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Bats are the major reservoir of coronaviruses worldwide

Results of a 20-country, USAID-funded PREDICT study combine fieldwork and viral testing to discover viruses with potential to spark a pandemic like SARS or MERS

Results of a five-year study in 20 countries on three continents have found that bats harbor a large diversity of coronaviruses (CoV), the family of viruses that cause Severe Acute Respiratory Syndrome Coronavirus (SARS) and Middle East Respiratory Syndrome Coronavirus (MERS). Findings from the study--led by scientists in the USAID-funded PREDICT project at the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health and the University of California, Davis' One Health Institute in the School of Veterinary Medicine--are published in the journal Virus Evolution. PREDICT is a globally coordinated effort to detect and discover viruses of pandemic potential and reduce risk for future epidemics.

With the cooperation of local governments, researchers sampled and tested 19,192 bats, rodents, non-human primates, and humans in areas where the risk of animal-to-human transmission is greatest, including sites of deforestation, ecotourism, and animal sanctuaries. The researchers identified 100 different CoVs and found that more than 98 percent of the animals harboring these viruses were bats, representing 282 bat species from 12 taxonomic families. Extrapolating to all 1,200 bat species, they estimate a total of 3,204 CoV are carried by bats worldwide, most of which have yet to be detected and described. They also found that CoV diversity correlated with bat diversity with high numbers of CoVs concentrated in areas where there are the most bat species, suggesting CoVs coevolved with or adapted to preferred families of bats.

"This study fills in a huge gap in what we know about the diversity of coronaviruses in animal hosts," says first author Simon Anthony, assistant professor of Epidemiology in CII. "Charting the geographic and genetic diversity of coronaviruses in animals is a critical first step towards understanding and anticipating which specific viruses could pose a threat to human health."

The First Step to Identifying Suspect Viruses

The researchers used consensus PCR, a cost-effective technique that targets a small section of the viral genome--sufficient to locate the position of each virus in the family tree of all CoVs. To go a step further, researchers are using more powerful genome-wide sequencing to take a detailed look at those viruses that resemble known threats to humans. In a study published in April, they reported that a MERS CoV-like virus did not have the genetic prerequisites to jump to humans--a sign that MERS-CoV had evolved to become more capable of transmission. A similar effort is now underway to sequence viruses similar to SARS-CoV.

Regional Variation in Risk of Virus "Jumping" Outside Its Genus

Researchers report preliminary evidence that CoVs in bats in Latin America were less likely than CoVs in Africa and Asia to "jump" outside their genus or family, potentially a sign of relatively lower risk of bat-to-human transmission on that continent. However, the authors caution that these regional differences may reflect variation in the ecology of bats in the various areas, and more work needs to be done to understand this.

Bats Play an Important Role

The researchers say their findings should not be interpreted as a call to cull bats. Bats play an important role in the ecosystem, and most of the coronaviruses they carry are harmless to humans. Additionally, culling may have unintended consequences: destabilizing host ecology can actually increase risk for disease transmission, as seen in studies of Marburg and rabies viruses.

"Our goal is to shed light on the ecology of virus-host interactions to better understand and address the conditions that give rise to outbreaks like SARS and MERS," says senior author Tracey Goldstein, associate

professor at the One Health Institute at the University of California, Davis.

The study was supported by USAID through the Emerging Pandemic Threats PREDICT project. Additional co-authors include W. Ian Lipkin, Sarah Kramer, Xiaoyu Che, Heather Wells, Allison L. Hicks, and Stephen S. Morse at the Mailman School of Public Health; Christine K. Johnson, Denise J. Grieg, and Jonna A. K. Mazet (PI and project director) at the University of California Davis; Damien O. Joly and Nathan D. Wolfe at Metabiota, Inc.; Peter Daszak and William Karesh at EcoHealth Alliance; and the PREDICT Consortium. The authors declare no conflicts.

http://bit.ly/2sH3wpz

Pig brain cells implanted into brains of people with Parkinson's

Would you have pig cells implanted in your brain? Some people with Parkinson's disease have, in the hope it will stop their disease progressing.

By Clare Wilson

The approach is still in the early stages of testing, but initial results from four people look promising, with all showing some improvement 18 months after surgery. People with Parkinson's disease, which causes tremors and difficulty moving, usually get worse over time.

The disease is caused by the gradual loss of brain cells that make dopamine, a compound that helps control our movements. Current medicines replace the missing dopamine, but their effectiveness wears off over the years.

So Living Cell Technologies, based in Auckland, New Zealand, has been developing a treatment that uses cells from the choroid plexus in pigs. This brain structure makes a cocktail of growth factors and signalling molecules known to help keep nerve cells healthy.

Neurochemical factory

Last month, surgery was completed on a further 18 people in a placebo-controlled trial, using the choroid plexus cell implants. The hope is that compounds made by these cells will nourish the remaining dopamine-producing cells in the patients' brains, slowing further loss.

The approach has been successful in a rat version of Parkinson's disease. "It's putting in a little neurochemical factory to promote new nerve cell growth and repair," says Ken Taylor of Living Cell Technologies.

The pig cells are placed inside a porous coating of alginate, made from seaweed, which allows growth factors to move into surrounding brain tissue, yet should stop patients' immune cells from entering to attack the pig cells. This approach is also being used with pig pancreas cells being implanted in people with diabetes.

Each alginate capsule is about half a millimetre wide and contains about a thousand pig cells. In the first small trial, four people had 40 capsules put in one side of the brain.

Symptom moderation

The team have recorded an average improvement among these people of 14 points, measured on a 199-point scale of symptom severity, which gauges things such as how well people can walk and cut up their food. But Steven Gill at the University of Bristol, UK, says that could have been due to a placebo effect, as people improved immediately after the surgery. "Nerve cells don't regrow that fast," he says.

Previous work has found that Parkinson's disease symptoms seem particularly responsive to the placebo effect, with some people showing improvements just because they expected to.

Gill also suggests that the people in the study appeared to improve so quickly because they initially exaggerated their symptom severity to get a place on the trial. However, the improvements seen among these four people have been maintained over a long period – 18 months. People with the disease normally deteriorate by a few points a year.

The larger, placebo-controlled trial should shed more light on the matter. Its results are due in November.

Larger trial

In this ongoing trial, people have had up to 120 capsules put in both sides of their brains. "The strategy is a good idea," says Roger Barker

at the University of Cambridge, who has previously acted as the company's scientific adviser, but isn't involved in the current trial. "The question is how competitive that will be compared with other cell therapies."

Another kind of cell therapy for Parkinson's that has shown some success uses implants of dopamine-making brain cells taken from aborted fetuses. But such tissue is hard to obtain. There are also hopes of turning adult stem cells into dopamine-producing cells. If this can be done using, for example, a patient's skin cells, it would rule out the risk of any immune rejection of the implants.

In addition, pig brain cells are being investigated as treatments for other diseases caused by nerve cells dying, including Alzheimer's and Huntington's, which causes movement and cognitive problems. As the choroid plexus cells release a cocktail of different growth factors, they may prove helpful for treating these other disorders involving nerve cell damage.

One concern with such animal-to-human transplants is that viruses lying dormant within the pig DNA – called porcine endogenous retroviruses – could cross over into people and start a new disease. But this hasn't happened so far in those who have received pig pancreas cells for diabetes. Other teams are attempting to use the gene-editing technology CRISPR to eliminate these viruses from the pig genome.

http://bit.ly/2rnIybo

Genomic sequencing could become household term with new hand-held device

Within five years, consumers may begin using a device smaller than a flip phone to monitor the air, test their food or diagnose what germ caused an upset stomach.

June 12, 2017 by Kathleen Phillips

And the root of this capability points to what now is only for scientists—genome sequencing. That's the message from a team of scientists from the U.K. and Canada teaching a weeklong class to about 40 fellow researchers from around the U.S. at Texas A&M AgriLife Research in College Station.

This course, a sort of "nerd summer camp for adults," was different, organizers said. Rather than instructing the art and science of genomics and bioinformatics on the multi-million-dollar equipment typically in labs, the class used the minION—a sequencing system made by Oxford Nanopore Technology. Basically, it's a hand-held device into which a sample is placed and then within minutes the sample's genome is translated into one's laptop.

"The mobility of this system is what is attractive about this device," said Dr. John Tyson, a minION instructor and research associate at the University of British Columbia in Vancouver.

The device has already been used to battle ebola in the remote jungles of Guinea and to sample both mosquitoes and humans for the presence of Zika virus in northeastern Brazil, according to minION instructor Dr. Nick Loman, independent research fellow at the University of Birmingham, England.

Knowing what pathogens are present early on, Loman said, can help scientists begin to work more toward surveillance and thus prevention rather than reacting to issues after they become problems.

The minION represents an enormous leap for researchers who need a highly portable system for a couple of reasons, according to Dr. Charlie Johnson, director of the Genomics and Bioinformatics Service with AgriLife Research in College Station. First, much research takes place in remote fields where larger equipment cannot be used. And second, the faster the results come, the more quickly they can be translated into actions.

"That being said, this type of portable technology is not a replacement for our workhouse enterprise-level Illumina sequencing systems, which can do the equivalent of 48 human genome projects in 48 hours," said Johnson, noting that the first human genome project took 13 years. "Rather, the minION is another fantastic tool in our genomics tool belt."

"Training others to use this type of technology helps empower research," said Johnson, who co-hosted the event with Dr. Robert Burghardt and Ashley Gustafson from the Texas A&M School of Veterinary Medicine. "It's easier to teach 250 students how to use a technology than to try to individually handle that many projects. And in agriculture, at least, our ultimate goal is to feed mankind, so this helps further our discoveries toward that end."

Indeed, though the technology ultimately may be used to glean typical household information, the testing ground has largely been agriculture, natural resources and medicine, Johnson noted.

Researchers attending the training, in fact, were required to bring actual samples of their current projects to use while learning the technology. Included in the mix were studies on lions, bears, cats, Alaskan ice cores, manatees and various insects such as fleas and scorpions. Finding out what makes those things tick, so to speak, can lead researchers to solutions.

"We're just scratching the surface," said Dr. Mick Watson, minION instructor and head of genomics at the University of Edinburgh, Scotland. "The technology is coming to a point where consumers will be able to use it in three to five years."

Watson also stressed the importance of farmers being able to use the low-cost technology on farms to determine the presence of pathogens before they do excessive damage to crops and livestock.

It's about rapid diagnosis so the correct treatments can be provided, and that in turn slows the rate of resistance to pesticides and medicine, he said.

Loman agreed.

"Often a doctor will prescribe a general antibiotic to make you feel better without knowing if it is the most effective on a particular bacteria, or if what you have is actually a virus," he said. "Being able to quickly get the genomic sequence of a germ rather than wait for a culture to grow in a lab could lead to the ability to use a more narrow spectrum of antibiotics, which would limit the rate of antibiotic resistance."

There also are some slightly more "off-the-wall" potential uses for the technology, such as quality control for craft brewers, the team noted.

The conclusion of the weeklong course was a field trip to Jester King Brewery in Austin, which boasts of its use of "natural surroundings and local agriculture." There, the newly equipped student researchers and the team collected yeast samples to run on the minIONs. Knowing what yeasts are present can help a brewery know how to manage the flavor of its content, Watson explained.

http://bit.ly/2sxtR8P

New cancer drug makes commonly prescribed chemo drug more effective when given together

Method found to increase the effectiveness of cancer drug while decreasing the risk of heart-damaging side effects

GALVESTON, Texas - Researchers have found a way to increase the effectiveness of a widely used cancer drug while decreasing the risk of heart-damaging side effects, according to a new study by researchers from The University of Texas Medical Branch at Galveston and Texas Tech University Health Sciences Center. The findings are currently available in the journal Scientific Reports Nature publishing group.

UTMB professor Satish Srivastava said that combining a newly-developed drug with a drug used to fight numerous kinds of cancers makes it better suited as a colon cancer treatment. The widely-used drug, doxorubicin, is effective in fighting cancer but can be toxic to the heart when higher doses are needed.

The research, Srivastava said, shows that using aldose reductase, an enzyme, when used with doxorubicin, reduces the toxins that can damage the heart.

The researchers have shown earlier that exposure to cancer-causing agents like pollutants triggers oxidative stress, which is a driving source of cancer tissue growth. The oxidative signals are also involved in growing the new blood vessels needed by the cancer tissues. An

effort to decrease the oxidative signals is one of the reasons for the popularity of antioxidant-containing foods, beverages, skin care products and vitamins.

"We've shown that oxidative signals can be blocked by aldose reductase, or AR, inhibitors," said lead author Srivastava, who is a professor in UTMB's departments of biochemistry and molecular biology as well as ophthalmology and visual sciences. "If we could prevent development of the new blood vessels in the cancer tissue driven by these signals, tumor growth and metastasis can be slowed down or prevented."

The researchers have been using an AR inhibitor called fidarestat to learn how well it prevents growth and metastasis of cancer. The drug has completed Phase II clinical trials in the U.S. and Phase III in Japan for preventing diabetic neuropathy and was found to have no major side effects.

Doxorubicin is commonly prescribed to fight several types of cancers including breast and lung cancers. It is also very cost effective, compared to other cancer drugs. However, colon cancers become resistant to this drug so a higher dosage must be used for it to be effective. The trouble with this is that at higher dosages, it can be toxic to the heart.

