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First proof of a direct association between coronavirus and neurological disease

A Great Britain-Quebec scientific collaboration

For the first time, researchers have found proof of a direct association between strain OC-43 of the human coronavirus (HCoV) and neurological disease in humans.

This major breakthrough was made by British and Quebec researchers, including Professor Pierre Talbot of the INRS-Institut Armand-Frappier Centre, who was the first not only to demonstrate the virus's ability to invade the human central nervous system, but also to suggest the neuropathological effects of this virus responsible for approximately 20% of common colds and more severe respiratory conditions in certain vulnerable individuals. The discovery was recently featured in the New England Journal of Medicine, one of the world's most prestigious scientific journals.

The researchers studied the case of a very young patient who died from encephalitis. The patient had presented severe immunodeficiency and received a stem cell transplant. Although most cases of encephalitis are caused by viruses or bacteria, it can be particularly difficult to pinpoint the cause in immunodeficient patients. As the case study shows, it was impossible to identify the pathogen using conventional techniques.

The researchers used various methods that allowed them to irrefutably identify the presence of strain OC-43 of the human coronavirus in the young patient's brain tissue.

"Among the methods used, deep sequencing of biopsy materials provides an important tool for the diagnosis of unexplained encephalitis, particularly in immunodeficient patients who have undergone stem cell transplantation," said Professor Talbot. This breakthrough is significant because it will make it possible to use specific treatments that are better tailored to patient conditions.

The results obtained confirm Professor Talbot's hypothesis that the human respiratory coronavirus can cause certain neurological diseases of unknown origin, such as multiple sclerosis, Alzheimer's disease, Parkinson's disease, and encephalitis.

http://bit.ly/2dPOwve

Respiratory tract bacterium uncovered as trigger for serious nervous system disease

The bacterium Mycoplasma pneumoniae has been under suspicion for quite a while.

Now, researchers at the University of Zurich, the University Children's Hospital Zurich, and the Erasmus University in Rotterdam have proved without a doubt that it is the culprit. In fact, mycoplasma is not only responsible for respiratory tract infections such as pneumonia in children and adults, it can also trigger Guillain-Barré syndrome (GBS) in infected individuals.

The scientists have succeeded for the first time in culturing mycoplasma from a GBS patient in a laboratory setting. Antibodies attack not only the bacteria but also the nerve pathways The reason for this is the similarity between structures on the surface of the bacteria and the body's own nerve-sheath structures (molecular mimicry).

This leads to an immune reaction, which attacks both the mycoplasma and the surrounding myelin sheath of nerve pathways. "Antibodies recognize a certain glycolipid structure present at the cell membrane of the bacteria. These antibodies cross-react with and bind to galactocerebroside (GalC), one of the most common components of human myelin", explains Patrick Meyer Sauteur, the study's first author.

This fatty substance ensures electrical conductivity of the nerve fibers. If it is destroyed, the patient experiences GBS, characterized by paralysis in arms and legs, weakness, and sensory disturbances.

Antibodies against GalC had already been described in patients with GBS.

Such anti-GalC antibodies were also found in the aforementioned patient, and there was a correlation between their concentration in the blood and the progression of the illness. Immunological tests demonstrated that anti-GalC antibodies of the patient reacted most strongly with the cultured isolate, less strongly with other subtypes of mycoplasmas, but not with other bacteria. These results confirmed the cross-reactivity of the anti-GalC antibody.

Antibody isotype class switch may be responsible for GBS

The researchers investigated a total of 189 adults and 24 children with GBS for the presence of antibodies to mycoplasma (as an indication of a recent bacterial infection) and GalC (as the suspected trigger for GBS), and compared them with 677 healthy individuals as controls. Three percent of the adults and 21 percent of the children were found to have had a recent mycoplasma infection - which was higher than in healthy control individuals.

Anti-GalC antibodies were found in their blood with almost the same frequency: in three percent of the adults and 25 percent of the children. These anti-GalC antibodies also reacted to several mycoplasma strains. Interestingly, the anti-GalC antibodies were also found in patients without GBS who had recently been infected with mycoplasma. However, these were all of the antibody isotype M (immunoglobulin M, IgM), the earliest antibody type elicited during an acute immune response.

By contrast, the anti-GalC antibodies in the GBS patients were of the isotype IgG. "We therefore assume that this class switch of the antibody isotype may contribute to the pathogenesis of GBS", explains Meyer Sauteur. "In fact, this antibody isotype class switch is also assumed as a critical step in the development of other autoimmune diseases. Immunotherapies based on that premise may thus be a new possible treatment option for GBS."

