted of a person with shoulder pain, who had been asked to perform a different movement and then rate their pain levels. The result was an algorithm that can use subtle differences in facial expressions to inform a guess about how a given person is feeling.

Certain parts of the face are particularly revealing, says Liu. Large amounts of movement around the nose and mouth tended to suggest higher self-reported pain scores.

There's evidence that even less sophisticated pain-recognition algorithms are less easily fooled than their human counterparts. A study from the University of California, San Diego, found that a computer system could weed out fakers 85 per cent of the time, whereas trained humans were only accurate 55 per cent of the time.

To help make it more accurate, Liu's system can be tweaked to take into account someone's age, sex and skin complexion. An individual's age had the most impact on their expression of pain levels, and Liu found that his personalised approach was better at estimating pain than one-size-fits-all systems.

Cohn is impressed with the results and says it's the first time he's seen a pain recognition algorithm that can be tweaked to give personalised results based on age, sex, and skin complexion. It's still early days, but Liu says there's nothing stopping the system eventually being made into an app that doctors could have on their smartphones.

Liu says the system could never be a replacement for real doctors. The videos his algorithm was trained on were taken in ideal lighting and photography conditions, so it's unlikely the system would be as accurate if it was used on real patients. Still, he's planning to further train the algorithm with more videos of people in pain to see if that boosts its pain-rating abilities. *Journal reference: arXiv, DOI: 1708.04670*

http://bit.ly/2ezMyEs

Is Zika Gone for Good?

While spraying to eradicate mosquito-breeding sites may have contributed to Zika's demise, it likely wasn't sufficient to account for the precipitous decline in cases this year.

By Jerome Groopman

Last summer, I received a telephone call from a relative who was terrified about Zika. A young woman in her early thirties, she was pregnant with her first child and was slated to travel to South Florida. At the time, the news was filled with stories of infected infants who had been born with shrunken heads and damaged brains—a condition known as microcephaly—and whose futures would be marked by severe debility. The Zika virus had spread to Florida from South and Central America; the pathogen was transmitted mainly by mosquitoes but could also be passed through sexual intercourse. There had already been several hundred cases of local transmission in the continental United States. The World Health Organization had declared Zika a global emergency.

While my relative's risk was low, her concerns were real, and she cancelled the trip. She was not alone in avoiding epicenters of the burgeoning epidemic. Even some Olympic athletes, who had spent years training, chose not to attend the Summer Games in Brazil, where there would be more than a million documented cases of infection and some thirty-five hundred infants born with microcephaly. Now, however, the spread of Zika in the continental United States has virtually ended. As September begins, there have been only two cases of local transmission reported in 2017—one in Hidalgo County, Texas, near the Mexican border. Dramatic declines in the numbers of new Zika cases have also been noted in South and Central America. How did the epidemic explode in the Americas and then withdraw so quickly? And is Zika gone for good?

Zika belongs to the genus *Flavivirus*, which includes yellow fever and dengue. It was originally identified seventy years ago, in monkeys in

Uganda's Zika Forest, and was contained for decades to a narrow equatorial belt in Africa. With today's global travel—a common vector for transporting epidemics—Zika arrived in Micronesia, in 2007, infecting nearly three-quarters of the population. The virus moved eastward across the Pacific Ocean and took root in South and Central America, with the first cases appearing in late 2015; within months, more than two hundred residents in the continental U.S. who had not travelled contracted the infection locally. Last year, it seemed we were poised for a major outbreak. Then it stopped.

Despite the powerful technologies that scientists currently have to characterize pathogens and treat the infections they cause, the course and consequences of epidemics are still a source of surprise. Modern tools of molecular biology have enabled researchers to tear apart the Zika virus and decipher all of its genes and proteins, to map the antibodies and blood cells it mobilizes in infected individuals. But we still don't know why some people contract the microbe with little or no illness, at most mild fever and muscle aches, while others suffer Guillain-Barré syndrome, a life-threatening paralysis. And we can't distinguish between those pregnant women whose babies will be born deformed and others who seem to escape the most devastating neurological effects of the virus.

