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UVA discovers powerful defenders of the brain -- with big implications for disease

Rare and potent immune cells found in unexpected place; may be missing link between brain and gut

CHARLOTTESVILLE, Va. - A rare and powerful type of immune cell has been discovered in the meninges around the brain, suggesting the cells may play a critical but previously unappreciated role in battling Alzheimer's, multiple sclerosis, meningitis and other neurological diseases, in addition to supporting our healthy mental functioning. By harnessing the cells' power, doctors may be able to develop new treatments for neurological diseases, traumatic brain injury and spinal cord injuries - even migraines.

Further, University of Virginia School of Medicine researchers suspect the cells may be the missing link connecting the brain and the microbiota in our guts, a relationship already shown important in the development of Parkinson's disease.

Unexpected Presence

The cells, known as "type 2 innate lymphocytes," previously have been found in the gut, lung and skin - the body's barriers to disease. Their discovery in the meninges, the membranes surrounding the brain, comes as a surprise. They were found as UVA researcher Jonathan Kipnis, PhD, explored the implications of his lab's game-changing discovery last year that the brain and the immune system are directly connected via vessels long thought not to exist

"This all comes down to immune system and brain interaction," said Kipnis, chairman of UVA's Department of Neuroscience. "The two were believed to be completely not communicating, but now we're slowly, slowly filling in this puzzle. Not only are these [immune] cells present in the areas near the brain, they are integral to its function. When the brain is injured, when the spinal cord is injured, without them, the recovery is much, much worse."

Curiously, the immune cells were found along the vessels discovered by Kipnis' team. "They're right on the lymphatics, which is really weird," noted researcher Sachin Gadani. "You have the lymphatics and they're stacked right on top. They're not inside of them - they're around them."

Important Immune Role

The immune cells play several important roles within the body, including guarding against pathogens and triggering allergic reactions. In exploring their role in protecting the brain, the Kipnis team has determined they are vital in the body's response to spinal cord injuries. But it's their role in the gut that makes Kipnis suspect they may be serving as a vital communicator between the brain's immune response and our microbiomes. That could be of great importance, because our intestinal flora is critical for maintaining our health and wellbeing.

"These cells are potentially the mediator between the gut and the brain. They are the main responder to microbiota changes in the gut. They may go from the gut to the brain, or they may just produce something that will impact those cells. But you see them in the gut and now you see them also in the brain," Kipnis said. "We know the brain responds to things happening in the gut. Is it logical that these will be the cells that connect the two? Potentially. We don't know that, but it very well could be."

While much more research needs to be done to understand the role of these cells in the meninges, Gadani noted that it's almost certain that the cells are important in a variety of neurological conditions. "It would be inconceivable they're not playing a role in migraines and certain conditions like that," he said. "The long-term goal of this would be developing drugs for targeting these cells. I think it could be highly efficacious in migraine, multiple sclerosis and possibly other conditions."

The findings have been published online by the Journal of Experimental Medicine. The article is by Gadani, of UVA's Medical Scientist Training Program; Igor Smirnov; Ashtyn T. Smith; Christopher C. Overall; and Kipnis, who, in addition to being department chairman, is the director of UVA's Center for Brain Immunology and Glia (BIG).

The work was supported by the National Institutes of Health, grant NS081026.

http://bit.ly/2hye4hC

Irish surgeon identifies emerging area of medical science

A University of Limerick (Ireland) professor has identified an emerging area of science having reclassified part of the digestive system as an organ.

The mesentery, which connects the intestine to the abdomen, had for hundreds of years been considered a fragmented structure made up of multiple separate parts. However, research by Professor of Surgery at UL's Graduate Entry Medical School, J Calvin Coffey, describes the mesentery as one, continuous structure.

In a review published in the November issue of one of the top medical journals, The Lancet Gastroenterology & Hepatology, Professor Coffey outlined the evidence for categorising the mesentery as an organ.

"In the paper, which has been peer reviewed and assessed, we are now saying we have an organ in the body which hasn't been acknowledged as such to date," Professor Coffey stated.

Better understanding and further scientific study of the mesentery could lead to less invasive surgeries, fewer complications, faster patient recovery and lower overall costs.

"When we approach it like every other organ...we can categorise abdominal disease in terms of this organ," professor Coffey said.

According to Professor Coffey, the Foundation Chair of Surgery at UL's Graduate Entry Medical School and University Hospitals Limerick, mesenteric science is its own specific field of medical study in the same way as gastroenterology, neurology and coloproctology.

"This is relevant universally as it affects all of us. Up to now there was no such field as mesenteric science. Now we have established anatomy and the structure. The next step is the function. If you understand the function you can identify abnormal function, and then you have disease. Put them all together and you have the field of mesenteric science...the basis for a whole new area of science," he said.

"During the initial research, we noticed in particular that the mesentery, which connects the gut to the body, was one continuous organ. Up to that it was regarded as fragmented, present here, absent elsewhere and a very complex structure. The anatomic description that had been laid down over 100 years of anatomy was incorrect. This organ is far from fragmented and complex. It is simply one continuous structure," Professor Coffey explained.

Already, medical students around the world are, from this year, learning about the mesentery as a continuous organ, after research by Professor Coffey prompted an update in one of the world's best-known medical textbooks Gray's Anatomy.

http://bit.ly/2hfLC6F

Earliest evidence discovered of plants cooked in ancient pottery

A team of international scientists, led by the University of Bristol, has uncovered the earliest direct evidence of humans processing plants for food found anywhere in the world.

Researchers at the Organic Geochemistry Unit in the University of Bristol's School of Chemistry, working with colleagues at Sapienza, University of Rome and the Universities of Modena and Milan, studied unglazed pottery dating from more than 10,000 years ago, from two sites in the Libyan Sahara.

The invention of cooking has long been recognised as a critical step in human development. Ancient cooking would have initially involved the use of fires or pits and the invention of ceramic cooking vessels led to an expansion of food preparation techniques.

Cooking would have allowed the consumption of previously unpalatable or even toxic foodstuffs and would also have increased the availability of new energy sources. Remarkably, until now, evidence of cooking plants in early prehistoric cooking vessels has been lacking.

The researchers detected lipid residues of foodstuffs preserved within the fabric of unglazed cooking pots. Significantly, over half of the vessels studied were found to have been used for processing plants based on the identification of diagnostic plant oil and wax compounds. Detailed investigations of the molecular and stable isotope compositions showed a broad range of plants were processed, including grains, the leafy parts of terrestrial plants, and most unusually, aquatic plants.

The interpretations of the chemical signatures obtained from the pottery are supported by abundant plant remains preserved in remarkable condition due to the arid desert environment at the sites.

The plant chemical signatures from the pottery show that the processing of plants was practiced for over 4,000 years, indicating the importance of plants to the ancient people of the prehistoric Sahara.

Dr Julie Dunne, a post-doctoral research associate Bristol's School of Chemistry and lead author of the paper, said: "Until now, the importance of plants in prehistoric diets has been under-recognised but this work clearly demonstrates the importance of plants as a reliable dietary resource.

"These findings also emphasise the sophistication of these early hunter-gatherers in their utilisation of a broad range of plant types, and the ability to boil them for long periods of time in newly invented ceramic vessels would have significantly increased the range of plants prehistoric people could eat."

Co-author Professor Richard Evershed, also from Bristol's School of Chemistry, added: "The finding of extensive plant wax and oil residues in early prehistoric pottery provides us with an entirely different picture of the way early pottery was used in the Sahara compared to other regions in the ancient world. "Our new evidence fits beautifully with the theories proposing very different patterns of plant and animal domestication in Africa and Europe/Eurasia."

The research was funded by the UK's Natural Environment Research Council (NERC) and is published today in *Nature Plants*.

http://bit.ly/2hjoUMH

Vitamin E and selenium don't prevent polyps that can lead to colorectal cancer

Vitamin E and selenium will not prevent colorectal adenomas

PORTLAND, OR - Eight years ago, results from a landmark cancer prevention trial run by SWOG showed that a daily dose of vitamin E and selenium did not prevent prostate cancer. In fact, the Selenium and Vitamin E Cancer Prevention Trial (SELECT) showed that vitamin E supplementation increased the risk of prostate cancer in healthy men.

Now, a SWOG review of ancillary SELECT results definitively shows that these two antioxidants also don't prevent colorectal adenomas - polyps that are the premalignant precursors to most colorectal cancers. Results are published in Cancer Prevention Research.

"The message to the public is this: Vitamin E and selenium will not prevent colorectal adenomas, which are surrogates for colorectal cancer," said Dr. Peter Lance, lead author of the journal article and deputy director of the University of Arizona Cancer Center. "We have no evidence that these supplements work to prevent cancer."

Despite the billions spent in the United States each year on vitamin supplements, there is scant evidence they prevent cancer. According to the National Cancer Institute, which funds SWOG through its National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP), results from nine randomized trials did not provide evidence that antioxidant supplements are beneficial in primary cancer prevention. An in-depth review conducted for the United States Preventive Services Task Force likewise found no clear evidence of benefit.

"There's a whole industry that has people dosing themselves thinking that vitamins will keep them healthy," Lance said. "But we have little evidence that they protect against cancer."

To arrive at their conclusions, Lance and his SWOG team used data from SELECT, a prostate cancer prevention trial that enrolled an

astonishing 35,533 healthy men - 21 percent men of color - in just 33 months at 427 study sites the United States, Canada, and Puerto Rico. Men were randomized into four groups. Some took a daily dose of vitamin E, others a dose of selenium, others took both antioxidants, and the rest took a placebo only.

A substantial number of SELECT participants incidentally underwent a lower endoscopy - colonoscopy or sigmoidoscopy - as part of their usual clinical care while taking part in the trial. In an ancillary study, Lance and his team went back into the SELECT data to review the lower endoscopy and pathology reports. They were able to evaluate information on 6,546 participants who received the procedure as part of SELECT, and found that 2,286 had more than one polyp detected by cameras used in the procedures. A statistical analysis showed that the occurrence of one or more premalignant polyps was about the same among men, regardless of whether men were taking selenium or vitamin E, alone or together, or double placebo.

What makes these results definitive, Lance said, is that SELECT was so large and was a randomized controlled study - a design that reduces bias and is considered the gold standard in clinical research.

Lance led another University of Arizona Cancer Center team that has just published similar results from a separate randomized trial of selenium and celecoxib. In December 2016, in the Journal of the National Cancer Institute, the team reported that selenium didn't prevent colorectal adenomas - and was associated with increased risk for Type 2 diabetes.

Lance's SWOG study team includes: Denise Row, Dr.P.H., of the University of Arizona Mel & Enid Zuckerman College of Public Health; Dr. David Alberts, University of Arizona Cancer Center; Patricia Thompson-Carino, Ph.D., of Stony Brook Cancer Center; Liane Fales of University of Arizona Cancer Center; Fang Wang of Stony Brook Cancer Center; Jerilyn San Jose of University of Arizona Cancer Center; Elizabeth Jacobs, Ph.D. of University of Arizona Cancer Center; Phyllis Goodman of the SWOG Statistical Center at Fred Hutchinson Cancer Research Center; Amy Darke of the SWOG Statistical Center at Fred Hutchinson Cancer Research Center; Monica Yee of SWOG Statistical Center at Cancer Research And Biostatistics; Dr. Lori Minasian of the Division of Cancer Prevention at the National Cancer Institute; and Dr. Ian Thompson of the University of Texas Health Sciences Center.

The work was funded by the National Institutes of Health Public Health Service, National Cancer Institute grants RO1 CA124862; U10 CA37429; and UM1 CA182883.

http://bit.ly/2i1YkqW

Pregnancy leads to changes in the mother's brain

Researchers explore for the first time the impact of pregnancy on the structure of the human brain

Pregnancy involves radical hormone surges and biological adaptations, but the effects on the brain are still unknown. In this study a team of researchers compared the structure of the brain of women before and after their first pregnancy. This is the first research to show that pregnancy involves long-lasting changes - at least for two years post-partum - in the morphology of a woman's brain.

Using magnetic resonance imaging, the scientists have been able to show that the brains of women who have undergone a first pregnancy present significant reductions in grey matter in regions associated with social cognition.