"In the study, using human colon cancer cell lines, we showed that the growth of cancer cells can be largely prevented using a combination of both drugs in a petri dish as well as in mouse models," said Srivastava. "Since doxorubicin is one of the cheapest drugs that is effective against many types of cancer but rarely used in colon cancer, the combination therapy could be highly effective in combating colon cancer while drastically lowering risk of cardiotoxic side effects."

Srivastava said that since the FDA-approved fidarestat is available through a company in Japan, his eventual goal is to use a combination of fidarestat and doxorubicin to combat various forms of cancer including colon cancer with the hope that combination therapy will require less doxorubicin, which will reduce the potential for toxicity.

Other authors include UTMB's Himangshu Sonowal, Pabitra Pal, Jian-Jun Wen and Kota Ramana as well as Sanjay Awasthi from Texas Tech University Health Sciences Center. The study was supported by the National Institutes of Health.

http://bit.ly/2siXpoy

Autism risk linked to fever during pregnancy

Prenatal exposure to maternal fever during the second trimester raised odds of autism spectrum disorder by 40 percent

Fever during pregnancy may raise the risk for autism spectrum disorder (ASD) in the child, according to a study led by scientists at the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health. The effect was most pronounced in the second trimester, raising odds for ASD by 40 percent. Risk of an ASD was increased by over 300 percent for the children of women reporting three or more fevers after the twelfth week of pregnancy.

The study is the most robust to date to explore the risk of ASD associated with fevers across the entire span of pregnancy, and of the capacity of two different types of commonly used anti-fever medications--acetaminophen and ibuprofen--to address that risk. Risks were minimally mitigated among the children of women taking acetaminophen for fever in the second trimester. Although there were no cases of ASD among children of mothers who took ibuprofen, a nonsteroidal anti-inflammatory drug, researchers could not ascertain whether risk was mitigated due to the extremely small number of women using this particular drug for fever. Results of the study appear in the journal Molecular Psychiatry.

The researchers followed 95,754 children born between 1999 and 2009, including 583 cases of ASD identified in Norway through the Autism Birth Cohort (ABC) Study. Mothers of 15,701 children (16 percent) reported fever in one or more four-week intervals throughout pregnancy, similar to rates reported in the U.S. ASD risk was increased by 34 percent when mothers reported fever at any time during pregnancy, and by 40 percent in the second trimester. The risk increased in a dose-dependent fashion from 1.3-fold with one or two

fever episodes after the twelfth prenatal week to 3.12-fold with three or more episodes.

"Our results suggest a role for gestational maternal infection and innate immune responses to infection in the onset of at least some cases of autism spectrum disorder," says first author Mady Hornig, associate professor of Epidemiology and director of Translational Research at CII.

Questionnaire analysis did not indicate an association between risk and maternally-reported symptoms of infection in individual organ systems that might implicate specific infectious agents. An ongoing study is testing blood samples collected at mid-pregnancy and at birth to explore the possible role of specific infectious agents and the contribution of distinctive patterns of immune response among mothers and children to understand the mechanisms creating vulnerability.

"Future work should focus on identifying and preventing prenatal infections and inflammatory responses that may contribute to autism spectrum disorder," says senior author W. Ian Lipkin, John Snow Professor of Epidemiology and director of CII.

Co-authors include Xiaoyu Che, Michaeline A. Bresnahan, Andrew F. Schultz, Joy E. Ukaigwe, Meredith L. Eddy, Bruce Levin, and Ezra S. Susser at Columbia; Deborah Hirtz at the National Institute of Neurological Disorders and Stroke; and Nina Gunnes, Kari Kveim Lie, Per Magnus, Siri Mjaaland, Ted Reichborn-Kjennerud, Synnve Schjølberg, Cand Psychol, Anne-Siri Øyen and Camilla Stoltenberg at the Norwegian Institute of Public Health.

The study was funded by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health (NS47537, NS086122), the Jane Botsford Johnson Foundation, Simons Foundation Autism Research Initiative, the Norwegian Ministry of Health and Care Services, the Norwegian Ministry of Education and Research, and the Research Council of Norway.

http://bit.ly/2rAxBqO

Mitochondria behind blood cell formation

Mitochondria play an important role in hematopoiesis

New Northwestern Medicine research published in Nature Cell Biology has shown that mitochondria, traditionally known for their role creating energy in cells, also play an important role in hematopoiesis, the body's process for creating new blood cells.

"Historically, mitochondria are viewed as ATP—energy—producing organelles," explained principal investigator Navdeep Chandel, PhD, the David W. Cugell Professor of Medicine in the Division of Pulmonary and Critical Care Medicine. "Previously, my laboratory provided evidence that mitochondria can dictate cell function or fate independent of ATP production. We established the idea that mitochondria are signaling organelles."

In the current study, Chandel's team, including post-doctoral fellow Elena Ansó, PhD, and graduate students Sam Weinberg and Lauren Diebold, demonstrated that mitochondria control hematopoietic stem cell fate by preventing the generation of a metabolite called 2-hydroxyglutarate (2HG). The scientists showed that mice with stem cells deficient in mitochondrial function cannot generate blood cells due to elevated levels of 2HG, which causes histone and DNA hyper-methylation.

"This is a great example of two laboratories complementing their expertise to work on a project," said Chandel, also a professor of Cell and Molecular Biology and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Paul Schumacker, PhD, professor of Pediatrics, Cell and Molecular Biology and Medicine, was also a co-author on the paper.

Chandel co-authored an accompanying paper in Nature Cell Biology, led by Jian Xu, PhD, at the University of Texas Southwestern Medical Center, which demonstrated that initiation of erythropoiesis, the production of red blood cells specifically, requires functional mitochondria.

"These two studies collectively support the idea that metabolism dictates stem cell fate, which is a rapidly evolving subject matter," said Chandel, who recently wrote a review in Nature Cell Biology highlighting this idea. "An important implication of this work is that diseases linked to mitochondrial dysfunction like neurodegeneration

or normal aging process might be due to elevation in metabolites like 2HG."

More information: Elena Ans? et al. The mitochondrial respiratory chain is essential for haematopoietic stem cell function, Nature Cell Biology (2017). DOI: 10.1038/ncb3529

http://bit.ly/2sIhR4Q

Loneliness contributes to self-centeredness for sake of self-preservation

Study finds positive feedback loop between behaviors

Research conducted over more than a decade indicates that loneliness increases self-centeredness and, to a lesser extent, self-centeredness also increases loneliness.

The findings by researchers at the University of Chicago show such effects create a positive feedback loop between the two traits: As increased loneliness heightens self-centeredness, the latter then contributes further to enhanced loneliness.

"If you get more self-centered, you run the risk of staying locked in to feeling socially isolated," said John Cacioppo, the Tiffany and Margaret Blake Distinguished Service Professor in Psychology and director of the Center for Cognitive and Social Neuroscience.

Cacioppo and co-authors Stephanie Cacioppo, assistant professor of psychiatry and behavioral science at the UChicago's Pritzker School of Medicine, and Hsi Yuan Chen, a researcher at the Center for Cognitive and Social Neuroscience, published their findings in Personality and Social Psychology Bulletin on June 13.

The researchers wrote that "targeting self-centeredness as part of an intervention to lessen loneliness may help break a positive feedback loop that maintains or worsens loneliness over time." Their study is the first to test a prediction from the Cacioppos' evolutionary theory that loneliness increases self-centeredness. Such research is important because, as many studies have shown, lonely people are more susceptible to a variety of physical and mental health problems as well as higher mortality rates than their non-lonely counterparts.

The outcome that loneliness increases self-centeredness was expected, but the data showing that self-centeredness also affected loneliness was a surprise, Stephanie Cacioppo said.

In previous research, the Cacioppos reviewed the rates of loneliness in young to older adults across the globe. Five to 10 percent of this population complained of feeling lonely constantly, frequently or all the time. Another 30 to 40 percent complained of feeling lonely constantly.

Their latest findings are based on 11 years of data taken from 2002 to 2013 as part of the Chicago Health, Aging and Social Relations Study of middle-aged and older Hispanics, African-Americans and Caucasian men and women. The study's random sample consisted of 229 individuals who ranged from 50 to 68 years of age at the start of the study. They were a diverse sample of randomly selected individuals drawn from the general population who varied in age, gender, ethnicity and socioeconomic status.

Early psychological research treated loneliness as an anomalous or temporary feeling of distress that had no redeeming value or adaptive purpose. "None of that could be further from the truth," Stephanie Cacioppo said.

The evolutionary perspective is why. In 2006, John Cacioppo and colleagues proposed an evolutionary interpretation of loneliness based on a neuroscientific or biological approach.

In this view, evolution has shaped the brain to incline humans toward certain emotions, thoughts and behavior. "A variety of biological mechanisms have evolved that capitalize on aversive signals to motivate us to act in ways that are essential for our reproduction or survival," the UChicago co-authors wrote. From that perspective, loneliness serves as the psychological counterpart of physical pain.

"Physical pain is an aversive signal that alerts us of potential tissue damange and motivates us to take care of our physical body," the UChicago researchers wrote. Loneliness, meanwhile, is part of a

warning system that motivates people to repair or replace their deficient social relationships.

The finding that loneliness tends to increase self-centeredness fits the evolutionary interpretation of loneliness. From an evolutionary-biological viewpoint, people have to be concerned with their own interests. The pressures of modern society, however, are significantly different from those that prevailed when loneliness evolved in the human species, researchers found.

"Humans evolved to become such a powerful species in large part due to mutual aid and protection and the changes in the brain that proved adaptive in social interactions," John Cacioppo said. "When we don't have mutual aid and protection, we are more likely to become focused on our own interests and welfare. That is, we become more self-centered."

In modern society, becoming more self-centered protects lonely people in the short term but not the long term. That's because the harmful effects of loneliness accrue over time to reduce a person's health and well-being.

"This evolutionarily adaptive response may have helped people survive in ancient times, but in contemporary society may well make it harder for people to get out of feelings of loneliness," John Cacioppo said.

When humans are at their best, they provide mutual aid and protection, Stephanie Cacioppo added. "It isn't that one individual is sacrificial to the other. It's that together they do more than the sum of the parts. Loneliness undercuts that focus and really makes you focus on only your interests at the expense of others."

The Cacioppos have multiple loneliness studies in progress that address its social, behavioral, neural, hormonal, genetic, cellular and molecular aspects, as well as interventions.

"Now that we know loneliness is damaging and contributing to the misery and health care costs of America, how do we reduce it?" John Cacioppo asked. That is the next big question to answer.

http://bit.ly/2rFqngk

Researchers discover what may be earliest stage of Alzheimer's disease

Clusters of a sticky protein -- amyloid plaque -- found in the brain signal mental decline years before symptoms appear, a new study finds

Older adults with elevated levels of brain-clogging plaques -- but otherwise normal cognition -- experience faster mental decline suggestive of Alzheimer's disease, according to a new study led by the Keck School of Medicine of USC that looked at 10 years of data.

Just about all researchers see amyloid plaques as a risk factor for Alzheimer's.

However, this study presents the toxic, sticky protein as part of the disease -- the earliest precursor before symptoms arise.

"To have the greatest impact on the disease, we need to intervene against amyloid, the basic molecular cause, as early as possible," said Paul Aisen, senior author of the study and director of the USC Alzheimer's Therapeutic Research Institute (ATRI) at the Keck School of Medicine. "This study is a significant step toward the idea that elevated amyloid levels are an early stage of Alzheimer's, an appropriate stage for anti-amyloid therapy."

Notably, the incubation period with elevated amyloid plaques -- the asymptomatic stage -- can last longer than the dementia stage.

"This study is trying to support the concept that the disease starts before symptoms, which lays the groundwork for conducting early interventions," said Michael Donohue, lead author of the study and an associate professor of neurology at USC ATRI.

The researchers likened amyloid plaque in the brain to cholesterol in the blood. Both are warning signs with few outward manifestations until a catastrophic event occurs. Treating the symptoms can fend off the resulting malady -- Alzheimer's or a heart attack -- the effects of which may be irreversible and too late to treat.

"We've learned that intervening before the heart attack is a much more powerful approach to treating the problem," Donohue said.

Aisen, Donohue and others hope that removing amyloid at the preclinical stage will slow the onset of Alzheimer's or even stop it.

The amyloid problem

One in three people over 65 have elevated amyloid in the brain, Aisen noted, and the study indicates that most people with elevated amyloid will progress to symptomatic Alzheimer's within 10 years.

If Alzheimer's prevalence estimates were to include this "preclinical stage" before symptoms arise, the number of those affected would more than double from the current estimate of 5.4 million Americans, the study stated.

Published in The Journal of the American Medical Association on June 13, the study uses 10 years of data from the Alzheimer's Disease Neuroimaging Initiative, an exploration of the biomarkers that presage Alzheimer's. USC ATRI is the coordinating center of this North American investigation. Aisen co-directs its clinical core.

USC plays a leading role in the only two anti-amyloid studies focused on the early, preclinical stage of sporadic Alzheimer's: The Anti-Amyloid Treatment in Asymptomatic Alzheimer's study (the A4 Study) and the EARLY Trial, Aisen said.

"We need more studies looking at people before they have Alzheimer's symptoms," Aisen said. "The reason many promising drug treatments have failed to date is because they intervened at the end-stage of the disease when it's too late. The time to intervene is when the brain is still functioning well -- when people are asymptomatic."