Further, there is no obvious reason for Zika's rapid demise in the Americas. While spraying to eradicate mosquito-breeding sites may have contributed, it likely wasn't sufficient to account for the precipitous decline in cases this year; the insects are simply too numerous and breed in too many areas. Nor would recommendations to refrain from unprotected sex be enough to blunt the virus's spread. More possible is that much of the population in South America and the Caribbean was infected and became immune, with body defenses purging Zika from the blood and semen. This widespread "herd immunity" can help snuff out a disease in a particular geographic region, since the odds a mosquito picks up the virus plummet when most people bitten cannot carry the pathogen.

While the spectre of Zika in the Americas is fading, it's wise to stay vigilant. Some experts worry that new cases of Zika recently reported in northern Mexico could presage another outbreak, with subsequent spread to U.S. border states. Relying on herd immunity is shortsighted, since over time fewer people will be infected and the virus can gain a new foothold. Indeed, the geographic distribution of *Aedes aegypti*, the mosquito species that transmits Zika, is expanding. The insect is infesting unexpected parts of North America and Europe; a population of *A. aegypti* was recently found in Washington, D.C., and appears to have survived four consecutive winters. The steady creep of climate change could bring *A. aegypti* farther north, where there is no herd immunity.

The definitive solution to prevent a return of the Zika epidemic is, of course, a broadly protective vaccine. Several efforts are ongoing, including a major trial sponsored by the National Institutes of Health. Ironically, the sharp drop in infections will make it difficult to demonstrate the efficacy of a candidate vaccine in field testing, since there is likely to be a relative dearth of new cases. Anticipating this obstacle, Anthony Fauci, who oversees the N.I.H. vaccine program, noted in *Science* that his team is poised to increase the number of participants in the trial, or to shift the location of testing to new hot spots.

But there is another concern about developing a Zika vaccine that has not received much attention. The virus does not exist alone in its ecosystem. The related pathogen dengue, which infects some four hundred million people annually and can cause excruciating skeletal pain and severe bleeding—breakbone fever—is carried by the same mosquitoes as Zika. Dengue has a boomerang biology: paradoxically, the antibodies produced after an infection can facilitate, rather than block, subsequent infections. The virus essentially uses the antibodies as Trojan horses, riding them covertly into our cells. In laboratory studies, Zika antibodies have appeared able to perform a similar deception, enhancing dengue's capacity to attack white blood cells.

An unintended consequence of a vaccine against Zika could be to elicit such antibodies and worsen dengue flareups. Although the W.H.O. declared, last November, that Zika is no longer a global emergency, we should not count on an end to outbreaks anytime soon—more likely, new beginnings.

Jerome Groopman, a staff writer since 1998, writes primarily about medicine and biology.

http://bit.ly/2x2RF7y

Study in early stage breast cancer shows that even small tumors can be aggressive

Even small tumours can be aggressive, according to a study in patients with early stage breast cancer that will be presented at the ESMO 2017 Congress in Madrid. [1]

LUGANO-MADRID - Researchers found that nearly one in four small tumours were aggressive and patients benefited from chemotherapy. Aggressive tumours could be identified by a 70-gene signature.

"Our results challenge the assumption that all small tumours are less serious and do not need adjuvant chemotherapy," said lead author Dr Konstantinos Tryfonidis, a researcher at the European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium.

The MINDACT study is managed and sponsored by the EORTC in collaboration with the Breast International Group (BIG) and included 6,693 women with early stage breast cancer (lymph node negative or 1-3 lymph node positive). [2] As previously reported, MINDACT showed that around 46% of patients who were at high clinical risk for recurrence, defined using Adjuvant! might not require chemotherapy. (3) These women had a low genomic risk for recurrence according to MammaPrint, a genomic signature that assists in predicting clinical outcomes in women with early stage breast cancer. [3,4]

The sub analysis presented at ESMO 2017 included the 826 patients in MINDACT with a primary tumour size of less than 1 cm (pT1abpN0). Clinical and genomic risks were assessed and 196 patients (24%) were found to be at clinical low risk and genomic high risk. These patients were randomised to receive, or not receive, chemotherapy. The researchers found that at five years, very few patients who received chemotherapy experienced disease relapses, showing high rates of distant metastases-free survival, disease-free survival and overall survival, which confirms that they derived benefit from chemotherapy.

"We found that nearly one in four patients with small tumours are at risk of distant metastases and do benefit from chemotherapy," said Dr Fatima Cardoso, senior author of the study, Co-Principal Investigator of MINDACT and Director of the Breast Unit of the Champalimaud Clinical Centre, Lisbon, Portugal. "This was striking because based on clinical criteria alone you would say that these tumours are not aggressive and therefore patients do not need chemotherapy. But 24% of small tumours had an aggressive biology, which shows that not all small tumours are the same."