The researchers believe that such changes correspond to an adaptive process of functional specialization towards motherhood. "These changes may reflect, at least in part, a mechanism of synaptic pruning, which also takes place in adolescence, where weak synapses are eliminated giving way to more efficient and specialized neural networks", says Elseline Hoekzema, co-lead author of the article.

According to Erika Barba, the other co-lead author, "these changes concern brain areas associated with functions necessary to manage the challenges of motherhood".

In fact, researchers found that the areas with grey matter reductions overlapped with brain regions activated during a functional neuroimaging session in which the mothers of the study watched images of their own babies.

In order to conduct the study, researchers compared magnetic resonance images of 25 first-time mothers before and after their pregnancy, of 19 male partners, and of a control group formed by 20 women who were not and had never been pregnant and 17 male

partners. They gathered information about the participants during five years and four months.

The results of the research directed by Òscar Vilarroya and Susanna Carmona demonstrated a symmetrical reduction in the volume of grey matter in the medial frontal and posterior cortex line, as well as in specific sections of, mainly, prefrontal and temporal cortex in pregnant women. "These areas correspond to a great extent with a network associated with processes involved in social cognition and self-focused processing", indicates Susanna Carmona.

The analyses of the study determine with great reliability whether any woman from the study had been pregnant depending on the changes in the brain structure. They were even able to predict the mother's attachment to her baby in the postpartum period based on these brain changes.

The study took into account variations in both women who had undergone fertility treatments and women who had become pregnant naturally, and the reductions in grey matter were practically identical in both groups.

Researchers did not observe any changes in memory or other cognitive functions during the pregnancies and therefore believe that the loss of grey matter does not imply any cognitive deficits, but rather: "The findings point to an adaptive process related to the benefits of better detecting the needs of the child, such as identifying the newborn's emotional state. Moreover, they provide primary clues regarding the neural basis of motherhood, perinatal mental health and brain plasticity in general", says Oscar Vilarroya.

Elseline Hoekzema (researcher at the UAB at the time of the study, but currently working at Leiden University) and Erika Barba-Müller (UAB) are the lead authors of the article published in Nature Neuroscience.

The study was directed by Òscar Vilarroya, from the Cognitive Neuroscience Research Unit of the Department of Psychiatry and Legal Medicine at the UAB, and coordinator of the research group Neuroimaging of Mental Disorders at the IMIM Foundation, and co-directed by Susana Carmona [researcher at the UAB at the time of the study and now at the University Carlos III, Madrid, and affiliated to the CIBER of Mental Health (CIBERSAM)].

Also collaborating in the research were Cristina Pozzobon, Florencio Lucco and Agustín Ballesteros (Valencian Infertility Institute, IVI); Marisol Picado (Hospital Clínic); Eveline A. Crone (Leiden University); David García-García and Manuel Desco (University Carlos III and Instituto de Investigación Sanitaria Gregorio Marañón, Madrid); and Juan Carlos Soliva and Adolf Tobeña (UAB).

http://bit.ly/2i9lSrc

Male or female physician: Does it matter in death, hospital readmission rates?

Do hospitalized Medicare beneficiaries treated by female internists have lower rates of 30-day mortality and hospital readmission than those patients treated by men?

A new study published online by JAMA Internal Medicine suggests that they do.

Previous research suggests men and women may practice medicine differently, with female physicians more likely to adhere to clinical guidelines and provide preventive care more often, among other things. However, some have suggested that factors such as career interruptions for childbearing and high-rates of part-time employment, may justify higher salaries for male physicians, despite research suggesting female physicians may provide better care.

Empirical evidence is needed so Yusuke Tsugawa, M.D., M.P.H., PhD., of the Harvard T. H. Chan School of Public Health, Boston, and coauthors examined 30-day mortality and readmission rates for hospitalized Medicare beneficiaries treated by male or female physicians.

The study analyzed more than 1.5 million patient hospitalizations for 30-day mortality rates and more than 1.5 million for hospital readmission rates from 2011 through 2014. During the study period, 58,344 internists treated at least one hospitalized Medicare beneficiary and, among those physicians, 18,751 were women (32.1 percent). Female physicians tended to be younger, were more likely to have had osteopathic training and treated fewer patients compared with their male counterparts.

Patients treated by female physicians had lower 30-day mortality rates (11.07 percent vs. 11.49 percent) and lower 30-day hospital readmission rates (15.02 percent vs. 15.57percent), according to the report. The study cannot identify why female physicians appear to have better patient outcomes than male physicians.

"These findings suggest that the differences in practice patterns between male and female physicians, as suggested in previous studies, may have important clinical implications for patient outcomes. Understanding exactly why these differences in care quality and practice patterns exist may provide valuable insights into improving quality of care for all patients, irrespective of who provides their care," the article concludes.

JAMA Intern Med. Published online 12/ 19, 2016. doi:10.1001/jamainternmed.2016.7875;

http://bit.ly/2i1Xw5u

UTMB researchers develop first chikungunya vaccine from virus that does not affect people

Newly developed vaccine quickly produces a strong immune defense and completely protects mice and nonhuman primates from disease

GALVESTON, Texas - Researchers from The University of Texas Medical Branch at Galveston have developed the first vaccine for chikungunya fever made from an insect-specific virus that doesn't have any effect on people, making the vaccine safe and effective. The newly developed vaccine quickly produces a strong immune defense and completely protects mice and nonhuman primates from disease when exposed to the chikungunya virus. The findings are detailed in Nature Medicine.

"This vaccine offers efficient, safe and affordable protection against chikungunya and builds the foundation for using viruses that only infect insects to develop vaccines against other insect-borne diseases," said UTMB professor Scott Weaver, senior author of this paper.

Chikungunya is a mosquito-borne virus that causes a disease characterized by fever and severe joint pain, often in hands and feet, and may include headache, muscle pain, joint swelling, or rash. Some patients will feel better within a week but many develop longer-term joint pain that can last up to years. Death is rare but can occur.

Traditionally, vaccine development involves tradeoffs between how quickly the vaccine works and safety. Live-attenuated vaccines that are made from weakened versions of a live pathogen typically offer rapid and durable immunity but reduced safety. On the other hand, the inability of inactivated vaccines to replicate enhances safety at the expense of effectiveness, often requiring several doses and boosters to work properly.

There may be a risk of disease with both of these vaccine types, either from incomplete inactivation of the virus or from incomplete or unstable weakening of the live virus that is only recognized when rare vulnerable individuals develop disease.

To overcome these tradeoffs, the researchers used the Eilat virus as a vaccine platform since it only infects insects and has no impact on people. The UTMB researchers used an Eilat virus clone to design a hybrid virus-based vaccine containing chikungunya structural proteins. The Eilat/Chikungunya vaccine was found to be structurally identical to natural chikungunya virus. The difference is that although the hybrid virus replicates very well in mosquito cells, it cannot replicate in mammals.

Within four days of a single dose, the Eilat/Chikungunya candidate vaccine induced neutralizing antibodies that lasted for more than 290 days. The antibodies provided complete protection against chikungunya in two different mouse models. In nonhuman primates, Eilat/Chikungunya elicited rapid and robust immunity - there was neither evidence of the virus in the blood nor signs of illness such as fever after chikungunya virus infection.

Other authors include UTMB's Jesse Erasmus, Albert Auguste, Huanle Luo, Shannan Rossi, Karla Fenton, Grace Leal and Tian Wang; Jason Kaelber and Wah Chiu from Baylor College of Medicine; Dal Kim and Ilya Frolov from the University of Alabama at Birmingham and Farooq Nasar from the United States Army Medical Research Institute of Infectious Diseases.

http://bit.ly/2hfWhhv

Ancient Chinese malaria remedy fights TB

A centuries-old herbal medicine, discovered by Chinese scientists and used to effectively treat malaria, has been found to potentially aid in the treatment of tuberculosis and may slow the evolution of drug resistance.

EAST LANSING, Mich. - In a promising study led by Robert Abramovitch, a Michigan State University microbiologist and TB expert, the ancient remedy artemisinin stopped the ability of TB-causing bacteria, known as Mycobacterium tuberculosis, to become dormant. This stage of the disease often makes the use of antibiotics ineffective.

The study is published in the journal Nature Chemical Biology.

"When TB bacteria are dormant, they become highly tolerant to antibiotics," Abramovitch said, an assistant professor in the College of Veterinary Medicine. "Blocking dormancy makes the TB bacteria more sensitive to these drugs and could shorten treatment times."

One-third of the world's population is infected with TB and the disease killed 1.8 million people in 2015, according to the Centers for Disease Control and Prevention.

Mycobacterium tuberculosis, or Mtb, needs oxygen to thrive in the body. The immune system starves this bacterium of oxygen to control the infection. Abramovitch and his team found that artemisinin attacks a molecule called heme, which is found in the Mtb oxygen sensor. By disrupting this sensor and essentially turning it off, the artemisinin stopped the disease's ability to sense how much oxygen it was getting.

"When the Mtb is starved of oxygen, it goes into a dormant state, which protects it from the stress of low-oxygen environments," Abramovitch said. "If Mtb can't sense low oxygen, then it can't become dormant and will die."

Abramovitch indicated that dormant TB can remain inactive for decades in the body. But if the immune system weakens at some point, it can wake back up and spread. Whether it wakes up or stays 'asleep' though, he said TB can take up to six months to treat and is one of the main reasons the disease is so difficult to control.

"Patients often don't stick to the treatment regimen because of the length of time it takes to cure the disease," he said. "Incomplete therapy plays an important role in the evolution and spread of multi-drug resistant TB strains."

He said the research could be key to shortening the course of therapy because it can clear out the dormant, hard-to-kill bacteria. This could lead to improving patient outcomes and slowing the evolution of drug-resistant TB.

After screening 540,000 different compounds, Abramovitch also found five other possible chemical inhibitors that target the Mtb oxygen sensor in various ways and could be effective in treatment as well.

"Two billion people worldwide are infected with Mtb," Abramovitch said. "TB is a global problem that requires new tools to slow its spread and overcome drug resistance. This new method of targeting dormant bacteria is exciting because it shows us a new way to kill it."

The National Institutes of Health, MSU AgBioResearch and the Bill and Melinda Gates Foundation funded the research. Other MSU researchers involved in the study include Huiqing Zheng, Christopher Colvin and Benjamin Johnson in the Department of Microbiology and Molecular Genetics, as well as collaborators from Sweet Briar College and the University of Michigan.

http://bit.ly/2icSbp9

Commercial brand of mouthwash can help kill off gonorrhea in the mouth

Daily use might be cheap and easy way of curbing spread of infection, say researchers

A commercial brand of mouthwash that is readily available from supermarkets and pharmacies can help curb the growth of the bacteria responsible for gonorrhoea, reveals preliminary research published online in the journal Sexually Transmitted Infections. Daily rinsing and gargling with the product might be a cheap and easy way of helping to control the spread of the infection, suggest the researchers.

New cases of gonorrhoea among men are on the rise in many countries amid declining condom use, with the bulk of cases among gay/bisexual men, say the researchers.

Rising rates of gonorrhoea heighten the risk of the emergence of antibiotic resistant strains of Neisseria gonorrhoeae, the bacteria responsible for the infection, making the need for a preventive measure that doesn't rely on condoms even more urgent, they say.

As far back as 1879, and before the advent of antibiotics, the manufacturer of Listerine, a commercial brand of mouthwash, claimed that it could be used to cure gonorrhoea. But no published research has tested out this claim.

In a bid to rectify this, the researchers assessed whether Listerine could curb the growth of N. gonorrhoeae in laboratory tests and in sexually active gay/bisexual men in a clinical trial.

For the laboratory tests, different dilutions (up to 1:32) of Listerine Cool Mint and Total Care, both of which contain 21.6% alcohol, were applied to cultures of N. gonorrhoeae to see which of any of them might curb growth of the bacteria. By way of a comparison, a salt water (saline) solution was similarly applied to an identical set of cultures.

Listerine at dilutions of up to 1 in 4, applied for 1 minute, significantly reduced the number of N. gonorrhoeae on the culture plates, whereas the saline solution did not.