Although elevated amyloid is associated with subsequent cognitive decline, the study did not prove a causal relationship.

For years, researchers have acknowledged age is the biggest risk factor when it comes to Alzheimer's. For more than 90 percent of people with Alzheimer's, symptoms do not appear until after age 60, according to the Centers for Disease Control and Prevention.

In 2014, about 46 million adults living in the United States -- 15 percent of the population -- were 65 or older. By 2050, that number is expected to expand to 88 million or 22 percent of the population.

The tipping point

Researchers measured amyloid levels in 445 cognitively normal people in the United States and Canada via cerebrospinal fluid taps or positron emission tomography (PET) scans: 242 had normal amyloid levels and 202 had elevated amyloid levels. Cognitive tests were performed on the participants, who had an average age of 74.

Although the observation period lasted 10 years, each participant, on average, was observed for three years. The maximum follow-up was 10 years.

The elevated amyloid group was older and less educated. Additionally, a larger proportion of this group carried at least one copy of the ApoE4 gene, which increases the odds that someone will develop Alzheimer's.

Based on global cognition scores, at the four-year mark, 32 percent of people with elevated amyloid had developed symptoms consistent with the early stage of Alzheimer's disease. In comparison, only 15 percent of participants with normal amyloid showed a substantial decline in cognition.

Analyzing a smaller sample size at year 10, researchers noted that 88 percent of people with elevated amyloid were projected to show significant mental decline based on global cognitive tests. Comparatively, just 29 percent of people with normal amyloid showed cognitive decline.

Alzheimer's disease research worldwide

Alzheimer's was recently a disease that could be diagnosed only after death with an autopsy.

Aisen and the researchers at USC ATRI have developed ways to identify early signs of Alzheimer's by creating a set of cognitive tests called the Preclinical Alzheimer Cognitive Composite. This battery of

tests and variations of it are widely used to detect Alzheimer's before dementia symptoms emerge, Aisen said.

"Our outcome measures are becoming the standard for early Alzheimer's disease intervention studies," Aisen said. "Drug companies will not invest in early intervention studies without a regulatory pathway forward. ATRI and USC are building a framework for drug development in Alzheimer's disease."

As a research institution devoted to promoting health across the life span, USC has more than 70 researchers dedicated to the prevention, treatment and potential cure of Alzheimer's disease.

Reisa Sperling at Harvard Medical School, Ronald Petersen at the Mayo Clinic, Chung-Kai Sun at USC ATRI and Michael Weiner at the University of California, San Francisco also contributed to this study.

http://bit.ly/2rFzbTt

Study sheds light on Neanderthal-Homo sapiens transition

Window into transition between Neanderthals and modern humans

Archaeologists at The Australian National University (ANU) and the University of Sydney have provided a window into one of the most exciting periods in human history -- the transition between Neanderthals and modern humans.

This is a stone tool thought to be a speartip made from radiolarite sourced over 100km to the east of the cave. **Miroslav Kralík**

An archaeological dig in a cave in the Moravian region of the Czech Republic has provided a timeline of evidence from 10 sedimentary layers spanning 28,000 to 50,000 years ago. This is the period when our modern human ancestors first arrived in Europe.

The dig, in a cave near the Czech border with Austria and around 150kms north of Vienna, has unearthed over 20,000 animal bones as well as stone tools, weapons and an engraved bone bead that is the oldest of its kind in Central Europe.

ANU archaeologist Dr Duncan Wright said the project was so important because it gives some of the earliest evidence of modern human activity in the region. This was a period when humans were moving substantial distances and bringing with them portable art objects.

"In the early layers the items we've found are locally made flakes, possibly used by small communities living and hunting in the vicinity to kill animals or prepare food, but around 40,000 years ago we start to see objects coming from long distances away," Dr Wright said.

"Dating from this same time we unearthed a bead made from mammal bone. This is the oldest portable art object of its type found anywhere in central Europe and provides evidence of social signalling, quite possibly used as a necklace to mark the identity of the wearer.

"So between these two periods, we've either seen a change in behaviour and human movement or possibly even a change in species."

Archaeologist Ladislav Nejman of the University of Sydney said one of the biggest questions is the beginnings of human exploration of this landscape by Homo sapiens who arrived in this area for the first time.

"We've found that somewhere between 40-48,000 years ago people became highly mobile," Dr Nejman said.

"Instead of moving short distances near the cave where they lived, they were walking for hundreds of kilometres quite often. We know that because we found various artefacts where the raw material comes from 100-200 kilometres away.

"The artefacts were also made of different materials from different regions. Some from the North-West, some from the North, some from the East."

However in layer 10, which represents an earlier time period between 48-45,000 years ago, all the recovered stone artefacts were made using local raw material, which indicates that the high residential mobility came later.

Dr Nejman said the study also revealed valuable new information about the climate of the region. "We haven't had such a long sequence of sedimentary layers before that we could test," he said.

"The climate changed quite often from warmer to colder, and vice versa, but at all times it was much colder than the interglacial period that we have lived in for the past 10,000 years."

Samples from the site have been sent through for analysis using a new technique, called ancient sediment DNA analysis. This is the first scientific method that can detect which species were present even without the bones of these species. It tests remnant DNA preserved in the sediment.

Dr Wright said the results will shed new light on a period of transition between two species of humans and also give clearer evidence about the activities of our modern human ancestors in a period and region where little is known.

"We can tell by the artefacts that small groups of people camped at this cave. This was during glacial periods suggesting they were well adapted to these harsh conditions" Dr Wright said. "It's quite possible that the two different species of humans met in this area."

The study was initially funded by a grant from SoMoPro program with a financial contribution from the European Community within the Seventh Framework Programme. The study has been published in the Journal of Human Evolution.

http://bit.ly/2sJjNtQ

State medical licensing boards' practices may hurt physician mental health

The intrusive methods licensing boards use to evaluate physician impairment may actually promote stigma around mental health -- without improving patient safety

Sharing a history of mental health issues with an employer is difficult for anyone. It's that much harder if reporting an old or well-controlled condition could lead to restrictions on your professional license -- as some physicians well know.

A new study found state medical boards ask physicians much more extensive and intrusive questions about mental health conditions than for physical health conditions. Despite national concern about physician suicide and well-being, research shows that even if physicians struggle with depression, they are reluctant to disclose and seek treatment because it could have serious consequences when they apply for their medical license.

Katherine J. Gold, M.D., M.S.W., M.S., assistant professor in the University of Michigan's Department of Family Medicine, recently led a study published in the Society of Teachers of Family Medicine that examined how state medical licensing boards across the 50 states and Washington, D.C., evaluated mental illnesses compared to physical illnesses or substance use on state licensing forms.

What she found is cause for alarm.

"The differences were really quite striking," says Gold. "States were significantly more likely to ask if physicians had been diagnosed, treated or hospitalized for mental health or substance abuse verses for physical health disorders, often asking about many years in the past."

Many of the questions violated the Americans with Disabilities Act as well, the study finds.

"The problem is that states don't ask, 'Do you have a problem right now that affects your ability to provide good care for patients?'" Gold explains. "(Instead) they ask broad questions that intrude on physician privacy and prevent doctors from seeking care, but don't necessarily pick up on impaired physicians."

A similar number of states asked about both physical and mental health, but the content and nature of the questions varied. Physical health questions tended to be much more lenient and vague while questions about mental health and substance abuse were much more specific, and at times, even intrusive, Gold says.

Fear and female physicians

Last year Gold led a survey that asked 2,100 female physicians who were also mothers about their mental health history and treatment.

Nearly half said they believed they met the definition for a mental illness at some point in their career, but had not sought treatment.

Two-thirds reported that fear of stigma, including fear of reporting to state medical boards, drove them to keep their worries quiet.

Only 6 percent who had ever been diagnosed had reported it to their state licensing board, as most felt their condition didn't affect the care they gave.

"I actually had a physician email me a month ago, and she was really worried because she had postpartum depression several years ago," says Gold. "[She] reported this to her state medical board and shared all of her treatment records but was still fearful that they would limit her license, despite the fact that there were no problems with her work and she was now doing much better. She was really terrified."

How state licensing boards respond to disclosures made by physicians about their mental health cannot be predicted and varies state by state, says Gold.

"It completely depends on the board," she says. "It could range from the board saying, 'Just send us a letter from your doctor, to send us all of your medical records from all of your treatment, to come before the board and give us your defense as to why you are fit to practice,' or even calling for ongoing monitoring and license restrictions."

Physician and patient safety

There is minimal data examining the impact of physician mental health on patient outcomes, Gold says. But conclusions can be drawn about how this issue affects doctors.

"Asking about prior problems or mental health diagnoses make it less safe for physicians because it creates an enormous pressure not to seek mental health treatment," says Gold.

"It affects physician identity. If you've trained for all these years as a physician and then you can't practice because back 10 years ago you had postpartum depression, that's really threatening. A lot of people just don't get help, and if they do get help, it's often off the books or informal help, which is not ideal."

Because of attention on the issue from the American Medical Association, there has been a sharp uptick in media focus on physician burnout and mental health, as well as the willingness of some doctors to tell their stories, and reporting on physician suicides.

A number of hospitals nationwide, including Michigan Medicine, are implementing programs to help residents and physicians individually improve their overall wellness and resilience. Although health systems should promote healthy lifestyles for doctors, more comprehensive and system-level changes should occur as well, Gold says.

"We're not going to improve physician health until we can take away some of the barriers to seeking help," she says. "We know that reporting this level of detail to state licensing boards is a huge barrier for physicians because of self-stigma and fears about their license and not being able to practice."

As a first step to make changes, Gold suggests making sure all questions about mental health on state medical licensing applications comply with the Americans with Disabilities Act. She also says questions should only ask about current conditions causing impairment. This ensures physicians aren't punished for disclosing an issue in their past that they've correctly addressed. Gold also indicates the Federation of State Medical Boards must take action.

"I think that's where change has to come from. It has to come from the group that is advising the state medical boards," she says. "They don't have regulatory authority over the boards, but certainly they can recommend best practices for the states."

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Statins may not be used for protection against Parkinson's disease

Use of statins may speed up the onset of Parkinson's disease symptoms in people who are susceptible to the disease, according to Penn State College of Medicine researchers.

Some previous research has suggested that statins, used to treat high cholesterol, may protect against Parkinson's disease. Research findings have been inconsistent, however, with some studies showing

a lower risk, some showing no difference and some showing a higher risk of Parkinson's disease in statin users.

"One of the reasons that may have explained these prior inconsistent results is that higher cholesterol, the main indication to use statins, has been related to lower occurrence of Parkinson's disease," said Xuemei Huang, professor of neurology. "This made it hard to know if the statin protective effect was due to the drug or preexisting cholesterol status."

Another reason for the inconsistent results is that there are two types of statins. Water-soluble statins cannot get into the brain, while fat-soluble statins, called lipophilic, can. Since people with high cholesterol are treated for both kinds, the interpretation of results as it relates to Parkinson's disease is not easy.

The researchers analyzed data in a commercially-available database of insurance claims for more than 50 million people.

They identified nearly 22,000 people with Parkinson's disease, and narrowed the number to 2,322 patients with newly diagnosed Parkinson's disease. They paired each Parkinson's patient with a person in the database who did not have Parkinson's -- called a control group.

Researchers then determined which patients had been taking a statin and for how long before Parkinson's disease symptoms appeared. Researchers reported their results in the journal Movement Disorders.

After analyzing the data, researchers found that prior statin use was associated with higher risk of Parkinson's disease and was more noticeable during the start of the drug use.

"Statin use was associated with higher, not lower, Parkinson's disease risk, and the association was more noticeable for lipophilic statins, an observation inconsistent with the current hypothesis that these statins protect nerve cells," Huang said. "In addition, this association was most robust for use of statins less than two-and-a-half years, suggesting that statins may facilitate the onset of Parkinson's disease."

Guodong Liu, assistant professor of public health sciences, said, "Our analysis also showed that a diagnosis of hyperlipidemia, a marker of high cholesterol, was associated with lower Parkinson's disease prevalence, consistent with prior research. We made sure to account for this factor in our analysis."

A recent study reported that people who stopped using statins were more likely to be diagnosed with Parkinson's disease, a finding interpreted as evidence that statins protect against Parkinson's disease.

"Our new data suggests a different explanation," Huang said. "Use of statins may lead to new Parkinson's disease-related symptoms, thus causing patients to stop using statins."

Huang stressed that more research needs to be completed and that those on statins should continue to take the medication their health care provider recommends.

"We are not saying that statins cause Parkinson's disease, but rather that our study suggests that statins should not be used based on the idea that they will protect against Parkinson's," Huang said.

"People have individual levels of risk for heart problems or Parkinson's disease. If your mom has Parkinson's disease and your grandmother has Parkinson's disease, and you don't have a family history of heart attacks or strokes, then you might want to ask your physician more questions to understand the reasons and risks of taking statins."

One limitation of this study was that the MarketScan data did not include Medicare patients, Medicaid patients or the uninsured. Also, because it was a private insurance sample, the patients were all under 65 years old, so the findings cannot be generalized to those who are older.

Other researchers on this study are Lan Kong and Douglas Leslie, Department of Public Health Sciences; Nicholas Sterling, Medical Scientist Training Program student; and Mechelle Lewis and Richard Mailman, Departments of Neurology and Pharmacology, all of Penn State College of Medicine; and Honglei Chen, Michigan State University.