Patrick M. Meyer Sauteur, Ruth Huizinga, Anne P. Tio-Gillen, Joyce Roodbol, Theo Hoogenboezem, Enno Jacobs, Monique van Rijn, Annemiek A. van der Eijk, Cornelis Vink, Marie-Claire Y. de Wit, Annemarie M.C. van Rossum, Bart C. Jacobs. Mycoplasma pneumoniae triggering the Guillain-Barré syndrome: a case-control study. Annals of Neurology. September 30, 2016. doi:10.1002/ana.24755

http://bit.ly/2dS0p8i

Parents' age and the risk for autism and schizophrenia: Is the connection real?

A new study published in Evolution, Medicine, and Public Health indicates that parents who reproduce later in life are more likely to have children who develop autism disorders.

Later reproduction was not, however, associated with increased risk for schizophrenia in offspring.

Multiple studies on this subject for over 30 years have found that risk patterns for these disorders are highly variable and often remain incomparable between public health studies due to substantial differences in study design. Now researchers from the Copenhagen Centre for Social Evolution have analyzed a massive single population sample from Denmark to compare risks based on maternal and paternal age, and parental age difference.

The authors used a sample of about 1.7 million Danish people born between January 1978 and January 2009, out of which approximately 6.5% were diagnosed with autistic or schizophrenic disorders during this time. Their data included the full spectrum of nation-wide autistic and schizophrenic diagnoses for up to 30 years of age and over twenty potentially confounding medical and socio-economic factors that they could statistically control for.

Unique personal identification numbers were used to link individuals' information between different Danish health registries, including the National Patient Registry (holding nationwide hospital admissions since 1977) and the Psychiatric Central Register (with diagnoses for all inpatient admissions since 1969). Combining these data sets also provided the ages of parents when children were born.

Above-average paternal and maternal ages were associated with increased risk of most autistic disorders in offspring and this effect was magnified in offspring of very old fathers. However, advanced

maternal and paternal ages were not associated with higher risk of any schizophrenic disorder. In contrast, children of young parents had reduced risks of autism and only children of very young mothers had increased risks of schizophrenia.

More dissimilarly aged parents meant enhanced risk for both autistic and schizophrenic disorders in offspring compared to parents with similar ages at childbirth, but only up to a certain point where risks leveled out. For example, higher risk for autism in offspring of older fathers (or mothers) would tend to be compensated if they had a child with a much younger partner.

"The magnitude of these increases and decreases in statistical risk need to be scaled against the fortunately rather modest absolute risks of being diagnosed with a mental disorder in Denmark, which is 3.7% for all autistic disorders and 2.8% for all schizophrenic disorders up to 30 years of age. The highest increases and decreases that we could relate to paternal and maternal age added only 0.2-1.8% to these absolute risks, but represented changes in relative risk of 76-104%.", says Dr. Sean Byars, the first author of the study.

The study also discusses why these risk patterns continue to exist in modern humans and suggests that they are remnants of our evolutionary past. In an earlier study of the same population the authors showed that autism risks are associated with above average sizes at birth and schizophrenia risks with smaller (but) still normal sizes at birth. The authors highlight that modern families of 1-3 children now typically originate at ages that our ancestors were completing families of 6-8 children provided these children survived.

"Natural selection has shaped how parents, and particularly mothers, allocated their reproductive investments best in the face of uncertain conditions during our prehistory and well into modern historical times," said Professor Jacobus Boomsma, the senior author of the study. "It was not very long ago that most mothers had their first child around the age of 20 and went through 10 pregnancies. Our modern reproductive patterns are thus a poor match to what humans are likely to be naturally adapted to. Our evolutionary interpretations suggest how we can possibly understand recently increased mental disease risks that have no direct medical explanation."

The paper "Opposite differential risks for autism and schizophrenia based on maternal and paternal age, and parental age differences" is available at:
http://emph.oxfordjournals.org/content/2016/1/286.full

http://bit.ly/2dxPY7D

Serious liver-related condition on the rise in the US

New analysis reveals ACLF represents a substantial and increasing health and economic burden in the United States

A new analysis reveals that cirrhosis and acute on chronic liver failure (ACLF, a deterioration of liver function in patients with cirrhosis that results in the failure of one or more organs) represent a substantial and increasing health and economic burden in the United States.