The clinical trial involved 196 gay/bisexual men who had previously tested positive for gonorrhoea in their mouths/throat, and who were returning for treatment at one sexual health clinic in Melbourne, Australia, between May 2015 and February 2016. Almost a third (30%; 58) tested positive for the bacteria in their throat on the return visit.

Thirty three of these men were randomly assigned to a rinse and gargle with Listerine and 25 of them to a rinse and gargle with the saline solution. After rinsing and gargling for 1 minute, the proportion of viable gonorrhoea in the throat was 52% among the men using Listerine compared with 84% among those using saline.

And the men using Listerine were 80% less likely to test positive for gonorrhoea in their throat five minutes after gargling than were the men using the saline solution.

The researchers admit that the monitoring period was short, so the possibility that the effects of the mouthwash might be short-lived can't be ruled out. But the laboratory test results would suggest otherwise, they say.

This research is preliminary, so a larger trial is currently under way to confirm these results and see whether the use of mouthwash could curb the spread of gonorrhoea, they say.

"If daily use of mouthwash was shown to reduce the duration of untreated infection and/or reduce the probability of acquisition of N. gonorrhoeae, then this readily available, condom-less, and low cost intervention may have very significant public health implications in the control of gonorrhoea in [men who have sex with men]," write the researchers.

Antiseptic mouthwash against pharyngeal Neisseria gonorrhoeae: a randomised controlled trial and an in vitro study http://sti.bmj.com/lookup/doi/10.1136/sextrans-2016-052753

http://bit.ly/2hbSkXS

Spicy molecule inhibits growth of breast cancer cells

Capsaicin, an active ingredient of pungent substances such as chilli or pepper, inhibits the growth of breast cancer cells.

This was reported by a team headed by the Bochum-based scent researcher Prof Dr Dr Dr habil Hanns Hatt and Dr Lea Weber, following experiments in cultivated tumour cells. In the journal "Breast Cancer - Targets and Therapy", the researchers from Ruhr-Universität Bochum presented their findings together with colleagues from the Augusta clinics in Bochum, the hospital Herz-Jesu-Krankenhaus Dernbach and the Centre of Genomics in Cologne.

The experiments were carried out with the SUM149PT cell culture, a model system for a particularly aggressive type of breast cancer, i.e.

the triple-negative type. Chemotherapy is currently the only available treatment for this type of cancer.

Frequently occurring receptor

In the cultivated cells, the team detected a number of typical olfactory receptors. One receptor occurred very frequently; it is usually found in the fifth cranial nerve, i.e. the trigeminal nerve. It belongs to the so-called Transient Receptor Potential Channels and is named TRPV1. That receptor is activated by the spicy molecule capsaicin as well as by helional - a scent of fresh sea breeze.

In collaboration with Dr Gabriele Bonatz from the Augusta clinics in Bochum (Brustzentrum), Hatt's team confirmed the existence of TRPV1 in tumour cells in nine different samples from patients suffering from breast cancer.

Cancer cells die

The researchers activated the TRPV1 receptor in the cell culture with capsaicin or helional, by adding the substances to the culture for a period of several hours or days. As a result, the cancer cells divided more slowly. Moreover, the treatment caused tumour cells to die in larger numbers. The surviving cells were no longer able to move as quickly as heretofore; this implies that their ability to form metastases in the body was impeded.

"If we could switch on the TRPV1 receptor with specific drugs, this might constitute a new treatment approach for this type of cancer," says Hanns Hatt. An intake via food or inhalation is insufficient for this purpose.

Effective in mice

Earlier studies had demonstrated that the chemical arvanil - with a chemical make-up similar to that of the spicy molecule capsaicin - was effective against brain tumours in mice; it reduces tumour growth in the animals. Due to its side effects, however, this substance is not approved for humans. In addition to capsaicin and helional, the endovanilloids, produced naturally in the body, also activate the TRPV1 receptor.

http://bit.ly/2hbFoBq

Traffic fatalities decline in states with medical marijuana laws

Most affected are those between the ages of 25 and 44

States that enacted medical marijuana laws, on average, experienced reductions in traffic fatalities, according to a study by researchers at Columbia University's Mailman School of Public Health. Overall, states that passed medical marijuana laws saw an 11 percent reduction in traffic fatalities, on average, after enacting the laws, and had 26 percent lower rates of traffic fatalities compared with states without the laws. The findings are published online in the American Journal of Public Health.

Reductions in traffic fatalities greatly impacted those between the ages of 15 and 44 and were especially striking among those aged 25 to 44 years, a group representing a high percentage of those registered patients for medical marijuana use.

Specifically, the researchers observed an 11 percent reduction of among those aged 15 to 24 years, 12 percent for ages 25 to 44, and 9 percent for those 45 years and older. Operational dispensaries were also associated with a significant reduction in traffic fatalities in those aged 25 to 44 years at 5 percent.

Lacking was strong evidence suggesting reductions among those aged 45 years and older, which is also a group overrepresented in the population of patients registered in state medical marijuana programs.

"This finding suggests that the mechanisms by which medical marijuana laws reduce traffic fatalities mostly operate in those younger adults, a group also frequently involved in alcohol-related traffic fatalities," said Julian Santaella-Tenorio, a doctoral student in Epidemiology at the Mailman School of Public Health. In 2004 and 2013, 47 percent of fatally injured drivers with a blood alcohol content of 0.08 or greater were 25 to 44 years old.

The researchers based their findings on data for 1985-2014 from the Fatality Analysis Reporting System, a nationwide census of traffic

fatalities information maintained by the National Highway Traffic Safety Administration. The association between medical marijuana laws and traffic fatalities for drivers, passengers, cyclists, and pedestrians was examined for each state enacting the laws. They also evaluated the link between marijuana dispensaries and traffic fatalities. Overall, a total of 1.22 million deaths were attributed to traffic crashes occurring in the 50 states during the study period.

Not all states with medical marijuana laws experienced reductions in traffic fatality rates, and a few states actually experienced increases. In California, after an initial immediate reduction of 16 percent in traffic fatalities and in New Mexico, after an immediate post-law reduction of 17.5 percent, the laws were actually associated with gradual increases in fatality rates. "These findings provide evidence of the heterogeneity of medical marijuana laws and indicate the need for further research on the particularities of implementing the laws at the local level. It also indicates an interaction of medical marijuana laws with other aspects, such as stronger police enforcement, that may influence traffic fatality rates," noted Santaella-Tenorio.

"It is also possible that states with medical marijuana laws and lower traffic fatality rates may be related to lower levels of alcohol-impaired driving behavior in these states," noted Silvia Martins, MD, PhD, associate professor at the Mailman School and senior author. "We found evidence that states with the marijuana laws in place compared with those which did not, reported, on average, lower rates of drivers endorsing driving after having too many drinks. We can also point to other characteristics such as the strength of public health laws related to driving, infrastructure characteristics, or the quality of health care systems, as a partial explanation for these findings."

"The evidence linking medical marijuana laws and traffic fatalities lays the groundwork for future studies on specific mechanisms," said Santaella-Tenorio. "We also expect another area of study will be the association between the laws and nonfatal traffic injuries."

Co-authors are Christine M. Mauro, Melanie M. Wall, June H. Kim, Katherine M. Keyes, and Deborah S. Hasin--all of the Mailman School of Public Health; Magdalena Cerdá, University of California, Davis; and Sandro Galea, Boston University.

This work was supported by the National Institute on Drug Abuse (grants R01DA037866, R01DA034244, T32 DA031099, K01 DA030449), the New York State Psychiatric Institute; and the National Institute on Alcohol Abuse and Alcoholism (grant K01 AA021511). Dr. Santaella-Tenorio is funded by the J. William Fulbright and the Colciencias doctoral scholarships.

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Arctic Inuit, Native American cold adaptations may originate from extinct hominids

Convincing evidence that the Inuit variant of a genetic region first came into modern humans from an archaic hominid population

In the Arctic, the Inuits have adapted to severe cold and a predominantly seafood diet.

After the first population genomic analysis of the Greenland Inuits (Fumagalli, Moltke et al. 2015, Science doi:10.1126/science.aab2319), a region in the genome containing two genes has now been scrutinized by scientists: TBX15 and WARS2.

This region is thought to be central to cold adaptation by generating heat from a specific type of body fat, and was earlier found to be a candidate for adaptation in the Inuits.

Now, a team of scientists led by Fernando Racimo, Rasmus Nielsen et al. have followed up on the first natural selection study in Inuits to trace back the origins of these adaptations.

To perform the study, they used the genomic data from nearly 200 Greenlandic Inuits and compared this to the 1000 Genomes Project and ancient hominid DNA from Neanderthals and Denisovans.

The results, published in the advanced online edition of Molecular Biology and Evolution, provide convincing evidence that the Inuit variant of the TBX15/WARS2 region first came into modern humans from an archaic hominid population, likely related to the Denisovans.

"The Inuit DNA sequence in this region matches very well with the Denisovan genome, and it is highly differentiated from other present-day human sequences, though we can't discard the possibility that the

variant was introduced from another archaic group whose genomes we haven't sampled yet." - said Fernando Racimo, lead author of the study.

The authors found that the variant is present at low-to-intermediate frequencies throughout Eurasia, and at especially high frequencies in the Inuits and Native American populations, but almost absent in Africa.

TBX15 is a gene known to affect the human body's response to cold, and is associated with a number of traits related to body fat distribution.

The authors speculate that the archaic variant may have been beneficial to modern humans during their expansion throughout Siberia and across Beringia, into the Americas.

The research team also worked to understand the physiological role of the region, which may be of interest to scientists concerned with factors that help determine BMI index and fat metabolism.

They found an association between the archaic region and the gene expression of TBX15 and WARS2 in various tissues, like fibroblasts and adipose tissue. They also observed that the methylation patterns in this region in the Denisovan genome are very different from those of Neanderthals and present-day humans.

"All this suggests that the introduced variant may have altered the regulation of these genes, thought the exact mechanism by which this occurred remains elusive." - said Racimo, who was a graduate student in UC Berkeley at the time of the study, and now works at the New York Genome Center.

The evidence adds to the remarkable number of recent examples of ancient interbreeding that may have conferred unique adaptive traits to modern humans, either from Neanderthals or Denisovans.

And it is the second major example ---the other being the EPAS1 genomic locus (found in the high altitude adaptation of Tibetans) to be passed on from archaic humans into the modern human gene pool.

http://bit.ly/2i4MnRq

Routine screening for genital herpes infection not recommended

U.S. Preventive Services Task Force (USPSTF) recommends against routine serologic screening (via a blood test) for genital herpes simplex virus infection

The U.S. Preventive Services Task Force (USPSTF) recommends against routine serologic screening (via a blood test) for genital herpes simplex virus infection in asymptomatic adolescents and adults, including those who are pregnant. The report appears in the December 20 issue of JAMA.

This is a D recommendation, indicating that there is moderate or high certainty that the screening has no net benefit or that the harms outweigh the benefits.

Genital herpes is a prevalent sexually transmitted infection in the United States; the Centers for Disease Control and Prevention estimates that almost 1 in 6 persons ages 14 to 49 years have genital herpes. Genital herpes infection is caused by 2 subtypes of herpes simplex virus (HSV), HSV-1 and HSV-2. Unlike other infections for which screening is recommended, HSV infection may not have a long asymptomatic period during which screening, early identification, and treatment may alter its course. Antiviral medications may provide symptomatic relief from outbreaks; however, these medications do not cure HSV infection. Although transmission of HSV can occur between an infected pregnant woman and her infant during vaginal delivery, interventions can help reduce transmission.

To update its 2005 recommendation on screening for genital herpes, the USPSTF reviewed the evidence on the accuracy, benefits, and harms of serologic screening for HSV-2 infection in asymptomatic persons, including those who are pregnant, as well as the effectiveness and harms of preventive medications and behavioral counseling interventions to reduce future symptomatic episodes and transmission to others.

The USPSTF is an independent, volunteer panel of experts that makes recommendations about the effectiveness of specific preventive care services such as screenings, counseling services, and preventive medications.