The Center for Applied Studies in Health Economics and Penn State College of Medicine funded this research.

http://bit.ly/2rGK9bF

New study: Unsaturated fat associated with fatty liver disease

As the obesity epidemic continues, new data shed light on which nutrients and what quantity of those nutrients promote health or disease.

Bethesda, MD - In the American Gastroenterological Association journal, Cellular and Molecular Gastroenterology and Hepatology, scientists report on the role of macronutrients in the development of metabolically unhealthy obesity -- cases where patients have diseases with obesity as the root cause, specifically nonalcoholic fatty liver disease (NAFLD).1

Researchers from the University of California, San Francisco (UCSF), studied two groups of mice fed diets supplemented with either saturated fat or unsaturated fat. Surprisingly, they found that ingestion of starch and the monounsaturated fatty acid oleate led to fatty liver disease, mimicking the effects of a high-fat "western diet."

"Although purported to have many health benefits, including a favorable lipid profile, too much unsaturated fat can have significant adverse effects on metabolism," said lead author Caroline C. Duwaerts, PhD, of the department of medicine and The Liver Center at UCSF. "Our research adds new information to the understanding of metabolically unhealthy obesity and should lead to additional studies focusing on saturated vs. unsaturated fats and macronutrient concentration."

Writing in an accompanying editorial ("In NAFLD, You Are What You Eat, Not Simply How Much You Eat"2), Rotonya Carr, MD, of the University of Pennsylvania notes that "this study demonstrates clearly that nutrient composition (not simply total caloric intake) matters in the pathogenesis of NAFLD and supports the findings of other groups who have demonstrated similarly that the combination of high carbohydrate/high fat diet promotes liver injury."

Monounsaturated fats are a type of unsaturated fat that are thought to help lower cholesterol levels when used in place of saturated fats in a person's diet. Monounsaturated fats include oils, such as olive, peanut and canola, as well as avocados and some nuts and seeds. Saturated fats, which are found in animal-based foods, such as meat, cheese and butter, are thought to raise bad cholesterol and lead to increased risk of heart disease.

1 Duwaerts CC, et al. Specific Macronutrients Exert Unique Influences on the Adipose-Liver Axis to Promote Hepatic Steatosis in Mice, Cellular and Molecular Gastroenterology and Hepatology (2017), http://dx.doi.org/10.1016/j.jcmgh.2017.04.004.
http://www.cmghjournal.org/article/S2352-345X(17)30078-4/fulltext

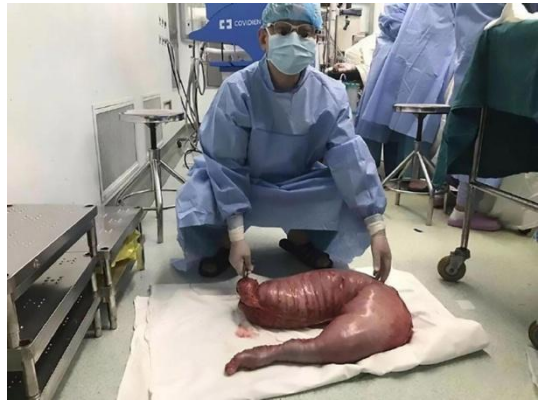
http://bit.ly/2ryFo8E

Man's 29 Lbs. of Poop Removed: What Is Hirschsprung's Disease?

When doctors in China removed 30 inches of a young man's colon, they also removed nearly 29 lbs. (13 kilograms) of his feces.

By Sara G. Miller, Staff Writer | June 14, 2017 11:30am ET

The 22-year-old's belly had swelled past the size that would be seen in a pregnant woman, at full-term, according to a Chinese news agency that reported his case. He told doctors that he had been constipated since birth, and that laxatives provided only slight relief.



The section of colon that was removed was 30 inches long and weighed nearly 29 lbs. **Shanghai Tenth People's Hospital**

The man had a very rare condition called Hirschsprung's disease, the website Inverse reported.

Hirschsprung's disease is a birth defect that affects about 1 in 5,000 babies in the U.S., according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD). People with the condition have no nerve cells within the wall of their colon, toward the end of its

length. The condition is more common in boys than in girls, and is also more common in children with other medical problems, including congenital heart defects and Down syndrome. [Get Gutsy About Your Digestive Health]

Normally, these nerve cells signal to the muscles of the bowel to alternatively contract and relax, to move stool along through the colon to the rectum. Without nerve cells, the bowel cannot effectively move stool through it, which can lead to severe constipation, according to the NIDDKD.

Nerve cells within the bowel wall form early in a fetus's development, the NIDDKD says. These cells first form at the top of the bowel and grow toward the opposite end. In those with Hirschsprung's disease, the nerves do not reach the end of the bowel. The condition can range in severity, depending on how far along the colon the nerve cells grew before they stopped. For example, in some cases, nerves are missing only from the very end of the large intestine, but in other cases, they can be missing from the entire large intestine and even parts of the small intestine.

The most obvious sign that a newborn has Hirschsprung's disease is that the baby does not have a bowel movement within the first 48 hours after birth, the Mayo Clinic says. Other symptoms can include a swollen belly, vomiting a green or brown substance, constipation, gas or diarrhea.

But in some cases, the condition isn't apparent until later in life. In older children, the symptoms can include a swollen belly, constipation, gas and fatigue, according to the Mayo Clinic. [5 Things Your Poop Says About Your Health]

Of course, many infants and children can develop constipation for other reasons. A key difference is that in infants or children with Hirschsprung's disease, constipation drugs taken by mouth, such as laxatives, typically do not have an effect, the NIDDKD says.

The only treatment for Hirschsprung's disease is surgery to remove the defective part of the colon, according to the NIDDKD.

Rarely, Hirschsprung's disease remains undiagnosed until a person reaches adulthood. In a 2006 report in the journal Annals of Diagnostic Pathology, researchers estimated that about 300 cases of adults or adolescents diagnosed with the condition have been described in the medical literature.

The disease is difficult to diagnose in adults, according to the case report. A number of other conditions can cause a large build-up of poop in the colon in adults, including problems with the movements of the colon, blockages and twists in the intestine called volvulus. A biopsy showing that the colon lacks nerve cells is needed to diagnose the condition.

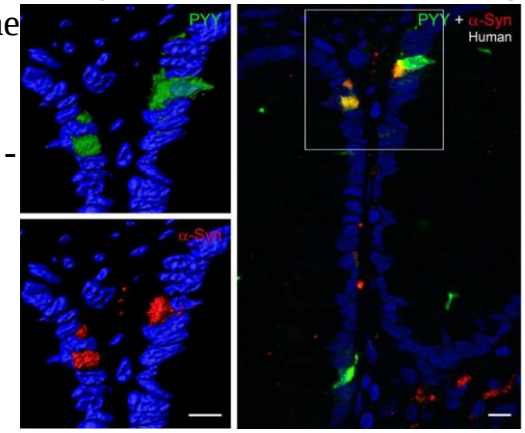
http://bit.ly/2rGZGbd

Pre-clinical study suggests Parkinson's could start in gut endocrine cells

Protein linked to Parkinson's could spread from gut to nervous system

DURHAM, N.C. - Recent research on Parkinson's disease has focused on the gut-brain connection, examining patients' gut bacteria, and even how severing the vagus nerve connecting the stomach and brain might protect some people from the debilitating disease.

But scientists understand little about what's happening in the gut - the ingestion of environmental toxins or germs, perhaps -- that leads to brain damage and the hallmarks of Parkinson's such as tremors, stiffness and trouble walking.



An image of tissue from a human colon uses fluorescent staining to show the presence of the protein alpha-synuclein (red) inside gut endocrine cells (green).
2017, JCI Insight

Duke University researchers have identified a potential new mechanism in both mice and human endocrine cells that populate the small intestines. Inside these cells is a protein called alpha-synuclein, which is known to go awry and lead to damaging clumps in the brains of Parkinson's patients, as well as those with Alzheimer's disease.

According to findings published June 15 in the journal JCI Insight, Duke researchers and collaborators from the University of California, San Francisco, hypothesize that an agent in the gut might interfere with alpha-synuclein in gut endocrine cells, deforming the protein. The deformed or misfolded protein might then spread via the nervous system to the brain as a prion, or infectious protein, in similar fashion to mad cow disease.

"There is abundant evidence that misfolded alpha-synuclein is found in the nerves of the gut before it appears in the brain, but exactly where this misfolding occurs is unknown," said gastroenterologist Rodger Liddle, M.D., senior author of the paper and professor of medicine at Duke. "This is another piece of evidence that supports the hypothesis that Parkinson's arises in the gut."

Alpha-synuclein is the subject of much ongoing research on Parkinson's, as it's the main component of Lewy bodies, or toxic protein deposits that take up residence in brain cells, killing them from the inside. The clumps form when alpha-synuclein develops a kink in its normally spiral structure, making it 'sticky,' and prone to aggregating, Liddle said.

But how would a protein go from traveling through the inner-most 'tube' of the intestine, where there are no nerve cells, into the nervous system? That's a question Liddle and colleagues sought to answer in a 2015 manuscript published in the Journal of Clinical Investigation. Although the main function of gut endocrine cells is to regulate digestion, the Duke researchers found these cells also have nerve-like properties.

Rather than using hormones to communicate indirectly with the nervous system, these gut endocrine cells physically connect to nerves, providing a pathway to communicate with the brain, Liddle said. The researchers demonstrated this in a stunning time-lapse video (2015, Journal of Clinical Investigation) in which a gut endocrine cell is placed under the microscope near a neuron. In just a few hours, the endocrine cell moves toward the neuron and fibers appear between them as they establish communication.

Liddle and other scientists were astonished at the video, he said, because the endocrine cells -- which are not nerves -- were behaving like them. This suggests they are able to communicate directly with the nervous system and brain.

With the new finding of alpha-synuclein in endocrine cells, Liddle and colleagues now have a working explanation of how malformed proteins can spread from the inside of the intestines to the nervous system, using a non-nerve cell that acts like a nerve.

Liddle and colleagues plan to gather and examine the gut endocrine cells from people with Parkinson's to see if they contain misfolded or otherwise abnormal alpha-synuclein. New clues about this protein could help scientists develop a biomarker that could diagnose Parkinson's disease earlier, Liddle said.

New leads on alpha-synuclein could also aid the development of therapies targeting the protein. Scientists have been investigating treatments that could prevent alpha-synuclein from becoming malformed, but much of the research is still in its early stages, Liddle said.

"Unfortunately, there aren't great treatments for Parkinson's disease right now," he said. "It's conceivable down the road that there could be ways to prevent alpha-synuclein misfolding, if you can make the diagnosis early."

In addition to Liddle, study authors include Rashmi Chandra of Duke, Annie Hiniker and Yien-Ming Kuo of the University of California, San Francisco (UCSF), and Robert L. Nussbaum of UCSF and the Invitae Corporation.

The research was supported by the National Institutes of Health (R01 DK098796, R01 DK109368), the U.S. Department of Veterans Affairs (BX002230), the Duke Clinical & Translational Science Institute (UL1TR001117), and the UCSF Program for Breakthrough Biomedical Research, which is funded in part by the Sandler Foundation.

http://bit.ly/2rIkL51

Police warned of drug so powerful it can kill in one breath

Do not inhale

IN A bid to thwart the opioid epidemic, the US Food and Drug Administration has asked Endo Pharmaceuticals to withdraw its opioid pain medication – Opana ER – over concerns that the drug is too easily abused, the first time the agency has made such a move.

In a statement, the drug-maker said it is "reviewing the request and is evaluating the full range of potential options".

It is a small step in fighting the rising tide of opioid abuse. In a speech last week, Rod Rosenstein of the US Drug Enforcement Administration said that deaths from drug overdose rose nearly 20 per cent in 2016, compared with the previous year. Rosenstein also urged law enforcement agencies to practise extreme caution when handling fentanyl, a synthetic opioid 50 to 100 times more potent than morphine. It is prescribed for severe pain, but is increasingly being sold on the street.

"Inhaling just a few airborne particles [of fentanyl] could be fatal," said Rosenstein. Last month, a police officer in Ohio collapsed after merely brushing some fentanyl off his shirt. He survived, but required four doses of the overdose treatment naloxone.

There is good news on the horizon, though. Last week, researchers in California reported that a vaccine that blocks the "high" of heroin has proven effective in non-human primates – the first vaccine against an opioid to do so.

http://bit.ly/2rIjWJA

A more safe and efficient means for drug manufacturing

System uses continuous flow technology to produce pharmaceutical compounds

Scientists have developed a system that uses continuous flow technology, instead of a batch-by-batch approach, to produce pharmaceutical compounds, and they used it to manufacture a chemotherapy drug that's currently under evaluation in clinical trials. Most pharmaceutical compounds are made in massive batches, yet small-volume continuous (SVC) manufacturing systems - currently used to produce numerous commodity chemicals - offer a number of advantages, such as improved safety and yield. As well, these systems can be used to conveniently produce pharmaceutical ingredients on site, when needed. Yet, while a number of SVC manufacturing systems have successfully produced pharmaceutical compounds in laboratories, few adhere to "current good manufacturing practices," such that they are commercially scalable. Here, Kevin P. Cole and colleagues developed a SVC manufacturing system that does adhere to such standards. The system allows for concurrent mixing of ingredients, and is equipped with fully automated filters that required no manual work, eliminating the risk of exposing operators to toxins. In this approach, a number of different techniques are used to separate layers of ingredients and effectively clean compartments after each use. The team demonstrated the effectiveness of their system by producing the chemotherapy agent prexasertib, currently being assessed in a phase two trial as a chemotherapy agent, in aqueous form. The system yielded 24 kilograms of the compound over the course of three days, the authors report.