Commenting on the results for ESMO, Dr Evandro de Azambuja, Head of the Medical Support Team, Academic Promoting Team, Jules Bordet Institute, Brussels, Belgium, said: "This study shows that it's not only tumour size that is important for breast cancer patients but also tumour biology. All tumours in the study were small - less than 1 cm - and the lymph nodes were free of cancer (node negative), which in principle should be a signal of good prognosis. But nearly one in four patients - those identified as genomic high risk - derived benefit from chemotherapy."

"Small node negative tumours can be very aggressive, even if they are classified as clinical low risk," said de Azambuja. "Tumour biology needs to be taken into account when deciding adjuvant treatments in this patient population. One cannot forget the patient's age, performance status, comorbidities and preferences during the discussion."

References ***ESMO 2017 Congress European Society for Medical Oncology***

1 Abstract 150O_PR 'Not all small node negative (pT1abN0) breast cancers are similar: Outcome results from an EORTC 10041/BIG 3-04 (MINDACT) trial substudy' will be presented by Dr Konstantinos Tryfonidis during Proffered Paper Session 'Breast cancer, early stage' on Friday, 8 September 2017, 14:00 to 15:30 (CEST) in the Pamplona Auditorium.

2 The MINDACT study is managed and sponsored by the EORTC in collaboration with the Breast International Group (BIG), Agendia, and many other academic and commercial partners, as well as patient advocates.

3 Cardoso F, et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. N Engl J Med. 2016;375(8):717-729. doi: 10.1056/NEJMoa1602253.

4 van de Vijver MJ, et al. A gene expression signature as a predictor of survival in breast cancer. N Engl J Med. 2002; 347:1999-2009.

http://bit.ly/2xIqrjZ

FINESSE mission to investigate atmospheres of hundreds of alien worlds

Could greatly improve our understanding of extrasolar worlds

September 4, 2017 by Tomasz Nowakowski, Astrowatch.net

One of NASA's proposed missions, known as the Fast INfrared Exoplanet Spectroscopy Survey Explorer (FINESSE), could greatly improve our understanding of extrasolar worlds. If selected for development, the spacecraft will investigate at least 500 exoplanet atmospheres, providing detailed information about climate processes on distant alien planets.

FINESSE has been recently chosen by NASA for concept studies and evaluations. It is one of the agency's six astrophysics Explorers Program proposals, which could be selected by 2019 to proceed with construction and launch.

The mission's main objective is to study the processes that govern planet formation and global climate. It will investigate the mechanisms that establish atmospheric chemical composition and shape atmospheric evolution.

"FINESSE will spectroscopically observe the atmospheres of many hundreds of transiting exoplanets to measure their molecular abundances and thermal profiles," Robert Zellem, FINESSE science team member at NASA's Jet Propulsion Laboratory (JPL), told Astrowatch.net.

In order to conduct the planned studies, FINESSE will use the transit method. It will measure how a planet's atmosphere absorbs light from its host star as a function of wavelength. This will allow researchers to infer the molecules in the planet's atmosphere.

"By doing this for hundreds of planets, FINESSE will determine how planets form and the crucial factors that establish planetary climate," Zellem said.

These observations will require a proper imaging system. That is why the FINESSE spacecraft will be equipped in a telescope with a 75-centimeter (29.5-inch) primary mirror and a spectrometer that will observe planets in the visible and infrared wavelengths (from 0.5 to 5 microns).

According to Zellem, wide spectral coverage will enable FINESSE to measure the abundances of molecules such as water, methane, carbon dioxide and carbon monoxide, as well as look for the presence of clouds and hazes.

Data collected by the spacecraft could improve our knowledge of exoplanet types, from rocky terrestrial planets to gas giants like Jupiter. FINESSE could help us discover what these alien worlds are like, determining how they evolved, and allowing researchers to apply this knowledge in the broader planetary context, including the search for life outside of our solar system.

If selected for development, FINESSE is targeted for the launch around 2023. Zellem hopes that during its operational lifetime of two years, it will carry out important observations of even more than 1,000 extrasolar worlds.

"FINESSE has the capability in its two-year mission to observe the atmospheres of over 1000 transiting exoplanets," he concluded.