Detection

In the past, most cases of genital herpes in the United States have been caused by infection with HSV-2. Adequate evidence suggests that the most widely used, currently available serologic screening test for HSV-2 approved by the U.S. Food and Drug Administration is not suitable for population-based screening, based on its low specificity, the lack of widely available confirmatory testing, and its high false-positive rate. Rates of genital herpes due to HSV-1 infection in the United States may be increasing. While HSV-1 infection can be identified by serologic tests, the tests cannot determine if the site of infection is oral or genital; thus, these serologic tests are not useful for screening for asymptomatic genital herpes resulting from HSV-1 infection.

Benefits of Early Detection and Intervention

Based on limited evidence from a small number of trials on the potential benefit of screening and interventions in asymptomatic populations and an understanding of the natural history and epidemiology of genital HSV infection, the USPSTF concluded that the evidence is adequate to bound the potential benefits of screening in asymptomatic adolescents and adults, including those who are pregnant, as no greater than small.

Harms of Early Detection and Intervention

Based on evidence on potential harms from a small number of trials, the high false-positive rate of the screening tests, and the potential anxiety and disruption of personal relationships related to diagnosis, the USPSTF found that the evidence is adequate to bound the potential harms of screening in asymptomatic adolescents and adults, including those who are pregnant, as at least moderate.

Summary

Based on the natural history of HSV infection, its epidemiology, and the available evidence on the accuracy of serologic screening tests, the USPSTF concluded that the harms outweigh the benefits of serologic screening for genital HSV infection in asymptomatic adolescents and adults, including those who are pregnant.

(doi:10.1001/jama.2016.16776; the full report is available pre-embargo to the media at the For the Media website)

http://bit.ly/2hc1G6h

UTHealth research could lead to blood test to detect Creutzfeldt-Jakob disease

Could lead to a noninvasive diagnosis prior to symptoms

HOUSTON - The detection of prions in the blood of patients with variant Creutzfeldt-Jakob disease could lead to a noninvasive diagnosis prior to symptoms and a way to identify prion contamination of the donated blood supply, according to researchers at McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth).

The results of the research, led by senior author Claudio Soto, M.D., professor in the Department of Neurology and the director of the George and Cynthia Mitchell Center for Alzheimer's disease and Related Brain Disorders at UTHealth, were published today in Science Translational Medicine, a journal of the American Association for the Advancement of Science. First author of the paper is Luis Concha-Marambio, senior research assistant in the Department of Neurology at McGovern Medical School.

" Our findings, which need to be confirmed in further studies, suggest that our method of detection could be useful for the noninvasive diagnosis of this disease in pre-symptomatic individuals," Soto said. "Early diagnosis would allow any potential therapy to be given before substantial brain damage has occurred. In the case of the blood supply, availability of a procedure to efficiently detect small quantities of the infectious agent would allow removal of blood units contaminated with prions, so that new cases can be minimized substantially."

Human prion diseases are infectious and invariably fatal neurodegenerative diseases. They include sporadic Creutzfeldt-Jakob disease (sCJD), the most common form, and variant Creutzfeldt-Jakob disease (vCJD), which is caused by the transmission of bovine spongiform encephalopathy - commonly known as mad cow disease - from infected cattle to humans.

Since 1990, 178 people in the United Kingdom have died from vCJD, according to the National CJD Research & Surveillance Unit at the University of Edinburgh. The disease has claimed an additional 49 people worldwide, including four United States residents, according to the European Centre for Disease Prevention and Control. In a handful of cases, the disease was spread through the donated blood supply.

The disease can lay silent in the body for decades as damage slowly builds in the brain from the misfolded infectious proteins called prions. On average, people infected with vCJD die two years after the development of the first symptoms, which can include psychiatric alterations such as depression, anxiety and hallucinations that progress to more severe dementia, muscle contractions and loss of coordination.

Soto's team analyzed blood samples from 14 cases of vCJD and 153 controls, which included patients affected by sCJD and other neurodegenerative or neurological disorders as well as healthy subjects. To detect the prions, the team used a protein misfolding cyclic amplification assay, invented in Soto's lab, which mimics the prion replication process in vitro that occurs in prion disease.

The results showed that prions could be detected with 100 percent sensitivity and specificity in blood samples from vCJD patients.

The new study builds on years of research by Soto's team, whose detection of prions in urine was published in the New England Journal of Medicine in August 2014. In June of this year, Soto received $11 million from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, to study the pathogenesis, transmission and detection of prion diseases including chronic wasting disease in deer.

Soto is also on the faculty and Concha-Marambio is a student at The University of Texas Graduate School of Biomedical Sciences at Houston.

Co-authors are Sandra Pritzkow, Ph.D., from McGovern Medical School; Paul Schulz, M.D., professor of neurology from McGovern Medical School and Memorial Hermann Mischer Neuroscience Institute at the Texas Medical Center; Fabio Moda, Ph.D., and Fabrizio Tagliavini, M.D., from Istituto Neurologico Carlo Besta in Milan; and James W. Ironside, FMedSci, FRSE, professor of clinical neuropathology at the National CJD Research and Surveillance Unit at the University of Edinburgh.

The research was supported by grants from the National Institutes of Health (P01AI106705, R42NS079060, R01NS049173).

http://bit.ly/2iqKV8n

Rejuvenating the brain's disposal system

Microglia are the scavenger cells of the brain's immune system that keep the brain tidy and free of any damaging material

Heidelberg - A characteristic feature of Alzheimer's disease is the presence of so called amyloid plaques in the patient's brain - aggregates of misfolded proteins that clump together and damage nerve cells. Although the body has mechanisms to dispose these aggregates, it apparently cannot keep up with the load in the diseased brain. Researchers from the German Center for Neurodegenerative Diseases (DZNE), Munich and the Ludwig Maximilians University (LMU) Munich have now discovered a strategy to help the brain remove amyloid plaques. More precisely: they uncovered a factor that can activate microglial cells to engulf newly forming clumps in the brain. Microglia are the scavenger cells of the brain's immune system that function in keeping the brain tidy and free of any damaging material. The work is published today in The EMBO Journal.

Previous research addressing the function of microglia in Alzheimer's disease was hampered by methodological constraints. Researchers often used microglial cells cultured in a dish, but only microglia from newborn mice survive outside the body. However, young microglia are not ideal to investigate an age-related illness, especially since it was known that microglia change in the course of the disease. All in all, the role of microglia in clearing the brain of amyloid plaques was still under debate.

The research team from Munich, headed by Christian Haass and Sabina Tahirovic, devised a new tissue culture system to address these issues. The scientists took aged brain tissue from mouse model of Alzheimer's disease and co-cultured it with tissue from younger brains. They observed that, within a few days of culturing, amyloid plaques were starting to clear away.

A detailed analysis of this process revealed that microglia from the aging tissue were engulfing the plaques on site, but they received some long-distance assistance from the younger tissue in the dish. In fact, young microglia were secreting factors that helped old microglia rejuvenate, resume cell division and take up their work: clear the brain from plaques. One of the factors that reactivated aged microglia is called "granulocyte-macrophage colony stimulating factor", or GM-CSF for short. The researchers found that GM-CSF alone could do the job.

GM-CSF has previously been reported to reduce plaques and improve cognition in a mouse model of Alzheimer's disease. However, it is not yet known if GM-CSF could potentially work as a new drug for Alzheimer's disease in humans. Caution is advised, because activating microglia may also have its downsides. Microglia secrete small proteins that induce inflammatory reactions and may harm neurons. The new model system of Tahirovic, Haass and their colleagues, however, can be explored further to search for additional factors that enhance the clearance of amyloid plaques.

The EMBO Journal (2016) e201694591 Young microglia restore amyloid plaque clearance of aged microglia Daria A, Colombo A, Llovera G, Hampel H, Willem M, Liesz A, Haass C, Tahirovic S

Read the paper: emboj.embopress.org/content/early/2016/12/20/embj.201694591

http://bit.ly/2iddLtm

Speeding up comprehension with grasping actions

Researchers at the CITEC Cluster of Excellence discover a catalyzer for cognition

Privatdozent Dr. Dirk Koester and his colleagues reported the findings of their discovery in the research journal "PLOS One." According to the researchers, the method could offer an approach for new therapies, such as treating stroke patients.

"Latest theories in cognitive science research hypothesize that our memory also records physical sensations as part of the words stored," says Dirk Koester, who works in the CITEC research group "Neurocognition, Action and Biomechanics" led by Prof. Dr. Thomas Schack. "Similar to an entry in a reference book, the brain records a word like 'whisk', associating it with concepts such as 'inanimate' and 'kitchen device.' In addition to this, the brain connects the word to one's own experience - how a whisk feels, for instance, and that a spinning motion is related to it." In their new study conducted with 28 participants, Koester and his colleagues lend support for the thesis of the embodiment of knowledge.

Koester explains the central finding of their study: "When the study participants had to grasp an object while reading, their brain processed parts of the meaning of the words earlier than in previous studies in which words were evaluated without something being gripped."

The participants sat in front of a computer screen, where three cubes were lying next to each other on the tabletop: one about the size of an apple, one the size of a table tennis ball, and one the size of a dice. On the screen behind the cubes, three white fields were displayed. Words then appeared in one of the fields on the screen - sometimes made-up words, sometimes real ones. When a pseudo-word such as "whask" was displayed, the participants did not have to do anything. But if a real noun like "orange" appeared, they were supposed to grip the cube corresponding to that respective field. An EEG electrode cap recorded brain activity, allowing the researchers to then evaluate how the word was processed.

As demonstrated in previous studies, it takes the brain a third of a second to process a word. "In our study, however, we were able to show that comprehension can already begin much earlier, after just a tenth of a second - if a grasping action is required," explains Koester. This study not only provides evidence that the brain has a common

control center for language and movement, but "it also shows that our brain's processing steps shift very quickly and adjust to current tasks - in this case, the task of grasping something while reading."

Koester believes that the findings from this study could also be used in the future for various therapies, such as treatments for aphasia, a language disorder that can occur after a stroke in which one's ability to comprehend or formulate words is impaired or lost. "Similar as in our experiment, patients could practice words they cannot access by indicating not only verbally but also with grip movements to show they recognize a word. In short, motor training," explains Koester. "As such, one's knowledge of words would be strengthened through the 'back door' of motor control."

Dirk Koester, Thomas Schack: Early neurophysiological interaction of conceptual and motor representations. PLOS ONE, http://dx.doi.org/10.1371/journal.pone.0165882, published on 14 Dezember 2016.

http://wb.md/2hkEZ2O

'Incredibly Exciting': Diabetes Drug With CV Benefits

Empagliflozin reduces cardiovascular death in patients with type 2 diabetes and known cardiovascular disease

Anne L. Peters, MD |December 21, 2016

Hello. I'm Dr Anne Peters. Approximately 1 year ago I brought you news of the EMPA-REG trial. I was quite excited about the value of empagliflozin for reducing cardiovascular risk in patients with type 2 diabetes. Now, the US Food and Drug Administration finally agrees and has added a new indication for empagliflozin—to reduce cardiovascular death in patients with type 2 diabetes and known cardiovascular disease.

I believe this is the first cardiovascular indication for a diabetes drug. As I have said previously, I am quite excited that our diabetes drugs are having benefits for cardiovascular disease risk reduction.

This new indication was supported by data from the EMPA-REG trial. To review, EMPA-REG was a cardiovascular outcomes trial that compared empagliflozin with placebo in older patients with type 2 diabetes and existing cardiovascular disease. Empagliflozin is an SGLT-2 inhibitor, essentially a diuretic for glucose. These drugs increase glucose excretion in urine and thus lower blood glucose levels. As we have learned, empagliflozin also lowers the risk for subsequent cardiovascular events in people who have cardiovascular disease. We are now convinced that these benefits are real.

In the EMPA-REG trial, 7020 patients were randomly assigned to one of three treatment arms: placebo; empagliflozin 10 mg; or empagliflozin 25 mg. They were then followed for three years. The investigators believed that the study would show that empagliflozin was safe for the heart, but it proved much more than this.

The study found a 38% reduction in cardiovascular disease mortality, a 32% reduction in overall mortality, and a 35% reduction in hospitalization for congestive heart failure in the patients who received empagliflozin. Those are huge benefits that began to be seen quite early on in the study, seemingly within a few months of patients starting the drug.