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Egocentric hearing: Study clarifies how we can tell where a sound is coming from

Neurons in the brain's auditory cortex detect a sound's origin relative to the head its source's actual position in the world

A new UCL and University of Nottingham study has found that most neurons in the brain's auditory cortex detect where a sound is coming from relative to the head, but some are tuned to a sound source's actual position in the world.

The study, published in PLOS Biology, looked at whether head movements change the responses of neurons that track sound location.

"Our brains can represent sound location in either an egocentric manner - for example, when I can tell that a phone is ringing to my left - or in an allocentric manner - hearing that the phone is on the table. If I move my head, neurons with an egocentric focus will respond differently, as the phone's position relative to my ears has changed, while the allocentric neurons will maintain their response," said the study's first author, Dr Stephen Town (UCL Ear Institute).

The researchers monitored ferrets while they moved around a small arena surrounded by speakers that emitted clicking sounds. Electrodes monitored the firing rates of neurons in the ferrets' auditory cortex, while LEDs were used to track the animals' movement.

Among the neurons under investigation that picked up sound location, the study showed that most displayed egocentric orientations by tracking where a sound source was relative to the animal's head, but approximately 20% of the spatially tuned neurons instead tracked a sound source's actual location in the world, independent of the ferret's head movements.

The researchers also found that neurons were more sensitive to sound location when the ferret's head was moving quickly.

"Most previous research into how we determine where a sound is coming from used participants with fixed head positions, which failed to differentiate between egocentric and allocentric tuning. Here we found that both types coexist in the auditory cortex," said the study's senior author, Dr Jennifer Bizley (UCL Ear Institute).

The researchers say their findings could be helpful in the design of technologies involving augmented or virtual reality.

"We often hear sounds presented though earphones as being inside our heads, but our findings suggest sound sources could be created to appear externally, in the world, if designers incorporate information about body and head movements," Dr Town said.

The study was funded by the Medical Research Council, Human Frontiers Science Foundation, Wellcome and the Biotechnology and Biological Sciences Research Council.

http://bit.ly/2sLc1Qf

Evolutionary hot start, followed by cold shock

The initial phases of animal evolution proceeded faster than hitherto supposed: New analyses suggest that the first animal phyla emerged in rapid succession – prior to the global Ice Age that set in around 700 million years ago.

The fossil record reveals that almost all of the animal phyla known today had come into existence by the beginning of the Cambrian Period some 540 million years ago. The earliest known animal fossils already exhibit complex morphologies, which implies that animals must have originated long before the onset of the Cambrian. However, taxonomically assignable fossils that can be confidently dated to pre-Cambrian times are very rare. In order to determine what the root of their family tree looked like, biologists need reliable dating information for the most ancient animal subgroups – the sponges, cnidarians, comb jellies and placozoans. Dr. Martin Dohrmann and Professor Gert Wörheide of the Division of Palaeontology and Geobiology in the Department of Earth and Environmental Sciences at LMU Munich have now used a new strategy based on the so-called molecular-clock to investigate the chronology of early animal evolution and produce a new estimate for the ages of the oldest animal groups. Their findings appear in the journal Scientific Reports.

The molecular clock approach is based on the principle that mutations accumulate in the genomes of all organisms over the course of time. The extent of the genetic difference between two lineages should therefore depend on the time elapsed since they diverged from their last common ancestor. "Our study is based on a combination of genetic data from contemporary animals and information derived from well dated fossils, which we analyzed with the help of complex computer algorithms," Dohrmann explains. For the study, the researchers used an unusually large dataset made up of the sequences of 128 proteins from 55 species, including representatives of all the

major animal groups, focusing in particular on those that diverged very early.

The analysis confirms the conclusion reached in an earlier study, which dated the origin of animals to the Neoproterozoic Era, which lasted from 1000 to 540 million years ago. However, much to their surprise, the results also suggested that the earliest phyla, and the ancestors of all bilateral animal species (the so-called Bilateria), originated within the – geologically speaking – short time-span of 50 million years. "In addition, this early phase of evolutionary divergence appears to have preceded the extreme climate changes that led to Snowball Earth, a period marked by severe long-term global glaciation that lasted from about 720 to 635 million years ago," Dohrmann says. In order to assess the plausibility of the new findings, the researchers plan to carry out further analyses using more extensive datasets and improved statistical methods." To arrive at well-founded conclusions with respect to the morphology and ecology of the earliest animals, we also need to know more about the environmental conditions that prevailed during the Neoproterozoic, and we need more fossils that can be confidently assigned to specific taxonomic groups", Wörheide says.

More information: Martin Dohrmann et al. Dating early animal evolution using phylogenomic data, Scientific Reports (2017). DOI: 10.1038/s41598-017-03791-w

http://bit.ly/2tfob1b

US is still first in science, but China rose fast as funding stalled here & elsewhere

U-M team examines global cooperation and output in original biomedical research publications and funding

ANN ARBOR, MI - American scientific teams still publish significantly more biomedical research discoveries than teams from any other country, a new study shows, and the U.S. still leads the world in research and development expenditures.

But American dominance is slowly shrinking, the analysis finds, as China's skyrocketing investing on science over the last two decades begins to pay off. Chinese biomedical research teams now rank fourth in the world for total number of new discoveries published in six top-tier journals, and the country spent three-quarters what the U.S. spent on research and development during 2015.

Meanwhile, the analysis shows, scientists from the U.S. and other countries increasingly make discoveries and advancements as part of teams that involve researchers from around the world.

The last 15 years have ushered in an era of "team science" as research funding in the U.S., Great Britain and other European countries, as well as Canada and Australia, stagnated. The number of authors has also grown over time. For example, in 2000 only two percent of the research papers the new study looked include 21 or more authors -- a number that increased to 12.5 percent in 2015.

The new findings, published in JCI Insight by a team of University of Michigan researchers, come at a critical time for the debate over the future of U.S. federal research funding. The study is based on a careful analysis of original research papers published in six top-tier and four mid-tier journals from 2000 to 2015, in addition to data on R&D investment from those same years.

The study builds on other work that has also warned of America's slipping status in the world of science and medical research, and the resulting impact on the next generation of aspiring scientists.

"It's time for U.S. policy-makers to reflect and decide whether the year-to-year uncertainty in National Institutes of Health budget and the proposed cuts are in our societal and national best interest," says Bishr Omary, M.D., Ph.D., senior author of the new data-supported opinion piece and chief scientific officer of Michigan Medicine, U-M's academic medical center. "If we continue on the path we're on, it will be harder to maintain our lead and, even more importantly, we could be disenchanting the next generation of bright and passionate biomedical scientists who see a limited future in pursuing a scientist or physician-investigator career."

The analysis charts South Korea's entry into the top 10 countries for publications, as well as China's leap from outside the top 10 in 2000 to fourth place in 2015. They also track the major increases in support for research in South Korea and Singapore since the start of the 21st Century.

Meticulous tracking

First author of the study, U-M informationist Marisa Conte, and Omary co-led a team that looked carefully at the currency of modern science: peer-reviewed basic science and clinical research papers describing new findings, published in journals with long histories of accepting among the world's most significant discoveries.

They reviewed every issue of six top-tier international journals (JAMA, Lancet, the New England Journal of Medicine, Cell, Nature and Science), and four mid-ranking journals (British Medical Journal, JAMA Internal Medicine, Journal of Cell Science, FASEB Journal), chosen to represent the clinical and basic science aspects of research.

The analysis included only papers that reported new results from basic research experiments, translational studies, clinical trials, metanalyses, and studies of disease outcomes. Author affiliations for corresponding authors and all other authors were recorded by country.

The rise in global cooperation is striking. In 2000, 25 percent of papers in the six top-tier journals were by teams that included researchers from at least two countries. In 2015, that figure was closer to 50 percent. The increasing need for multidisciplinary approaches to make major advances, coupled with the advances of Internet-based collaboration tools, likely have something to do with this, Omary says.

The authors, who also include Santiago Schnell, Ph.D. and Jing Liu, Ph.D., note that part of their group's interest in doing the study sprang from their hypothesis that a flat NIH budget is likely to have negative consequences but they wanted to gather data to test their hypothesis.

They also observed what appears to be an increasing number of Chinese-born scientists who had trained in the U.S. going back to China after their training, where once most of them would have sought to stay in the U.S. In addition, Singapore has been able to recruit several top notch U.S. and other international scientists due to their marked increase in R&D investments.

The same trends appear to be happening in Great Britain, Australia, Canada, France, Germany and other countries the authors studied - where research investing has stayed consistent when measured as a percentage of the U.S. total over the last 15 years.

The authors note that their study is based on data up to 2015, and that in the current 2017 federal fiscal year, funding for NIH has increased thanks to bipartisan Congressional appropriations. The NIH contributes to most of the federal support for medical and basic biomedical research in the U.S. But discussion of cuts to research funding that hinders many federal agencies is in the air during the current debates for the 2018 budget. Meanwhile, the Chinese R&D spending is projected to surpass the U.S. total by 2022.

"Our analysis, albeit limited to a small number of representative journals, supports the importance of financial investment in research," Omary says. "I would still strongly encourage any child interested in science to pursue their dream and passion, but I hope that our current and future investment in NIH and other federal research support agencies will rise above any branch of government to help our next generation reach their potential and dreams."

Omary is professor of physiology and internal medicine at the U-M Medical School, where Schnell is professor of physiology and computational medicine and bioinformatics. Conte is the Assistant Director, Research and Informatics, at U-M's Taubman Health Sciences Library, and Liu is a research specialist at the Michigan Institute for Data Science. Reference: JCI Insight, https://doi.org/10.1172/jci.insight.95206

http://bit.ly/2rIQm6L

New flu test: One drop of blood could save your life

World first test to identify which influenza patients will need urgent, life-saving, medical treatment

Australian researchers have developed a world first test to identify which influenza patients will need urgent, life-saving, medical treatment.

The High-risk Influenza Screen Test (HIST) measures 'an early warning signal' released by the patient's body into their blood to 'kick start' their immune system's fight against the infection.

The test, developed by Dr Benjamin Tang -- a doctor from the Department of Intensive Care Medicine, Nepean Hospital and medical researcher at Westmead Institute for Medical Research -- needs only a single drop of blood and a few hours to predict, with 91 percent accuracy, which influenza patients will develop potentially deadly secondary infections, such as pneumonia.

Previously doctors could only test for influenza infection but didn't know which patients would be at risk of rapid deterioration.

"Influenza can sometimes kill otherwise healthy people in the prime of their lives," says Dr Tang.

"By using the High-risk Influenza Screen Test we're eavesdropping on the immune system to pick up when the body first mounts a defence against a serious, life-threatening, infection. The early warning means we have a greater chance to treat the patient's infection before it overwhelms them and potentially kills them," says Dr Tang.

The research, published today by Dr Tang and colleagues in the European Respiratory Journal, deciphered the genetic codes that immune cells release to warn the body of a serious infection, such as pneumonia, caused by the influenza virus.

HIST will be particularly useful during pandemics when there is a delay in developing vaccines for strains of the influenza virus.

"We can now test people during a pandemic, or outbreak of a new flu virus, to identify those who might be at greater risk of developing serious complications. The test works with any flu infection as it looks at how the body reacts rather than the strain or type of virus."

Dr Tang says HIST could also be used to track the effectiveness of new drugs in clinical trials by accurately plotting the patient's immune response.

The patented High-risk Influenza Screen Test runs on equipment already available in most pathology laboratories.

http://bit.ly/2sCN5dx

Massachusetts General researchers explore why those with autism avoid eye contact

Imaging studies reveal overactivation of subcortical brain structures in response to direct gaze

Individuals with autism spectrum disorder (ASD) often find it difficult to look others in the eyes. This avoidance has typically been interpreted as a sign of social and personal indifference, but reports from people with autism suggests otherwise. Many say that looking others in the eye is uncomfortable or stressful for them - some will even say that "it burns" - all of which points to a neurological cause. Now, a team of investigators based at the Athinoula A. Martinos Center for Biomedical Imaging at Massachusetts General Hospital has shed light on the brain mechanisms involved in this behavior. They reported their findings in a Scientific Reports paper published online this month.

"The findings demonstrate that, contrary to what has been thought, the apparent lack of interpersonal interest among people with autism is not due to a lack of concern," says Nouchine Hadjikhani, MD, PhD, director of neurolimbic research in the Martinos Center and corresponding author of the new study. "Rather, our results show that this behavior is a way to decrease an unpleasant excessive arousal stemming from overactivation in a particular part of the brain."

The key to this research lies in the brain's subcortical system, which is responsible for the natural orientation toward faces seen in newborns and is important later for emotion perception. The subcortical system can be specifically activated by eye contact, and previous work by Hadjikhani and colleagues revealed that, among those with autism, it was oversensitive to effects elicited by direct gaze and emotional expression. In the present study, she took that observation further, asking what happens when those with autism are compelled to look in the eyes of faces conveying different emotions.