I do not know the true mechanism by which empagliflozin provides these cardiovascular benefits; many researchers are looking into this. But we are now convinced that these benefits are real, at least for empagliflozin. Studies are being conducted with other SGLT-2 inhibitors to see if the same is true with them.

Safety Considerations

All drugs have side effects. Empagliflozin is not indicated for patients with an estimated glomerular filtration rate (eGFR) below 45 mL/min/1.73 m^2, and in fact, some individuals have developed acute renal failure when started on empagliflozin. This is uncommon but does happen in those higher-risk patients who are more at risk for dehydration and may have more marginal renal function, even aside from diuretics.

For example, think of patients with an eGFR of around 55 mL/min/1.73 m^2; they are taking diuretics, they may be older, they may be a little frail, they may be taking a nonsteroidal anti-inflammatory drug because their joints hurt. Those are the individuals

with whom I am more cautious. In those individuals, I often will reduce the diuretic they are already taking, and perhaps use half of the lowest dose of empagliflozin when initiating the drug, to help patients become accustomed to the change in volume status and be sure they do well.

In the long term, patients on empagliflozin actually experience improvements in renal function. There is a reduction in the numbers of patients who develop significant renal disease, especially patients with preexisting proteinuria. Thus, we see a long-term benefit to using empagliflozin in patients with some degree of renal insufficiency. But one needs to be aware that initially, there can be some risk for acute renal failure.

In terms of other side effects, patients will urinate more often because this is a diuretic for glucose. There is also an increased risk for genital mycotic infections in both men and women. Patients need to be aware of this and be treated quickly should they develop any early signs or symptoms so that it does not progress into a more severe genital mycotic infection. I tell patients that this may happen, and in general, once forewarned, patients are actually able to get medical help quickly when they need it.

Dosing Strategy

In this trial, A1c reductions and cardiovascular outcomes were similar in patients who received the 25-mg dose and those who received the 10-mg dose. This leads me to believe that a 12.5-mg dose, or half of a 25-mg tablet, may be a good and potentially more cost-effective dose for some of our patients who cannot afford medications or have issues paying for their pills.

It is easier for patients to take a whole 10-mg tablet, but in settings where patients have to stretch their medication dollars, I have told them to split the 25-mg tablet and take it once a day. They seem to do well.

In summary, this new indication for empagliflozin is for cardiovascular disease risk reduction in our high-risk patients. It is incredibly exciting to have a diabetes drug that can provide this additional benefit.

I hope you will include this in your treatment of patients with type 2 diabetes, particularly those who have preexisting cardiovascular disease. Thank you.

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Ten people to get NHS bionic eyes

The NHS will pay for 10 blind patients to have "bionic eyes" to help treat an inherited form of blindness.

By James Gallagher Health and science reporter, BBC News website

The bionic eye is a retinal implant which interprets images captured by a miniature video camera worn on a pair of glasses.

Five patients will be treated at Manchester Royal Eye Hospital and five at Moorfields Eye Hospital in 2017. They will be monitored for a year afterwards to see how they get on in everyday life.

"I'm delighted," said Prof Paulo Stanga from the Manchester hospital.

He has been involved in earlier trials of the Argus II Bionic Eye, made by the company Second Sight, in retinitis pigmentosa.

He added: "It surpassed all of our expectations when we realised that one of the retinitis pigmentosa patients using the bionic eye could identify large letters for the first time in his adult life."

This disease, which is often passed down through families, destroys the light-sensing cells in the retina. It leads to vision loss and eventually blindness.

Twinkling lights

Keith Hayman, who is 68 and from Lancashire, was fitted with the bionic eye in Manchester. The former butcher was forced to retire

early because of the disease and had been blind for more than two decades.

He said: "Having spent half my life in darkness, I can now tell when my grandchildren run towards me and make out lights twinkling on Christmas trees. "I would be talking to a friend, who might have walked off and I couldn't tell and kept talking to myself, this doesn't happen any more, because I can tell when they have gone. "These little things make all the difference to me."

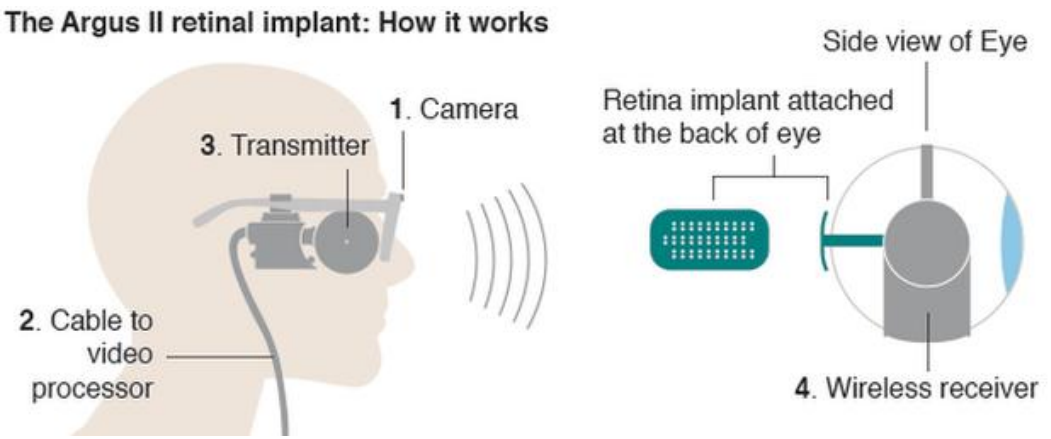
How it works

The bionic eye implant receives its visual information from a miniature camera mounted on glasses worn by the patient.

The images are converted into electrical pulses and transmitted wirelessly to an array of electrodes attached to the retina.

The electrodes stimulate the remaining retina's remaining cells which send the information to the brain.

Camera receives images which are sent to a video processor and converted into



electronic signals, which are then transmitted to an array of electrodes attached to the retina

Gregoire Cosendai, from Second Sight, says: "This is the first time in history that any treatment for this type of blindness has existed and now it is to be offered free of charge to blind patients.

"This is a major victory for blind people in the UK who have supported us in our six-year mission to fund Argus II in England."

Dr Jonathan Fielden, from NHS England, said: "This highly innovative NHS-funded procedure shows real promise and could change lives.

"The NHS has given the world medical innovations ranging from modern cataract surgery, new vaccines and hip replacements, now once again the NHS is at the forefront of harnessing ground-breaking science for the benefit of patients in this country."

http://bit.ly/2hkNL0O

Scientists discover concussion biomarker

Discovery takes guesswork out of concussion diagnosis and management

EVANSTON, Ill. --- The secret to reliably diagnosing concussions lies in the brain's ability to process sound, according to a new study by researchers from Northwestern University's Auditory Neuroscience Laboratory.

Widely considered a crisis in professional sports and youth athletic programs, sports-related concussions have had devastating neurological, physical, social and emotional consequences for millions of athletes. Still, no single test has been developed to reliably and objectively diagnose concussions.

The groundbreaking research, to be published Dec. 22 in the journal Nature, Scientific Reports, has found a biological marker in the auditory system that could take the ambiguity and controversy out of diagnosing concussions and tracking recovery.

"This biomarker could take the guesswork out of concussion diagnosis and management," said lead author Nina Kraus, the Hugh Knowles Professor in the School of Communication and director of the Auditory Neuroscience Laboratory. "Our hope is this discovery will enable clinicians, parents and coaches to better manage athlete health, because playing sports is one of the best things you can do."

By observing research subjects' brain activity as they were exposed to auditory stimuli, Kraus and her team discovered a distinct pattern in the auditory response of children who suffered concussions compared to children who had not.

Kraus and colleagues placed three simple sensors on children's heads to measure the frequency following response, which is the brain's automatic electric reaction to sound. With this measure they successfully identified 90 percent of children with concussions and 95 percent of children in the control group who did not have concussions.

Children who sustained concussions had on average a 35 percent smaller neural response to pitch, allowing the scientists to devise a reliable signature neural profile. As the children recovered from their head injuries, their ability to process pitch returned to normal.

"Making sense of sound requires the brain to perform some of the most computationally complex jobs it is capable of, which is why it is not surprising that a blow to the head would disrupt this delicate machinery," Kraus said.

What was surprising, Kraus said, was the specificity of the findings.

"This isn't a global disruption to sound processing," she said. "It's more like turning down a single knob on a mixing board."

Kraus is a biologist who studies the auditory system, which is at the nexus of our cognitive, sensory and limbic systems. She described the research findings -- based on a small study of 40 children being treated for concussion and a control group -- as a major first step.

Dr. Cynthia LaBella, the director of the Institute of Sports Medicine at the Ann and Robert H. Lurie Children's Hospital of Chicago and professor of pediatrics at Northwestern University Feinberg School of Medicine, is Kraus' partner in the research.

"Our ambition is to produce a reliable, objective, portable, user-friendly, readily available and affordable platform to diagnose concussion," Kraus said.

Concussions, a type of mild traumatic brain injury, are the result of a direct or indirect blow to the head that causes the brain to be jostled within the skull. But there is little relation between the force of an impact and the potential for injury -- two athletes can suffer similar hits but experience vastly different outcomes.

"With this new biomarker, we are measuring the brain's default state for processing sound and how that has changed as a result of a head injury," Kraus said. "This is something patients cannot misreport, you cannot fake it or will your brain to perform better or worse."

See demonstration of the Auditory Neuroscience Laboratory's "biological approach" at http://www.brainvolts.northwestern.edu.

http://bit.ly/2hoz7Yb

These dinosaurs lost their teeth as they grew up

Dinosaurs had teeth as young juveniles that were gradually lost as they grew up

By comparing the fossilized remains of 13 ceratosaurian theropod dinosaurs known as Limusaurus inextricabilis collected from the Upper Jurassic Shishugou Formation of northwestern China, researchers have been able to reconstruct the dinosaur's growth and development from a young hatchling of less than a year to the age of 10. The findings, reported in Current Biology on December 22, uncovered something unexpected: the dinosaurs had teeth as young juveniles that were gradually lost as they grew up.

"We found a very rare, very interesting phenomenon in a ceratosaurian dinosaur whereby toothed jaws in juvenile individuals transition to a completely toothless beaked jaw in more mature individuals during development," says Shuo Wang of Capital Normal University in Beijing, China.

The findings make Limusaurus the first known reptile with the characteristic known as ontogenetic edentulism (meaning tooth reduction or loss in development). Together with other evidence, they led the researchers to conclude that the toothed juveniles were probably omnivorous meat-eaters. The beaked adults most likely transitioned to a plant-based diet.

Wang and colleagues first reported on this ceratosaurian back in 2001. At that point, they had collected just one fossilized juvenile, and they didn't yet know what it was. Over the course of the next several years, more specimens were found. But it wasn't clear that they all belonged to the same species.

"Initially, we believed that we found two different ceratosaurian dinosaurs from the Wucaiwan Area, one toothed and the other toothless, and we even started to describe them separately," Wang says.

As they started to code the dinosaurs' characteristics for phylogenetic analysis, they began to realize that they looked remarkably similar -- all except for the teeth. With more careful study, the researchers concluded that in fact the specimens did represent the same dinosaur. It's just that those dinosaurs lost their teeth over time.

The researchers identified 78 developmental changes in Limusaurus in all, with tooth loss being the most surprising. They say that the discovery has significant implications for understanding the evolution of the beak, an important feeding structure in many dinosaurs of the past, as well as modern birds.

Wang says that tooth loss isn't so unusual in animals alive today. There are fish and an amphibian that lose teeth as they grow. Platypuses lose their teeth too. But the discovery is still a first for the fossil record and for reptiles.

The findings suggest that the dietary habits and needs of some dinosaurs changed over the course of their development, most likely along with shifts in their digestive systems. Wang and colleagues will continue studying changes to the digestive system and skeleton in greater detail.

This study was supported by the National Natural Science Foundation of China, the U.S. National Science Foundation, and the Special Funds for Major States Basic Research Projects of China. The authors received addition support from the NSF, the National Basic Research Program of China , and the "Strategic Priority Research Program" of the Chinese Academy of Sciences.

Current Biology, Wang et al.: "Extreme Ontogenetic Changes in a Ceratosaurian Theropod" http://www.cell.com/current-biology/fulltext/S0960-9822(16)31269-6

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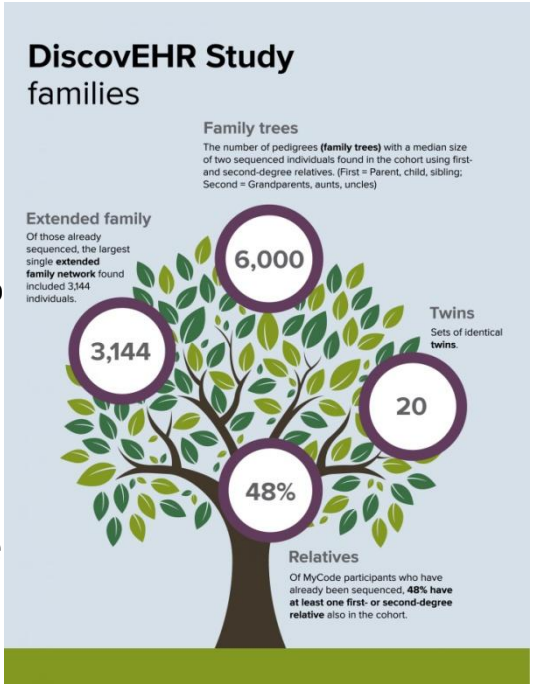
Analysis of 50,000+ genomes reveals detrimental mutations

Researchers found that genes that are more sensitive to loss-of-function variation are genes essential to life

Two new studies highlight the findings of an extensive analysis of exomes, coupled with electronic health records (EHR), which has led to the identification of a number of medically relevant genetic variants in humans. The results are part of DiscovEHR, a comprehensive project where more than 50,000 participants in the U.S. provided blood and DNA samples for genomic analyses, and consented to link the data to their individual EHRs. In the first study, Frederick Dewey et al. analyze the data, finding that individual participants had a median of 21 rare gene variants that were predicted to have lost their function (pLOFs), although several hundred common pLOFs were also identified.



An infographic depicting DiscoveEHR family trees. This material relates to a paper that appeared in theDec. 23, 2016, issue of Science, published by AAAS. The paper, by F.E. Dewey at Regeneron Genetics Center in Tarrytown, NY, and colleagues was titled, "Distribution and clinical impact of functional variants in 50,726 whole-exome sequences from the DiscovEHR study." **Brian Foelsch, Geisinger Health System**

Intriguingly, the researchers found that genes that were more sensitive to loss-of-function variation were genes essential to life, cancer-associated genes, and genes associated with autosomal dominant human diseases, compared to genes associated with autosomal recessive disease, drug targets, and olfactory receptors. The data also

yielded hundreds of genes that have been partially or fully disabled, which could provide valuable insights into their function in future research. About 3.5% of individuals were found to harbor deleterious variants in 76 clinically relevant genes.

In a separate study, Noura S. Abul-Husn et al. analyzed DiscovEHR data in order to better understand gene variants that contribute to the development of familial hypercholesterolemia (FH). FH is characterized by substantial, lifelong elevation of low-density lipoprotein cholesterol (LDL-C) and a much greater risk of premature cardiovascular disease. Among the three known genes - LDLR, PCSK9, and APOB - that are associated with FH, the authors identified 19 variants that can lead to development of the disease. Cholesterol levels, as well as increased risk of developing coronary artery disease, were significantly higher in people with the LDLR variants, the authors report. By surveying matching EHR records, they found that 58% of FH variant carriers were currently prescribed a statin medication, which helps reduce the risk of cardiovascular disease, and yet only 46% of those receiving treatment had cholesterol levels under the target recommended for FH patients. These findings are consistent with previous reports and highlight the undertreatment of FH, the authors conclude. These two studies are highlighted in a Perspective by Daniel Rader and Scott Damrauer.

http://bit.ly/2i5iCqw

Global climate target could net additional six million tons of fish annually

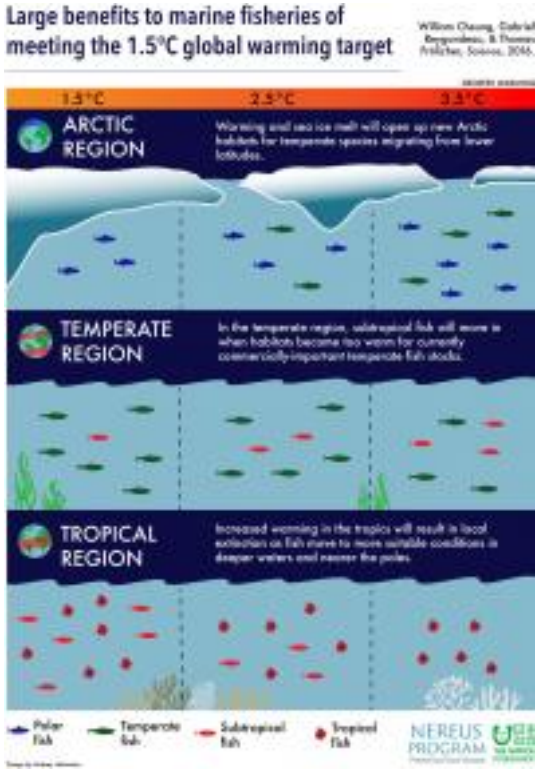
If countries abide by the Paris Agreement, potential fish catches could increase by six million metric tons per year

If countries abide by the Paris Agreement global warming target of 1.5 degrees Celsius, potential fish catches could increase by six million metric tons per year, according to a new study published in Science.

The researchers also found that some oceans are more sensitive to changes in temperature and will have substantially larger gains from achieving the Paris Agreement.

"The benefits for vulnerable tropical areas is a strong reason why 1.5 C is an important target to meet," said lead author William Cheung, director of science at the Nippon Foundation-Nereus Program and associate professor at UBC's Institute for the Oceans and Fisheries.

"Countries in these sensitive regions are highly dependent on fisheries for food and livelihood, but all countries will be impacted as the seafood supply chain is now highly globalized. Everyone would benefit from meeting the Paris Agreement."



If countries abide by the Paris Agreement global warming target of 1.5 degrees Celsius, potential fish catches could increase by six million metric tons per year, according to a new study published in Science. **Lindsay Lafreniere**

The authors compared the Paris Agreement 1.5 C warming scenario to the currently pledged 3.5 C by using computer models to simulate changes in global fisheries and quantify losses or gains. They found that for every degree Celsius decrease in global warming, potential fish catches could increase by more than three metric million tons per year. Previous UBC research shows that today's global fish catch is roughly 109 million metric tons.

"Changes in ocean conditions that affect fish stocks, such as temperature and oxygen concentration, are strongly related to atmospheric warming and carbon emissions," said author Thomas Frölicher, principal investigator at the Nippon Foundation-Nereus Program and senior scientist at ETH Zürich. "For every metric ton of carbon dioxide emitted into the atmosphere, the maximum catch potential decreases by a significant amount."

Climate change is expected to force fish to migrate towards cooler waters. The amount and species of fish caught in different parts of the world will impact local fishers and make fisheries management more difficult.

The findings suggest that the Indo-Pacific area would see a 40 per cent increase in fisheries catches at 1.5 C warming versus 3.5 C. Meanwhile the Arctic region would have a greater influx of fish under the 3.5 C scenario but would also lose more sea ice and face pressure to expand fisheries.

The authors hope these results will provide further incentives for countries and the private sector to substantially increase their commitments and actions to reduce greenhouse gas emissions.

"If one of the largest carbon dioxide emitting countries gets out of the Paris Agreement, the efforts of the others will be clearly reduced," says author Gabriel Reygondeau, Nippon Foundation-Nereus Program senior fellow at UBC. "It's not a question of how much we can benefit from the Paris Agreement, but how much we don't want to lose."

The study "Large benefits to marine fisheries of meeting the 1.5 °C global warming target" was published in Science: http://science.sciencemag.org/cgi/doi/10.1126/science.aag2331.

http://bit.ly/2hEtMI5

'Necrobiome' Reveals a Corpse's Time of Death

The microbial ecosystems inhabiting corpses could help forensic scientists determine a person's time of death, even after almost two months. Christopher Intagliata reports.

By Christopher Intagliata on December 22, 2016

Download MP3

Tens of trillions of microbes call our living bodies home. But when we die? "The first thing that happens is basically ecosystem collapse—where you have a tremendous loss of diversity." Nathan Lents, a molecular biologist at John Jay College in New York. "And then it bottoms out and starts to get rich again."

That microbial phoenix, rising from our extinguished mortal coils, is called the "necrobiome." Lents and his team tracked the necrobiome, by swabbing the ears and noses of 21 cadavers at a body farm in Tennessee. It's a sort of outdoor lab for forensic scientists, where bodies are left to the elements to decompose.

They tracked the genetic signatures of that microbial community as it waned and waxed after death. And they used that data to build an algorithm that could pinpoint a corpse's time of death, to an accuracy of just two summertime days. "And that held out for up to six to seven weeks. And that's way better than entomology can tell you." Entomology being the study of the insects that colonize a corpse. "Entomology's ok for giving you upper and lower limits within five to seven days, but beyond that, entomology's not helpful."

The study is in the journal PLOS ONE. [Hunter R. Johnson et al, *A Machine Learning Approach for Using the Postmortem Skin Microbiome to Estimate the Postmortem Interval*]

The method isn't quite ready for primetime. There's still a lot of 'biological noise' in the system. "We're talking about living things here. Well.. living and dead things." But as with any machine learning, more info will help it see beyond the noise. "It will forever learn. So the more data we pump into this system, the better it will get." Ultimately, Lents says, the algorithm will have to be smart enough to hold up in a court of law, when it could determine the fate of someone accused of turning someone into a corpse.

http://bit.ly/2i7uhOI

Final trial results confirm Ebola vaccine provides high protection against disease

An experimental Ebola vaccine was highly protective against the deadly virus in a major trial in Guinea, according to results published today in The Lancet.

The vaccine is the first to prevent infection from one of the most lethal known pathogens, and the findings add weight to early trial results published last year.

The vaccine, called rVSV-ZEBOV , was studied in a trial involving 11,841 people in Guinea during 2015. Among the 5,837 people who received the vaccine, no Ebola cases were recorded 10 days or more

after vaccination . In comparison, there were 23 cases 10 days or more after vaccination among those who did not receive the vaccine.

The trial was led by the World Health Organization, together with Guinea's Ministry of Health and other international partners.

"While these compelling results come too late for those who lost their lives during West Africa's Ebola epidemic, they show that when the next Ebola outbreak hits, we will not be defenceless," said Dr Marie-Paule Kieny, WHO's Assistant Director-General for Health Systems and Innovation, and the study's lead author .

The vaccine's manufacturer, Merck, Sharpe & Dohme, this year received Breakthrough Therapy Designation from the United States Food and Drug Administration and PRIME status from the European Medicines Agency, enabling faster regulatory review of the vaccine once it is submitted.

Since Ebola virus was first identified in 1976, sporadic outbreaks have been reported in Africa. But the 2013-2016 West African Ebola outbreak, which resulted in more than 11,300 deaths, highlighted the need for a vaccine.

The trial took place in the coastal region of Basse-Guinée, the area of Guinea still experiencing new Ebola cases when the trial started in 2015. The trial used an innovative design, a so-called "ring vaccination" approach - the same method used to eradicate small pox.

When a new Ebola case was diagnosed, the research team traced all people who may have been in contact with that case within the previous 3 weeks, such as people who lived in the same household, were visited by the patient, or were in close contact with the patient, their clothes or linen, as well as certain "contacts of contacts". A total of 117 clusters (or "rings") were identified, each made up of an average of 80 people.

Initially, rings were randomised to receive the vaccine either immediately or after a 3-week delay, and only adults over 18 years were offered the vaccine. After interim results were published showing the vaccine's efficacy, all rings were offered the vaccine immediately and the trial was also opened to children older than 6 years.