Using functional magnetic resonance imaging (fMRI), Hadjikhani and colleagues measured differences in activation within the face-processing components of the subcortical system in people with autism and in control participants as they viewed faces either freely or when constrained to viewing the eye-region. While activation of these structures was similar for both groups exhibited during free viewing, overactivation was observed in participants with autism when concentrating on the eye-region. This was especially true with fearful faces, though similar effects were observed when viewing happy, angry and neutral faces.

The findings of the study support the hypothesis of an imbalance between the brain's excitatory and inhibitory signaling networks in autism - excitatory refers to neurotransmitters that stimulate the brain, while inhibitory refers to those that calm it and provide equilibrium. Such an imbalance, likely the result of diverse genetic and environmental causes, can strengthen excitatory signaling in the subcortical circuitry involved in face perception. This in turn can result in an abnormal reaction to eye contact, an aversion to direct gaze and consequently abnormal development of the social brain.

In revealing the underlying reasons for eye-avoidance, the study also suggests more effective ways of engaging individuals with autism. "The findings indicate that forcing children with autism to look into someone's eyes in behavioral therapy may create a lot of anxiety for them," says Hadjikhani, an associate professor of Radiology at Harvard Medical School. "An approach involving slow habituation to eye contact may help them overcome this overreaction and be able to handle eye contact in the long run, thereby avoiding the cascading effects that this eye-avoidance has on the development of the social brain."

The researchers are already planning to follow up the research. Hadjikhani is now seeking funding for a study that will use magnetoencephalography (MEG) together with eye-tracking and other behavioral tests to probe more deeply the relationship between the subcortical system and eye contact avoidance in autism.

The co-authors of the Scientific Reports study are Nicole R. Zürcher, Amandine Lassalle and Noreen Ward of the MGH Martinos Center; Jakob Åsberg Johnels, Eva Billstedt and Christopher Gillberg of Gothenburg University, Gothenburg, Sweden; Quentin Guillon of the Lyon Neuroscience Research Center, Lyon, France; Loyse Hippolyte of the University of Lausanne, Lausanne, France; and Eric Lemonnier of CRA, of Limoges, France. The study was supported by the Swiss National Science Foundation (grant PP00P3-130191), the Centre d'Imagerie BioMédicale of the University of Lausanne, as well as the Foundation Rossi Di Montalera, the LifeWatch Foundation, the AnnMarie and Per Ahlqvist Foundation, the Torsten Soderberg Foundation and the Swedish Science Council.

http://bit.ly/2sepqI0

Why is one twin smaller than the other? Answer could lie in the placenta

MRI study finds differences in prenatal oxygen transport from mother to baby

BOSTON - When a baby is born small, it's often attributed to genetic factors or maternal risk factors like poor nutrition or smoking. But a twin study led by researchers at Boston Children's Hospital now find that slower transport of oxygen from mother to baby across the placenta predicts slower fetal growth, as well as a smaller brain and liver.

The study, published today in Scientific Reports (Nature.com) is the first to make a direct connection between birth outcomes and placental oxygen transport.

By studying identical twins, the researchers were uniquely able to control for both genetic factors and maternal risk factors. Although identical twins also share a placenta, it is divided into two separate compartments, and one may be healthier than the other.

P. Ellen Grant, MD, director of Boston Children's Fetal-Neonatal Neuroimaging and Developmental Science Center, and Elfar Adalsteinsson, PhD at MIT have developed a noninvasive method that uses MRI to map the timing of oxygen delivery across the placenta in real time. Using this technique, called Blood-Oxygenation-Level-

Dependent (BOLD) MRI, they showed that dysfunctional placentas have large regions with slow oxygen transport to the fetus.

"Until now, we had no way to look at regional placental function in vivo," says Grant.

"Prenatal ultrasound or routine clinical MRI can assess placental structure, but cannot assess regional function, which is not uniform across the placenta. Doppler ultrasound, the current clinical method of assessing placental function, measures blood flow in the umbilical arteries and other fetal vessels, but it cannot tell how well oxygen or nutrients are being transported from mother to fetus."

Real-time placental oxygen mapping

In the new study, part of the NIH-funded Human Placenta Project, Grant, co-senior investigator Julian Robinson, MD, chief of obstetrics at Brigham and Women's Hospital (BWH), and their colleagues followed seven sets of identical twins all the way to birth, specifically tracking pregnancies in which one twin was smaller than the other.

At 29 to 34 weeks of pregnancy, the seven mothers underwent BOLD MRI for about 30 minutes.

While they inhaled pure oxygen for 10-minute stretches, Grant's team measured how long it took oxygen to reach its maximum concentration in the placenta, known as the time to plateau (TTP), and then how long it took for the oxygen to pass through the umbilical cord into the fetus and penetrate the brain and liver. Researchers led by Polina Golland, PhD, at MIT CSAIL used image-correction algorithms developed by MIT to adjust for fetal motion.

They found that a longer TTP in the placenta correlated with lower liver and brain volumes and lower newborn birth weights. TTP also correlated with placental pathology when placentas were examined after birth by placental pathologist Drucilla Roberts, MD, at Massachusetts General Hospital (MGH).

Grant hopes her team's work will be used to better understand pregnancy risk factors, develop a prenatal test for mothers in whom placental dysfunction is suspected and ultimately improve prenatal care.

"Our next goal is to figure out what causes variation in oxygen transport in the placenta and identify a cutoff value that would be of concern in a pregnancy, including singleton pregnancies," she says. "Then, we can think about potential treatments to improve placental oxygen transport, and use our methods to immediately assess the success of these treatments."

Future directions

Grant believes placental oxygen transport is a prime example of how environmental factors can modify the DNA we all inherit. Future studies will investigate how placental oxygen transport affects fetal gene expression and specific measures of brain development and organ metabolism.

These studies will use a special MRI coil to improve image accuracy, developed for pregnant mothers by collaborator Larry Wald, PhD, at the Athinoula A. Martinos Center. William Barth, MD, chief of Maternal-Fetal Medicine at MGH and Chloe Zera, MD, MPH, a BWH obstetrician, have also joined the team to guide the development of novel MR imaging strategies to improve the management of pregnant mothers.

"The placenta plays a key role in fetal development and maternal health," says David Weinberg, project lead for NIH's Human Placenta Project, launched by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

"Understanding how it functions is essential for developing interventions to improve the health of mothers and their infants."

Jie Luo, PhD, and Esra Abaci Turk, PhD, both research fellows at Boston Children's Hospital and the Madrid-MIT M+Vision Consortium, were co-first authors on the study. The research was funded by the NIH (U01 HD087211 and R01 EB017337) and the Consejeria de Educacion, Juventud y Deporte de la Comunidad de Madrid through the Madrid-MIT M+Vision Consortium. Luo, Abaci Turk, Grant, and co-authors Norberto Malpica, PhD, and Elfar Adalsteinsson, PhD (both of Madrid-MIT M+Vision Consortium) are co-inventors on a patent applications describing the MRI based method for measuring placental transport.

http://bit.ly/2sLlKGa

5 kilograms of broccoli in a pill slashes diabetics' blood sugar

Concentrated broccoli extract could prove indispensable to people with type 2 diabetes

By Andy Coghlan

Doctors frequently tell us to eat our greens, but soon they could be prescribing broccoli. A powder that contains concentrated extract from the vegetable could prove indispensable to people with type 2 diabetes. The extract reduced blood sugar levels by up to 10 per cent in people with the disease.

Get your five a day – 5 kilograms that is **Adam Gault/Getty**

Type 2 diabetes usually develops around middle age, often in people who are overweight. Their body stops responding to insulin, which controls the level of glucose in the blood. Abnormal insulin regulation causes a rise in blood sugar levels, which can raise people's chances of heart attacks, blindness and kidney problems.

People with the condition are often prescribed metformin, which helps to lower blood glucose. However, as many as 15 per cent cannot take this therapy because of kidney damage risks.

"More research is needed to see if this repurposed drug can be used to treat Type 2 diabetes, as it was only tested in a small number of people and only helped a subset of those who are taking it," says Elizabeth Robertson, of the charity Diabetes UK. "For now, we recommend that people continue with the treatment prescribed by their healthcare team."

Clever greens

A chemical called sulforaphane, found in broccoli sprouts, has previously demonstrated an ability to reduce glucose levels in diabetic rats. Anders Rosengren of the University of Gothenburg in Sweden, and his colleagues wondered whether the same might be true for humans. To test the theory, his team gave 97 people with type 2 diabetes a concentrated dose of sulforaphane every day for three months, or a placebo. All but three people in the trial continued taking metformin. Those who didn't take metformin were able to control their condition relatively well without it.

The concentration of sulforaphane given was around 100 times that found naturally in broccoli. "It was the same as eating around five kilograms of broccoli daily," says Rosengren.

On average, those who received the broccoli extract saw their blood glucose reduce by 10 per cent more than those on the placebo. The extract was most effective in obese participants with "dysregulated" diabetes, whose baseline glucose levels were higher to start with.

"We're very excited about the effects we've seen and are eager to bring the extract to patients," says Rosengren. "We saw a reduction of glucose of about 10 per cent, which is sufficient to reduce complications in the eyes, kidneys and blood," he says.

Complimentary medicine

Further investigations showed that while both metformin and sulphoraphane cut blood glucose, they do it in different ways. Metformin makes cells more sensitive to insulin, so they sponge more surplus glucose out of the bloodstream. Sulphoraphane reduces glucose by suppressing liver enzymes that otherwise stimulate the production of glucose.

For this reason, Rosengren thinks the broccoli extract is complementary to metformin, not competitive. But he points out that many people with diabetes can't take metformin because of kidney complications, so the broccoli extract could be an ideal substitute in these cases. In collaboration with the Swedish Farmers' Association, Rosengren and his colleagues are applying to regulatory authorities to seek approval for the powder, which could take as little as two years.

Rosengren also plans to explore potential benefits of the extract in people who are pre-diabetic, and so not yet taking metformin.

Journal reference: Science Translational Medicine, DOI: 10.1126/scitranslmed.aah4477

http://bit.ly/2se6NM0

Bacteria found to be common in open-heart surgical equipment

A study of North American hospitals found potentially deadly bacteria in more than a third of heater-cooler units used in open heart surgery.

Surgical operating theatres are supposed to be some of the most hygienic and sterile places in the world, and that goes double for those used for open-heart surgery.

However, a recent study has found that many heater-cooler units used to maintain the temperature of a patient's blood and organs during heart bypass provide a home for potentially lethal bacteria.

The research, presented to the 2017 APIC conference by John Rihs of Special Pathogens Laboratory, examined 653 water samples from 89 heater-cooler units located in hospitals around the US and Canada.

Of these, 33 units tested positive for the bacterium Mycobacterium chimaera, 4 were colonised with Legionella and 97 cultures were deemed uninterpretable due to extremely high levels of bacterial and fungal contamination.

Even though heater-cooler units use water tanks that provide temperature-controlled water through closed circuits, contamination presents an issue, as the water in them can still aerosolise and has the potential to transmit bacteria through the air to patients.

This transmission of bacteria can cause infections with non-specific symptoms that are slow to develop and difficult to diagnose.

Such infections can go untreated for years, which makes them even more difficult to treat.

Rihs' research highlights the need for hospitals to remain vigilant in monitoring the decontamination and maintenance schedules of heater-cooler units.

http://bit.ly/2sDll8q

Scientists solve 30-year old mystery on how resistance genes spread

Scientists have revealed that certain disease-causing bacteria get their resistance genes in a complex process involving bacterial 'sex'; this can potentially lead to a more targeted effort in preventing the spread of antibiotic resistance

To win the war against antibiotic resistant super bugs, scientists seek to find the origin of resistance genes. Further, they try to identify how the genes are introduced to disease-causing bacteria - so-called pathogens. Identifying where resistance genes come from and how they spread somewhat compares to finding patient zero in an outbreak, which is not an easy task.

For more than 30 years, scientists have proposed that resistance genes actually originate from the microorganisms producing the antibiotic. But even though this has been a hypothesis, scientists have not been able to find direct proof of this transfer.

Now, research conducted at The Novo Nordisk Foundation Center for Biosustainability - DTU Biosustain - at Technical University of Denmark for the very first time shows that antibiotic resistance genes originate from the same place as the antibiotic compounds, i.e. from a group of soil bacteria called Actinobacteria.

The study is now published in Nature Communications.

More than three fourths of all current antibiotics used to treat human infections are produced by Actinobacteria, which at the same time carry antibiotic resistance genes.

In these experiments, the researchers surprisingly found that many resistance genes in disease-causing microbes (gram negative pathogens) were very similar to resistance genes found in Actinobacteria. Especially in one case, the genes were 100% identical.

"It has been suspected that pathogens can obtain resistance genes from Actinobacteria for half a century. So now with the 100 % identical

genes we find the smoking gun," says Postdoc Xinglin Jiang from DTU Biosustain.

Gram negative pathogens constitute a big group of different species; amongst others pseudomonas, which can cause lung and urinary tract infections.

At first, it was difficult to imagine how pathogens can acquire genes from Actinobacteria, because they are so different and not at all related with each other. But by investigating the DNA sequence around the resistance genes, the team figured out how the resistance genes transfer occurred through a new mechanism named "carry back", where the pathogen basically has a primitive form of "sex" with the Actinobacterium and takes up its resistance genes after it dies.

This gene transfer by carry back could in principle happen where pathogens come into contact with Actinobacteria, like in an animal farm or in soil polluted with untreated hospital waste. In this way, the pathogen can become resistant and endanger human lives in the next round of infection.