In addition to showing high efficacy among those vaccinated, the trial also shows that unvaccinated people in the rings were indirectly protected from Ebola virus through the ring vaccination approach (so-called "herd immunity"). However, the authors note that the trial was not designed to measure this effect, so more research will be needed.

"Ebola left a devastating legacy in our country. We are proud that we have been able to contribute to developing a vaccine that will prevent other nations from enduring what we endured" said Dr KeÏta Sakoba, Coordinator of the Ebola Response and Director of the National Agency for Health Security in Guinea .

To assess safety, people who received the vaccine were observed for 30 minutes after vaccination, and at repeated home visits up to 12 weeks later. Approximately half reported mild symptoms soon after vaccination, including headache, fatigue and muscle pain but recovered within days without long-term effects. Two serious adverse events were judged to be related to vaccination (a febrile reaction and one anaphylaxis) and one was judged to be possibly related (influenza-like illness). All three recovered without any long term effects.

It was not possible to collect biological samples from people who received the vaccine in order to analyse their immune response. Other studies are looking at the immune response to the vaccine including one conducted in parallel to the ring trial among frontline Ebola workers in Guinea.

"This both historical and innovative trial was made possible thanks to exemplary international collaboration and coordination, the contribution of many experts worldwide, and strong local involvement," said Dr John-Arne Røttingen, Specialist Director at the Norwegian Institute of Public Health, and the chairman of the study steering group .

In January, GAVI, the Vaccine Alliance provided US$5 million to Merck towards the future procurement of the vaccine once it is approved, prequalified and recommended by WHO. As part of this agreement, Merck committed to ensure that 300,000 doses of the vaccine are available for emergency use in the interim, and to submit the vaccine for licensure by the end of 2017. Merck has also submitted the vaccine to WHO's Emergency Use and Assessment Listing procedure, a mechanism through which experimental vaccines, medicines and diagnostics can be made available for use prior to formal licensure.

Additional studies are ongoing to provide more data on the safety of the vaccine in children and other vulnerable populations such as people with HIV. In case of Ebola flare-ups prior to approval, access to the vaccine is being made available through a procedure called "compassionate use" that enables use of the vaccine after informed consent. Merck and WHO's partners are working to compile data to support license applications.

The rapid development of rVSV-EBOV contributed to the development of WHO's R&D Blueprint, a global strategy to fast-track the development of effective tests, vaccines and medicines during epidemics.

Also published in The Lancet (embargo as above), is a phase 2 trial of a different Ebola vaccine candidate, the recombinant adenovirus type-5 Ebola vaccine. The trial was led by the Beijing Institute of Biotechnology and was conducted in Sierra Leone in 2015. It involved 500 healthy participants, followed for 6 months - 250 were given a high dose vaccine, 125 a low-dose and 125 a placebo. The study found that the vaccine was safe and induced an immune response that peaked at 28 days, but decreased during the six months post injection. One serious adverse event was reported, in an individual with a history of asthma. Further research on this vaccine is needed in order to assess its efficacy.

NOTES TO EDITORS

The rVSV-ZEBOV trial is funded by WHO, with support from the Wellcome Trust, the United Kingdom Department for International Development, the Norwegian Ministry of Foreign Affairs to the Norwegian Institute of Public Health through the Research Council of Norway, the Canadian Government through the Public Health Agency of Canada, Canadian Institutes of Health Research, International Development Research Centre and Department of Foreign Affairs, Trade and Development and Médecins Sans Frontières.

The trial team includes experts from The University of Bern, the University of Florida, the London School of Hygiene and Tropical Medicine, Public Health England, the European Mobile Laboratories among others. The trial was designed by a group of experts including the late Professor Donald A. Henderson of John Hopkins University, who led the WHO smallpox eradication effort by using the ring vaccination strategy.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)61117-5/abstract

VSV-EBOV was developed by the Public Health Agency of Canada. The vaccine was licensed to NewLink Genetics, who in turn licensed it to Merck & Co. The vaccine works by replacing a gene from a harmless virus known as vesicular stomatitis virus (VSV) with a gene encoding an Ebola virus surface protein. The vaccine does not contain any live Ebola virus. Earlier trials have shown the vaccine to be protective in animals, and be safe and produce an immune response in humans.

Analysis only included cases occurring 10 days after receiving the vaccine to account for the incubation period of the Ebola virus.

Quotes direct from authors and cannot be found in the text of the Article.

http://bit.ly/2hfLbWN

5,000-Year-Old Nativity Scene Found in Egypt

Italian researchers have discovered what might be the oldest nativity scene ever found — 5,000-year-old rock art that depicts a star in the east, a newborn between parents and two animals.

By Rossella Lorenzi, Seeker | December 23, 2016 08:06am ET

The scene, painted in reddish-brown ochre, was found on the ceiling of a small cavity in the Egyptian Sahara desert, during an expedition to sites between the Nile valley and the Gilf Kebir Plateau.

"It's a very evocative scene which indeed resembles the Christmas nativity. But it predates it by some 3,000 years," geologist Marco Morelli, director of the Museum of Planetary Sciences in Prato, near Florence, Italy, told Seeker.

Morelli found the cave drawing in 2005, but only now his team has decided to reveal the amazing find. "The discovery has several implications as it raises new questions on the iconography of one of the more powerful Christian symbols," Morelli said.

Researchers discovered 5,000-year-old rock art on the ceiling of a cave in the Egyptian Sahara desert. **Marco Morelli**

The scene features a man, a woman missing the head because of a painting detachment, and a baby. "It could have been interpreted as a normal depiction of a family, with the baby between the parents, but other details make this drawing unique," Morelli said.

He noted the newborn is drawn slightly above, as if raising to the sky. Such position, with the baby not yet between the parents, would have meant a birth or a pregnancy.

"As death was associated to Earth in contemporary rock art from the same area, it is likely that birth was linked to the sky," Morelli said.

The scene becomes more symbolically complex if the other figures, two animals and a small circular feature, are taken into consideration.

On the upper part is a headless lion, a mythical beast which appears in several rock art drawings from the same area, while below in the scene a baboon or an anthropomorphic monkey can be seen.

In the east, the Neolithic artist drawn what appears to be star.

The researchers called the site the "Cave of the Parents."

"No doubt it's an intriguing drawing," Morelli said. "We didn't find similar scenes until the early Christian age."

http://bit.ly/2i9bmD9

Guillotined Acorn Worms Simply Regrow Their Heads

Studying the worms' miraculous abilities could one day lead to treatments for dementia, paralysis and amputations

By Jennifer Frazer on December 23, 2016

Humans have noted with frustration our conspicuous inability to regenerate organs, limbs, and heads. But there is an animal – a close relative -- that can do not only that, it can regenerate the entire front half of its body after bisection: head, heart, central nervous system and all. That animal is the acorn worm (This is the third time I have written about these humble and apparently vastly under-appreciated animals in just the last few months. Clearly, they need a better PR team).

Don't believe me? Here's a time-lapse video that shows one accomplishing this show stopping feat in a mere two weeks. The images of regeneration go by a little quickly -- try pausing and restarting the video to slow them down.

OK, this is a cool party trick, you may concede. But why should we care? Because these invertebrates are just about as close to being a chordate – an animal like ourselves with a dorsal spinal cord -- as you can get without being one. They grow a hollow neural tube along their backs, just like us. As such, they use many of the same developmental genes we use to develop our brains to grow their heads, "brains", and bodies.

Those shared genes means that understanding how they can regrow the entire upper half of their bodies and central nervous system from scratch in a matter of just two weeks could help unlock doors that could produce radically better treatments for people with brain and spinal cord injuries, dementia, paralysis, and amputations. I should emphasize, however, that these scientists are not suggesting humans can regrow entire heads. They are suggesting we may be able to regenerate parts of our brains, central nervous systems, and perhaps

even bodies that have been damaged or lost. This could obviously help a lot of people, should it pan out. And it may not.

Regeneration is, perhaps surprisingly, not unusual among animals. "Popularized in myths, science fiction, and even horror movies, regeneration of missing and damaged tissue is a common reality in the animal kingdom," the authors write. Unfortunately, that reality does not include us. Yet nearly every phylum of animals contains at least a few species able to regenerate. Sea stars and other echinoderms can famously regenerate large sections of their body should they be cut into pieces. Even among the chordates and vertebrates it is not uncommon. Lancelets, tunicates(sea squirts), frogs, fish, and salamanders can all regenerate parts of their bodies to one degree or another. Fish and amphibians even regenerate parts of their central nervous systems.

However, in a stroke of bad luck for scientists, the vertebrates that can regenerate have also, for unrelated reasons, had their genomes duplicated more than once. That makes it much harder to tinker with their genetics for the purposes of studying regeneration. Normally, scientists amp up production of, suppress, or knock out a gene – effectively, breaking it -- to study what the effect of that tinkering tells us about what the normal version does. But because there are so many different versions of the same gene to deal with in the vertebrates, the usual strategy is impractical. Invertebrate genomes, like that of the acorn worms, lack duplication issues.

Of course, that this seemingly magical ability exists among a group of animals so closely related to our own begs a more basic question: when did the ability to regenerate evolve? Was it an ability the first animals possessed and passed down to their descendants, or has it evolved multiple times in many different animal groups? That the earliest evolved living animals, like sponges, jellyfish, coral, and comb jellies, all have great powers of regeneration, suggests the former is true.

This matters because if regeneration was a trait present in the first animals and persisted a long time before groups like our own lost the ability, it is probable, the authors say, that humans still retain many or all of the genetic switches that control it, but they have been disabled somehow. It may be possible to reactivate these regenerative molecular pathways in us using insights we gain from studying animals like the acorn worm whose gene networks are still operational. To that end, the scientists chose to study the acorn worm Ptychodera flava, whose regeneration you witnessed above. Before scientists can begin breaking the worm's genes to see what they do, however, they need to know what normal worm regeneration looks like. A new study published in September in the journal Developmental Dynamics lays this out the normal course of acorn worm regeneration.

Acorn worms are, as I wrote in October, made up of a proboscis which sits in a collar attached to a tail. The mouth is inside the collar, and the proboscis is used by the worm to wriggle through the mud or sand in which it feeds.

The experiment employed a simple, if drastic, intervention: slice the worm in two. The surviving halves recuperated from this grave insult with remarkable speed – particularly the unlucky rear end. On this half, the wound sealed and healed within two days. A little round construction pod called a regeneration blastema formed within 3 days. Cells accumulated and assembled there to form a rudimentary head by 5 days post cut. Four to five days later, a mouth formed and opened. An acorn worm can actually start eating again just five days after being sliced in half! Blood vessels regenerated quickly too. This makes sense: both obtaining fuel and distributing that fuel along with oxygen to growing, energetically-needy tissues is critical for regeneration.

The worm then regenerated all the structures of the head , collar, heart, nervous system, and upper trunk, going in order from front to back. Just two weeks later, you have a shiny new acorn worm where there was only the decidedly non-business end of one before.

When the scientists closely examined the sequence of regeneration, they also made an intriguing discovery: there were differences between how the worms develop as embryos and juveniles and how they regenerate after grave injury. Small differences, but differences which nonetheless show a separate regenerative program may be operating.

An unsolved puzzle remains: from where do the cells that migrate to the regeneration blastema come? Are they genuine stem cells always present somewhere in the worm's body? Stem cells are undifferentiated cells that can divide indefinitely or produce cells of any other tissue types. In human adults, they're found in bone marrow, fat, and blood. Or are these construction cells ex-body cells that have been de-programmed and returned to a stem-cell like state so they can be assigned a new role in the regenerating tissue?

One clue comes from the first gill slit that forms during regeneration (all original gills were removed by cutting the worm in half). The part closer to the proboscis is white, wall the part closer to the pre-fabbed worm is pigmented like the rest of the worm's original body. That suggests the front end is being generated from new cells, while the back end is being constructed from cells recycled from old tissue that has been dissolved and its cells re-assigned.

Human cells are not normally capable of shedding their identity once they have been assigned a tissue type. If acorn worms can do this, we might be able to similarly remodel our own tissues, these scientists say. These are magical superpowers indeed. But it is worth remembering that should we come by any or all of the abilities I've described, it would be thanks not to a yellow sun or a radioactive spider bite, but to an ugly, humble but fascinating little worm, quietly digging its way through seafloor mud.