Understanding the origin is hence key to counteracting the spread of antibiotic resistance, explains Senior Researcher Tilmann Weber from DTU Biosustain:

"We can't stop this gene transfer, but when you know, which resistance genes pathogens may harbor, you can personalize the antibiotic treatment. Also, with this knowledge you can try to develop new antibiotics with other properties that the pathogens don't have a defense against."

Bacterial sex act reveals the mechanism:

By following the DNA-transfer, scientists for the very first time showed an unknown mechanism called carry back in which pathogens were able to snatch genes from far-related bacteria via the carry back mechanism. Here is how, in short, the carry back process works:

1. The Gram negative pathogen injects its DNA into the Actinobacteria. Gram negative bacteria naturally have an ability called conjugation by which bacterial cells can inject their own DNA into other bacterial cells. It is called the bacterial equivalent of sex, because it is usually used to exchange gene information between Gram negative bacteria. But sometimes Gram negative bacteria can also use this mechanism to inject DNA into far-related Gram positive bacteria like Actinobacteria.

2. Inside the Actinobacteria, the injected DNA recombines with the host's DNA containing resistance genes. After the Actinobacterium dies, the recombinant DNA is released into the environment.

3. Lastly, the injected DNA can act as "gluing DNA" and mediate the uptake of resistance gene back to the pathogens through a phenomenon called natural transformation.

http://bit.ly/2sD0CBM

Increase in ciguatera fish poisoning cases in Europe

European cooperation project EuroCigua investigates risks and spread of ciguatoxin poisoning

BfR Federal Institute for Risk Assessment

The substance ciguatoxin is only found in fish from tropical and subtropical seas. For some years now, cases of ciguatera have been reported with increasing frequency in Europe, in particular on the Spanish and Portuguese islands in the Atlantic but also in Germany. New information indicates that these toxins are increasingly prevalent in the Mediterranean. The global trade of imported fish is another reason for the increasing occurrence of ciguatoxin poisoning in Europe. "Fish should be a regular part of the diet", says BfR-President Professor Dr. Dr. Andreas Hensel. "Ciguatera is a very rare form of fish poisoning in Germany. The reported cases have been caused by the consumption of contaminated tropical predatory fish such as various snapper species." These include Lutjanus bohar (two-spot red snapper), Lutjanus argentimaculatus, Lutjanus erythropterus (crimson snapper) or Pinjalo pinjalo.

European scientists have combined their expertise in the EuroCigua project on the "determination of the incidence and epidemiological characteristics of ciquatera cases in Europe". The aim is to characterise the risks of ciguatoxin poisoning in Europe. The EuroCigua project is developing reliable methods for the identification

and quantification of ciguatoxin in fish and microalgae in European waters. Under the umbrella of the European Food Safety Authority (EFSA), 14 further European organisations from six member states are involved in the project, including the BfR.

Ciguatoxin poisoning is triggered by metabolites of microalgae whose natural habitat is in the coral reefs of the Caribbean as well as the Pacific and Indian Oceans. Herbivorous fish feed on these microorganisms. If the small fish are eaten by larger predatory fish, the ciguatoxins can accumulate and subsequently find their way into the human food chain. The initial focus of the EuroCigua project is to determine the frequency of ciguatera cases and ciguatoxic fish in Europe. Alongside this, the involved parties are developing and establishing new, reliable methods to detect the presence of ciguatoxin in fish and microalgae. The detection of ciguatoxins is putting high demands on the analytical methods, as the toxins are effective in very low concentrations. Moreover, these toxins occur in many different chemical structures -- depending on the catch area. At the present time, no analytical methods are available for the routine testing of fish for ciguatoxins.

While ciguatera cases used to be confined to tropical and subtropical regions of the world, Spain and Portugal have been reporting outbreaks of ciguatoxin poisoning on the Canary Islands and Madeira since 2008. In Germany as well, there has been at least one ciguatera outbreak with up to 20 affected people every year since 2012. By means of the EuroCigua project, the scientists hope to gain a better understanding of the time-based and geographic distribution in European waters of the Gambierdiscus spp. microorganism responsible for poisoning. They are also investigating whether fish from EU waters might contain ciguatoxin.

One important part of the project is ciguatera prevention. The experts have created a leaflet outlining recommendations to reduce the risk of food poisoning in the affected regions. Fish should be a regular part of the diet, but the experts advise against eating the offal of tropical predatory fish, as they contain the highest ciguatoxin levels. Ciguatoxin is heat-stable and is therefore not destroyed during the preparation of fish. It is colourless, odourless and tasteless and can therefore not be detected by the naked eye. Ciguatoxin poisoning is accompanied by a variety of clinical symptoms, including gastrointestinal and especially neurological disorders such as the reversal of cold-hot sensitivity. When the first symptoms appear, the affected persons should seek immediate medical attention and inform the competent veterinary authority.

FAO link on ciguatera: http://www.fao.org/docrep/007/y5486e/y5486e0q.htm

Link to the EuroCigua project ***Link to the EuroCigua leaflet***

http://bit.ly/2sG7z5T

Goat testicles in men, human organs in pigs: the past and future of xenotransplantation

The road to growing organs in pigs is paved with ethical questions

by Angela Chen@chengela

In 2003, a South Korean company called Maria Biotech announced its newest success: it had created mouse embryos with human cells in them.

The idea is that the mice could be born with human cells in all their tissues, and this would make them more accurate animal models for research. The problem came when a reporter asked whether there would truly be human cells in *every* tissue. (Yes.) Does that include human cells in ovaries and testes? (Presumably, yes.) So what happens if two of these mice get together, and a human sperm meets a human egg in the Fallopian tube of a mouse?

“That ended the project,” says Kevin FitzGerald, a bioethicist at Georgetown University. The scenario described by the reporter was almost certainly impossible, but the incident represents some of the ethical questions around transplanting organs between species, or xenotransplantation.

There’s a big organ shortage, and xenotransplantation has long been floated around as a possible solution. Once, attempts at

xenotransplantation meant putting chimpanzee kidneys in humans, which usually wasn't successful. The big problem with transplantation of any kind is that the immune system can reject the donated organ, even if it's human. Now imagine how bad the rejection would be for an animal organ. Additionally, animals contain viruses that are harmful to humans, and a number of dangerous diseases (including HIV, SARS, and MERS) have all jumped from animals to humans, causing concern that xenotransplantation "might save one person's life and cause a plague that kills 10,000 others," as FitzGerald puts it.

But we might be able to get around some of these issues with advances in genome editing. Just a few months ago, scientists debuted the world's first human-pig chimeras, or pig embryos injected with human stem cells. The pigs, which weren't allowed to develop past the fetal stage, started to grow organs with human cells in them. They set the stage for a world where we could grow human organs in other animals. One day, we may even be able to use stem cells to grow our *own* organs in other animals. But all of this comes with ethical questions.

Xenotransplantation has a long history, with some pointing out that the procedure is mentioned in Greek mythology — specifically, when Icarus and Daedalus attached bird wings to their arms to try to fly. (As the author of one history of xenotransplantation put it: though Icarus died, "Daedalus successfully made the journey, providing this pair with an enviable 50 percent success rate.")

In the early 20th century, Nobel Prize-winning surgeon Alexis Carrel developed a method of connecting blood vessels, which made xenotransplantation possible for the first time. It also made horrific experiments possible: by the 1920s, a doctor named Serge Voronoff decided that the best way to revive men's "zest for life" (read: sex drive) was by transplanting monkey testicles into human men. It wasn't a full transplant. Rather, he sliced up the monkey testicle and then inserted slices into the human testicle. Despite the seeming horror of this approach, it became rather popular, and at least several hundred operations were performed. Later, the American "doctor" John Brinkley (he had no degree) did the same thing with goat testicles for the low, low price of what would be $9,000 today. He became rich, famous, and was probably responsible for many deaths.

More medically sound transplants came in the 1960s, with chimpanzee kidneys transplanted into 13 patients, one of whom lived for almost nine months. The decade also brought an attempt at transplanting a monkey heart, but the patient died immediately. More optimistically, one patient survived for 70 days after he received a baboon liver in 1992.

In the 1980s, things began to heat up. Danish scientist Steen Willadsen, a pioneer of cloning, combined portions of both sheep and goat embryos to made chimeras — animals that were half sheep and half goat, colloquially called "geep."

"That was the breakthrough insight that mammals may be a bit more compatible than we thought," says FitzGerald. "If you could put goat and sheep together, what else could you do?" Maybe you could get past the immune rejection problem if you created something that was part animal and part human because the immune system would then develop seeing both sides as itself, he continues. Interest grew even more after Dolly the sheep was successfully cloned in the '90s.

Today, the bellwether for tracking further developments isn't necessarily academic research or federal policy, but rather, business. These developments tend to be driven much more by a practical analysis of just how market-friendly a technology is, and how much investment it can get, says FitzGerald. And each advancement raises questions.

The first question is always, where does the needle stop? Is this an ethical use of animals? If we're putting animal organs into humans, at what point do we start asking if this changes what it means to be a human being? "Do we really want to say human beings are reducible to the brain? Because that's not necessarily a good way to go ethically

either," says FitzGerald, "and that would require a lot of thought and reviews."

Even if growing full organs in animals were successful, questions of money and scale remain. "We can grow pigs in large numbers for food, but the necessary housing and development for organ transplant pigs would be much more expensive than for regular pigs," says FitzGerald. How many organs would be available, and how much would they cost, and who would pay? "Xenotransplantation is fascinating in so many ways scientifically, but it could be that it's not really the solution to the organ shortage problem," he adds.

Ultimately, though, FitzGerald thinks that xenotransplantation doesn't have to be an end in itself. "I don't think people should wrestle with this as sort of 'this is the solution or it isn't' situation," he says. This type of technology could lead the way to other solutions — like growing organs successfully in labs — with fewer ethical complications. "My guess would be that this is just merely another step along the way and merely an intermediate step to try to get where we want to be."

http://wb.md/2sokaHY

Kids With Belly Pain: What Does It Mean When You Can't See the Appendix?

Ultrasound Evaluation in Abdominal Pain

William T. Basco, Jr, MD, MS

In an attempt to limit radiation exposure from CT in the evaluation of abdominal pain, many centers have adopted an "ultrasound first, followed by CT if needed" approach. CT is typically used when the ultrasound findings are equivocal or the appendix is not visualized. Although CT has a high sensitivity and specificity for identification of the appendix, ultrasound does not, owing to such factors as technician experience and skill and even body habitus of the patient.

A recent study[1] sought to evaluate whether children in whom ultrasound fails to visualize the appendix are likely to have appendicitis. This study was conducted at a large pediatric emergency department (ED) in Singapore. Data from 641 children (mean age, 10.8 years; 46.3% boys) who made ED visits in 2013 that resulted in admission for abdominal pain were reviewed.

The ultrasound evaluation failed to visualize the appendix in 160 (24.9%) of the children, 17 of whom subsequently underwent appendectomy. On ultrasound, 14 of these 17 children had secondary findings suggesting intra-abdominal inflammation (including intra-abdominal fluid). The remaining three children had normal ultrasound findings, and appendicitis was confirmed by CT. Therefore, the sensitivity of ultrasound in detecting appendicitis when the appendix could not be visualized, and secondary signs were present, was 82.4%. When the appendix was visualized by ultrasound, the sensitivity and specificity were very high for detecting appendicitis. In 51 children, the appendix was incompletely visualized, but a partial view of a normal appendix was reassuring. Among 34 children with normal, partially viewed appendices and no secondary features, none were diagnosed with appendicitis. The remaining 17 children with partially viewed appendices (13 abnormal and 4 equivocal) all underwent appendectomy for appendicitis.

Looking at the data another way, among the 145 children whose appendices could not be visualized at all, and who had no secondary features of appendicitis, only three (2.1%) had appendicitis. The authors concluded that the risk for appendicitis is very low in children with abdominal pain in whom ultrasound fails to visualize the appendix.

Viewpoint

The study authors acknowledge that the experience of this single pediatric center may not be applicable to all pediatric settings, especially in the United States, which has so many personnel variables to consider. Still, I hope that this study can spark discussion at pediatric EDs about the proper approach to determining whether appendicitis is the source of abdominal pain in a child. I suspect that

busy centers with dedicated pediatric ultrasonographers would be able to produce similar promising outcomes.

It is also important to refrain from overapplying these findings. These data do not support an approach that would discharge children with abdominal pain from the ED because they have a nonvisualized appendix. The approach taken after a negative or nonvisualized appendix in this study was to admit the child for a period of observation, and only 35 children had CT. I assume that in most US hospitals, CT would be more quickly pursued.

References

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http://nyti.ms/2rJDb5C

Scientists Discover a Key to a Longer Life in Male DNA

Researchers recently found that a genetic mutation may add about 10 years to men's life spans

Carl Zimmer

A common genetic mutation is linked to an increase in life span of about 10 years among men, researchers reported on Friday.

The mutation, described in the journal Science Advances, did not seem to have any effect on women. Still, it joins a short list of gene variants shown to influence human longevity.

By studying these genes, scientists may be able to design drugs to mimic their effects and slow aging. But the search for them has been slow and hard.

When it comes to how long we live, nurture holds powerful sway over nature. In 1875, for example, life expectancy in Germany was less than 39 years; today it is over 80.