Reference

Luttrell, Shawn M., Kirsten Gotting, Eric Ross, Alejandro Sánchez Alvarado, and Billie J. Swalla. "Head regeneration in hemichordates is not a strict recapitulation of development." Developmental Dynamics 245, no. 12 (2016): 1159-1175.

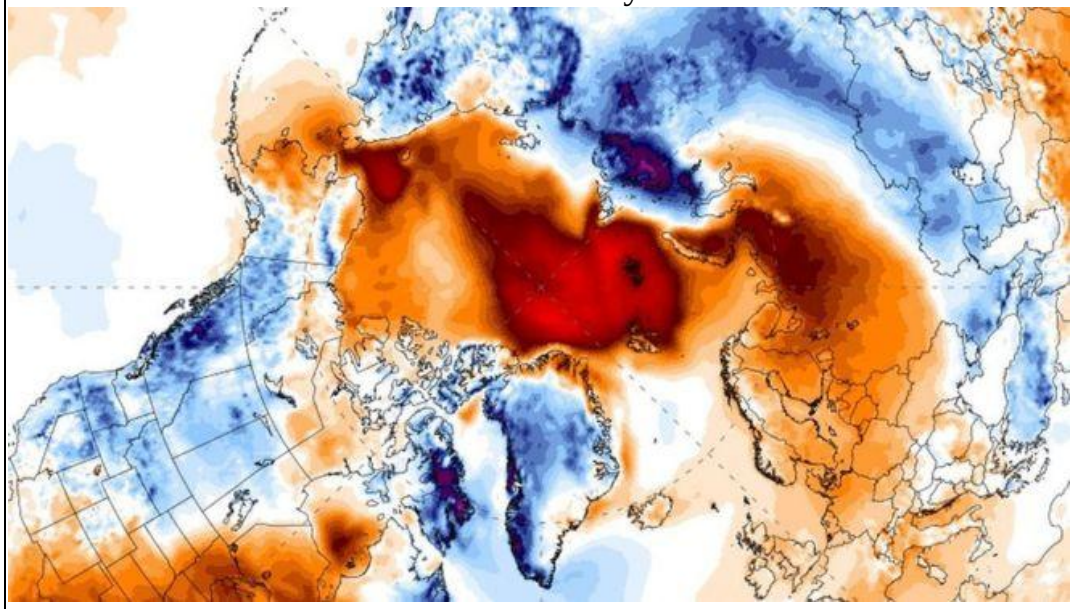
http://bbc.in/2hYyLGR

Arctic heatwave could break records

Temperatures at the North Pole could be up to 20 degrees higher than average this Christmas Eve, in what scientists say is a record-breaking heatwave.

By Victoria Gill Science reporter, BBC News

Climate scientists say these unseasonably warm weather patterns in the Arctic region are directly linked to man-made climate change. Temperatures throughout November and December were 5C higher than average. It follows a summer during which Arctic sea ice reached the second-lowest extent ever recorded by satellites.



Temperatures on Christmas Eve at the North Pole could reach close to freezing on Christmas Eve 2016 University of Maine/ ClimateReanalyzer.org Dr Friederike Otto, a senior researcher at Oxford's Environmental Change Institute told BBC News that in pre-industrial times "a heatwave like this would have been extremely rare - we would expect it to occur about every 1,000 years".

Dr Otto added that scientists are "very confident" that the weather patterns were linked to anthropogenic climate change.

"We have used several different climate modelling approaches and observations," she told BBC News.

"And in all our methods, we find the same thing; we cannot model a heatwave like this without the anthropogenic signal."

Temperatures are forecast to peak on Christmas Eve around the North Pole - at near-freezing. The warm air from the North Atlantic is forecast to flow all the way to the North Pole via Spitsbergen, giving rise to clouds that prevent heat from escaping.

And, as Dr Otto explained to BBC News, the reduction in sea ice is contributing to this "feedback loop".

"If the globe is warming, then the sea ice and ice on land [shrinks] then the darker water and land is exposed," she said. "Then the sunlight is absorbed rather than reflected as it would be by the ice."

Forecasting models show that there is about a 2% chance of a heatwave event occurring every year.

"But if temperatures continue to increase further as they are now," said Dr Otto, "we would expect a heatwave like this to occur every other year and that will be a huge stress on the ecosystem."

Dr Thorsten Markus, chief of NASA's Cryospheric Sciences Laboratory, said the heatwave was "very, very unusual".

"The eerie thing is that we saw something quite similar (temperatures at the North Pole of about 0C in December) almost exactly a year ago," he told BBC News.

The freeze and thaw conditions are already making it difficult for reindeer to find food - as the moss they feed on is covered by hard ice, rather than soft, penetrable snow.

Asked if the conditions on Christmas Eve were likely to affect Santa's all-important journey, Dr Markus said he was confident that his sled would cope with the conditions.

He added: "Santa is most likely overdressed though. Maybe in the future we'll see him in a light jacket or plastic mac."

http://bit.ly/2i6HJzN

Laser therapy with deep-sea drug kills prostate cancer in trial

A non-surgical treatment for low-risk prostate cancer in which doctors inject a light-sensitive drug derived from deep-sea bacteria into a patient's bloodstream was shown in a trial to kill cancer cells without destroying healthy tissue.

LONDON - Results of a trial in 413 patients showed that the drug, which is activated with a laser to destroy tumor tissue in the prostate, was so effective that half the patients went into remission, compared with 13.5% in a control group.

"These results are excellent news for men with early localised prostate cancer, offering a treatment that can kill cancer without removing or destroying the prostate," said Mark Emberton, a University College London consultant urologist who led the trial. "This is truly a huge leap forward."

The treatment, called vascular-targeted photodynamic therapy or VTP, was developed by scientists at the Weizmann Institute of Science in Israel in collaboration with the privately-owned STEBA Biotech.

The light-sensitive drug used, called WST11, is derived from bacteria found at the bottom of the ocean. To survive with very little sunlight, they have evolved to convert light into energy with incredible efficiency, Emberton's team said in a study published in the journal Lancet Oncology.

The Weizmann scientists exploited this feature to develop WST11, a compound that releases free radicals to kill surrounding cells when activated by laser light.

Men with low-risk prostate cancer are currently put under active surveillance, where the disease is monitored and only treated when it becomes more severe. Radical therapy, which involves surgically removing or irradiating the whole prostate, has significant long-term side effects, so is only used to treat high-risk cancers.

While radical therapy causes lifelong erectile problems and incontinence, VTP only caused short-term urinary and erectile

problems which resolved within three months, the researchers said. No significant side-effects remained after two years.

In the trial, only 6 percent of patients treated with VTP needed radical therapy compared with 30 percent of patients in the control arm who were under active surveillance.

The trial involved 47 treatment sites in 10 European countries, most of which were performing VTP for the first time. “The fact that the treatment was performed so successfully by non-specialist centres in various health systems is really remarkable,” Emberton said.

The VTP treatment is now being reviewed by the European Medicines Agency (EMA) for possible licence, but it likely to be several years before it can be offered to patients more widely.

http://bbc.in/2hmk93c

Doctors confirm 200-year-old diagnosis

Doctors have confirmed a diagnosis made more than 200 years ago by one of medicine's most influential surgeons.

By James Gallagher Health and science reporter, BBC News website

John Hunter had diagnosed a patient in 1786 with a "tumour as hard as bone". Royal Marsden Hospital doctors analysed patient samples and case notes, which were preserved at the museum named after him - the Hunterian in London. As well as confirming the diagnosis, the cancer team believe Mr Hunter's centuries-old samples may give clues as to how cancer is changing over time.

"It started out as a bit of fun exploration, but we were amazed by John Hunter's insight," Dr Christina Messiou told the BBC News website.

Mr Hunter became surgeon to King George III in 1776 and is one of the surgeons credited with moving the medical discipline from butchery to a science. He's also rumoured to have given himself gonorrhoea as an experiment while writing a book about venereal diseases.

His huge medical collection is now housed at the Hunterian Museum at the Royal College of Surgeons.

It includes his colourful notes describing a man who arrived at St George's Hospital, in 1786, with a hard swelling on his lower thigh.

"It appeared to be a thickening of the bone, it was increasing very rapidly... On examining the diseased part, it was found to consist of a substance surrounding the lower part of the thigh bone, of the tumour kind, which seemed to originate from the bone itself."

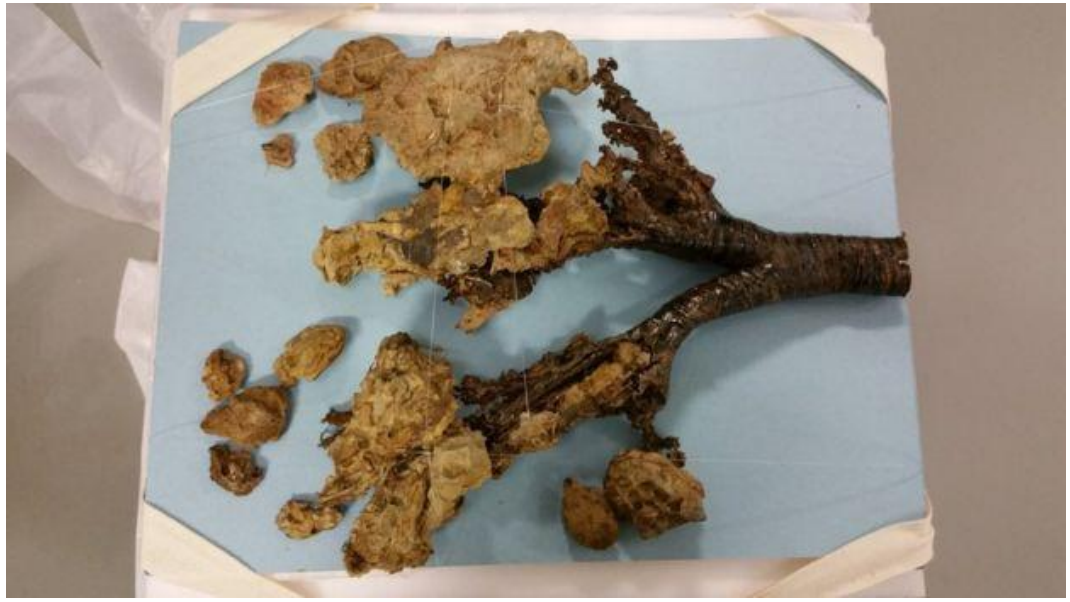
Mr Hunter amputated the man's leg and he recovered briefly for four weeks.

"From this time he began to lose flesh and sink gradually, his breathing more and more difficult," the notes continued.

The patient died seven weeks after the operation and an autopsy discovered bony tumours had spread to his lungs, the lining of the heart and on the ribs.

Bony growths had spread to the patient's lungs **Christina Messiou**

More than 200 years later, the samples fell under the gaze of Dr



Christina Messiou. She said: "Just looking at the specimens, the diagnosis of osteosarcoma came very quickly to me and John Hunter's write up was amazingly astute and fits with what we know about the behaviour of the disease. "The large volumes of new bone formation

and the appearance of the primary tumour are really characteristic of osteosarcoma."

She went to get a second opinion from her colleagues at the Royal Marsden in central London. And in an out-of-hours session at the hospital they used modern day scanning technology to confirm the centuries old diagnosis.

Dr Messiou, whose speciality is sarcoma, told the BBC: "I think his diagnosis is really impressive and in fact his management of the patient followed similar principles to what we would have done in the modern day." But she says the exciting stage of the research is still to come. They are now going to compare more of Hunter's historical samples with contemporary tumours - both microscopically and genetically - to see if there are any differences.

Dr Messiou told the BBC: "It's a study of cancer evolution over 200 years and if we're honest we don't really know what we're going to find. "But it would be interesting to see if we can link lifestyle risk factors with any differences that we see between historical and current cancers. "So we've got big ambitions for the specimens."

Writing in the British Medical Journal, the Royal Marsden team apologised for delay in analysing the samples from 1786 and the obvious breach of cancer waiting times, but point out their hospital was not built until 1851.