Germans didn't gain those extra decades because of evolving, life-extending changes in their genes. Instead, they gained access to clean water, modern medicine and other life-protecting measures.

Nevertheless, heredity clearly plays a modest role in how long people live. For example, a number of studies have shown that identical twins, who share the same genes, tend to have more similar life spans than fraternal twins. In a 2001 study of Amish farmers in Pennsylvania, researchers found that close relatives were more likely to live to similar ages than distant ones.

The impact of heredity on life span has turned out to be about as big as its influence on developing high blood pressure. But large-scale surveys of people's DNA have revealed few genes with a clear influence on longevity. "It's been a real disappointment," said Nir Barzilai, a geneticist at Albert Einstein College of Medicine.

Researchers are having better luck following clues from basic biology. In many species, for example, there is a relationship between an animal's size and its life span.

"If you look at dogs, flies, mice, whatever it is, smaller lives longer," said Gil Atzmon, a geneticist at the University of Haifa in Israel who collaborates with Dr. Barzilai.

Results like these have led researchers to look closely at the molecules that cause our bodies to grow. One of the most important is growth hormone, which is produced in the brain and courses through the body. The hormone latches on to cells, binding to a surface molecule called a growth hormone receptor. This signal can trigger cells to grow faster. The cells may also release signaling molecules of their own, known as growth factors.

About a quarter of people have a mutation in the gene for growth hormone receptors — a substantial chunk of DNA is missing.

People with this mutation can make working receptors, but their shape is slightly different. Studies in the mid-2000s suggested that this mutation might make children short.

The link between height and longevity led Dr. Atzmon and his colleagues to wonder if it might also influence how long people lived.

The researchers sequenced the gene for growth hormone receptors in 567 Ashkenazi Jews over 60 and their children, whom Dr. Barzilai had been studying for years.

The mutation, they found, was present in 12 percent of the men over age 100. That rate was about three times higher than in 70-year-old men. In women, however, the mutation was present in roughly the same fraction in both age groups.

Dr. Atzmon and his colleagues followed up by examining the gene in a group of long-lived people in the United States, another in France and a third in the Amish community, raising the total number of subjects to 814.

In all three groups, the researchers observed the same effect. Among men, the mutation in the gene for growth hormone receptors was linked to substantially longer lives. “The results look convincing to me,” said Ali Torkamani, the director of genome informatics at the Scripps Translational Science Institute in La Jolla, Calif.

Dr. Torkamani, who was not involved in the new study, said it was the first to establish a link between growth hormone receptors and longevity.

“I definitely think there’s some fire there,” said P. Eline Slagboom, a geneticist at Leiden University Medical Center in the Netherlands.

But she had some reservations about the results, given that only men showed an effect and that the study was relatively small.

“It’s calling out for larger studies,” she said.

In 2008, Dr. Barzilai and his colleagues discovered that a mutation in another growth-related gene could extend life — this time, only in women. Combined with the new study, this research suggests that men and women take different genetic paths toward living long lives.

But the researchers don’t know what those paths might be. “This whole issue has shocked us,” Dr. Barzilai said.

The new study also shows that the link between life span and height is more complex than the scientists had anticipated.

They had expected that long-lived men with the mutation would be short. However, just the opposite turned out to be true: The mutation seemed to raise men’s height by about an inch.

Dr. Barzilai and his colleagues suspect that the mutation triggers a cascade of changes in the growth-spurring signals in men’s bodies, leaving cells less sensitive to low levels of growth hormone.

When growth hormone levels surge, however, these cells divide faster than those in men without the mutation. Somehow, the receptor amplifies the signal’s growth.

That sensitivity may spur the growth of boys during adolescence, when their bodies are flooded with growth hormone. But as the amount of hormone drops in manhood, their cells may divide more slowly, and they may stop producing growth-spurring molecules of their own.

Numerous studies suggest that extra growth signals can speed up aging. One theory is that there may be a trade-off in the body between growth and repairing molecular damage in cells.

Men with a mutation in their growth hormone receptor may put more resources into repairing their bodies, thus slowing the aging process.

In recent years, some doctors have prescribed growth hormone to patients to restore youth and give them strength. Dr. Barzilai said the new study suggests that keeping growth hormone levels low may actually be a better strategy for living longer. “We’re worried about giving treatments that probably are going to do the opposite,” he said.

Dr. Barzilai and his colleagues now hope to mimic the effect of the newly discovered mutation by reducing growth hormone levels in older people. Already they have produced some promising results in animal studies using a diabetes drug called metformin.

“It’s not far from reality,” Dr. Barzilai said.

http://bit.ly/2so2coK

Oh, Lovely: The Tick That Gives People Meat Allergies Is Spreading

Over the last 15 years many protein-loving Americans have developed a dangerous allergy to meat

First comes the unscratchable itching, and the angry blossoming of hives. Then stomach cramping, and—for the unluckiest few—

difficulty breathing, passing out, and even death. In the last decade and a half, thousands of previously protein-loving Americans have developed a dangerous allergy to meat. And they all have one thing in common: the lone star tick.

Red meat, you might be surprised to know, isn't totally sugar-free. It contains a few protein-linked saccharides, including one called galactose-alpha-1,3-galactose, or alpha-gal, for short. More and more people are learning this the hard way, when they suddenly develop a life-threatening allergy to that pesky sugar molecule after a tick bite.

Yep, one bite from the lone star tick—which gets its name from the Texas-shaped splash of white on its back—is enough to reprogram your immune system to forever reject even the smallest nibble of perfectly crisped bacon. For years, physicians and researchers only reported the allergy in places the lone star tick calls home, namely the southeastern United States. But recently it's started to spread. The newest hot spots? Duluth, Minnesota, Hanover, New Hampshire, and the eastern tip of Long Island, where at least 100 cases have been reported in the last year. Scientists are racing to trace its spread, to understand if the lone star tick is expanding into new territories, or if other species of ticks are now causing the allergy.

The University of Virginia is deep in the heart of lone star tick country. It's also home to a world-class allergy research division, headed up by immunologist Thomas Platts-Mills. He'd been hearing tales of the meat allergy since the '90s—people waking up in the middle of the night after a big meal, sweating and breaking out in hives. But he didn't give it much thought until 2004, when he heard about another group of patients all suffering from the same symptoms.

This time, it wasn't a plate of pork chops they shared; it was a new cancer drug called cetuximab. The drug worked, but curiously, patients that lived in the southeast were 10 times as likely to report side effects of itching, swelling, and a dangerous drop in blood pressure.

Platts-Mills teamed up with cetuximab's distributor, Bristol-Myers Squibb, and began comparing patient blood samples. He discovered that all the patients who experienced an allergic reaction had pre-existing antibodies to alpha-gal, and cetuximab was full of the stuff, thanks to the genetically modified mice from which it was derived. With that mystery solved, Platts-Mills turned to figuring out what made patients so sensitive to alpha-gal.

The best hint he had was the geographic overlap between the cetuximab patients and previously reported meat allergies. The area perfectly matched where people came down with Rocky Mountain spotted fever—a disease carried by the lone star tick. But it wasn't until Platts-Mills and two of his lab members came down with tick-induced meat allergies of their own that they made the connection.

Over the next few years Platts-Mills and his colleague Scott Commins screened more meat allergy patients and discovered that 80 percent reported being bitten by a tick. What's more, they showed that tick bites led to a 20-fold increase in alpha-gal antibodies. Since ethics standards prevented them from attaching ticks to randomized groups of patients, this data was the best they could do to guess how meat allergy arises. Something in the tick's saliva hijacks humans' immune systems, red-flagging alpha-gal, and triggering the massive release of histamines whenever red meat is consumed.

Researchers are still trying to find what that something is. Commins has since moved to the University of North Carolina, where he's injecting mice with lone star tick extracts to try to understand which molecules are setting off the alpha-gal bomb. It's tricky: Tick saliva is packed with tons of bioactive compounds to help the parasite feed without detection. One of them might be an alpha-gal analogue—something similar-but-different-enough in shape that it sets off the human immune system. But it could also be a microbe—like a bacteria or virus—that triggers the response. Some have even suggested that residual proteins from the ticks' earlier blood meals could be the culprit.

Whatever it is, allergy researchers will be paying attention. Because, as far as anyone can tell, alpha-gal syndrome seems to be the only allergy that affects all people, regardless of genetic makeup. “There’s something really special about this tick,” says Jeff Wilson, an asthma, allergy, and immunology fellow in Platts-Mills’ group. Usually a mix of genes and environmental factors combine to create allergies. But when it comes to the lone star tick it doesn’t matter if you’re predisposed or not. “Just a few bites and you can render anyone really, really allergic,” he says.

In the meantime, Platts-Mills, Commins, and Wilson are busy communicating the scale of the public health problem. Every day they check local news headlines to log new cases of catastrophic hamburger aversion, and spend hours on the phone gathering the latest intel from allergy clinics and academic centers around the country. They’re building the first real red meat allergy incidence map of the US—because state health departments aren’t required to report alpha-gal syndrome to the Centers for Disease Control and Prevention. And it’s still rare enough outside the southeastern US that many doctors don’t correctly diagnose it.

Wilson is trying to get blood samples from all the new outbreaks, to figure out if the patients’ antibodies correspond to the saliva of lone star ticks or a different tick species. That will tell him if the increases in the allergy are the result of changing range patterns, or if other ticks have developed the capacity to rewire human immune systems in the same way. That information would also provide further clues to the mechanism itself. As for a cure? There’s not much science has to offer on that front, besides Epipens and veggie burgers.

http://bit.ly/2tE4wHR

Acupuncture relieves pain in emergency patients: Study

World's largest randomized controlled trial of acupuncture in emergency departments finds it is a safe and effective alternative to pain-relieving drugs

The world's largest randomised controlled trial of the use of acupuncture in emergency departments has found the treatment is a safe and effective alternative to pain-relieving drugs for some patients.

Led by RMIT University in Melbourne, Australia, the study found acupuncture was as effective as pain medicine in providing long-term relief for patients who came to emergency in considerable pain.

But the trial, conducted in the emergency departments of four Melbourne hospitals, showed pain management remains a critical issue, with neither treatment providing adequate immediate relief.

Lead investigator Professor Marc Cohen, from RMIT's School of Health and Biomedical Sciences, said pain was the most common reason people came to emergency, but was often inadequately managed.

"While acupuncture is widely used by practitioners in community settings for treating pain, it is rarely used in hospital emergency departments," Cohen said.

"Emergency nurses and doctors need a variety of pain-relieving options when treating patients, given the concerns around opioids such as morphine, which carry the risk of addiction when used long-term.

"Our study has shown acupuncture is a viable alternative, and would be especially beneficial for patients who are unable to take standard pain-relieving drugs because of other medical conditions.

"But it's clear we need more research overall to develop better medical approaches to pain management, as the study also showed patients initially remained in some pain, no matter what treatment they received."

The study, published in the Medical Journal of Australia and funded by a grant from the National Health and Medical Research Council, involved 528 patients with acute low back pain, migraine or ankle sprains who presented at the emergency departments of the Alfred Hospital, Cabrini Malvern, Epworth Hospital and Northern Hospital between January 2010 and December 2011.

Patients who identified their level of pain as at least 4 on a 10-point scale randomly received one of three types of treatment: acupuncture alone, acupuncture plus pharmacotherapy or pharmacotherapy alone.

One hour after treatment, less than 40 per cent of patients across all three groups felt any significant pain reduction (2 or more pain points), while more than 80% continued to have a pain rating of at least 4.

But 48 hours later, the vast majority found their treatment acceptable, with 82.8 per cent of acupuncture-only patients saying they would probably or definitely repeat their treatment, compared with 80.8 per cent in the combined group, and 78.2 per cent in the pharmacotherapy-only group.

"Some Australian emergency departments already offer acupuncture when trained staff are available but further studies are needed on ways to improve pain management overall in emergency departments, and the potential role for acupuncture in this," Cohen said.

"We need to determine the conditions that are most responsive to acupuncture, the feasibility of including the treatment in emergency settings, and the training needed for doctors or allied health personnel."

http://bit.ly/2tEh9lY

Yamagata town drafts in sniffer dogs to improve cancer detection rates

The mayor of a small Japanese town with high rates of stomach cancer among its residents has turned to a sniffer dog research program to improve the accuracy and effectiveness of health checkups.

TOKYO Facing the challenge of improving early cancer detection rates in Kaneyama, a town with 6,000 residents in the northeast of Japan, Mayor Hiroshi Suzuki reached out for professional help.

Knowing his town had among Japan's highest fatality rates due to stomach cancer, Suzuki consulted Masao Miyashita, a medical school professor who visited the town last year, and received a proposal to take part in a research program in which dogs are used to sniff out cancer from test samples.

At no cost to residents, the Yamagata Prefecture town sends frozen urine samples to Miyashita at the Nippon Medical School Chiba Hokusoh Hospital in Chiba Prefecture, east of Tokyo.

The hospital then has the samples tested at a facility in the prefecture where dogs are trained for the purpose.

The substances emitted by cancer cells which allow the dogs to sniff out the disease are unknown, as is how the dogs know what they are detecting. "In our research so far, cancer detection dogs have been able to find (signs of) cancer with an accuracy of nearly 100 percent," said Miyashita.

There are only five dogs trained to work as cancer detection dogs in Japan, according to St. Suger Japan which operates the training facility. It costs about 5 million yen ($45,000) to train each dog.