The number of hospitalizations for cirrhosis nearly doubled from 371,000 in 2001 to 659,000 in 2011. The prevalence of ACLF among those hospitalizations increased from 1.5 percent to 5 percent. The inpatient costs increased twofold for cirrhosis ($4.8 billion to $9.8 billion) and fivefold for ACLF ($320 million to $1.7 billion).

"This study is the first to illustrate the increase in prevalence and cost of ACLF hospitalizations in the U.S., which highlights important public health concerns", said Dr. Alina Allen, lead author of the Hepatology study. "The increasing number of hospitalizations for multiorgan failure in cirrhosis is partly explained by the increase in infectious complications, a recognized leading cause of decompensation and death in this patient population." Dr. Allen added that the care of hospitalized cirrhotic patients in general, and patients with ACLF in particular, is expensive because it requires highly specialized and resource-intensive care, organ-failure support, or liver transplantation.

"Despite major improvements in liver disease management, the care standards seem to be far from optimal, as evident by growing rates of hospitalizations for complications of cirrhosis," she said. "The concerning trends observed in this study will not change without

systematic and coordinated attempts that target healthcare, from risk-factor modification to early diagnosis and better disease management." Although the mortality rates during ACLF hospitalizations decreased over the decade of study, they remained high at 50 percent.

http://bit.ly/2dzno8p

Preliminary Zika vaccines prevent neurological disorders in newborn mice

Two vaccines against Zika virus developed at the University of Pittsburgh School of Medicine have successfully conveyed immunity from female mice to pups conceived weeks after the mother's vaccination.

PITTSBURGH - When challenged with Zika virus within a week of their birth, both vaccines protected the pups against neurological damage better than pups with no maternal-conferred immunity. The results are published online today and scheduled for the November issue of EBioMedicine, a journal supported by Cell Press and The Lancet.

"We've not only developed a promising vaccine candidate to move toward larger preclinical and, eventually, human clinical trials, but also a delivery format that would be inexpensive to produce and distribute to hundreds of thousands of people," said senior author Andrea Gambotto, M.D., associate professor of surgery in Pitt's School of Medicine.

Zika is a virus spread primarily through the bite of an infected mosquito of the Aedes species. When pregnant women are infected, the virus can pass to their fetus, which can damage the developing baby and cause severe neurological birth defects, including microcephaly, or an abnormally small head.

One of the two vaccines uses a "microneedle array" to deliver the vaccine just below the surface of the skin through tiny crystals that dissolve after being affixed to the skin by a Band-Aid-like patch. The technology was co-invented by Louis D. Falo, M.D., Ph.D., chair of Pitt's Department of Dermatology and co-author of the study.

The other vaccine uses the traditional needle delivery format and adenovirus, a type of common cold virus, to present Zika antigens to the immune system to induce immunity.

Both vaccines used proteins on the "envelope," or outer shell, of the virus as the antigen to prime the immune system so it can quickly recognize and fight off the actual virus. This approach has worked in the past to develop West Nile, yellow fever and dengue vaccines.

Three groups of female mice, with five mice per group, were immunized with either one of the two vaccines or a saline solution with no vaccine for the control group. Two weeks after the initial vaccination, the mice received a booster of the same vaccine they originally received.

Blood tests were performed at vaccination and every two weeks afterward. The mice showed immunity against Zika two weeks after immunization with the adenovirus Zika vaccine and six weeks after immunization with the microneedle array Zika vaccine.

Five weeks after initial immunization, the female mice were mated with unvaccinated males. Because mice do not develop microcephaly, giving the mothers Zika while pregnant would be unlikely to affect the pups. So the researchers waited until one week after the pups were born and then exposed them to Zika. All of the pups from the mothers immunized with adenovirus Zika vaccine and half of the pups from the mothers who received the microneedle array vaccine survived infection. Only 12.5 percent of the pups from mothers in the unimmunized control group survived.

Furthermore, all of the control group pups showed signs of neurological damage, including loss of balance, muscle weakness and hind-limb paralysis. Five out of six of the microneedle array group pups also exhibited neurological issues, though they weren't as severe as the control group's symptoms. None of the adenovirus vaccine pups showed significant neurological problems.

Although the adenovirus Zika vaccine definitely performed better in this study, Dr. Gambotto said it was used as a proof-of-principle

vaccine in mice to quickly develop and test if the envelope protein antigen would work in a mouse model. It wouldn't work well in humans because the vast majority of us have already had adenovirus colds so our immune systems would simply neutralize the vaccine and not develop proper Zika antibodies.

"We decided to move forward with the microneedle array Zika vaccine and have since developed a promising, second-generation vaccine," said Dr. Gambotto. "We are hopeful, now that Congress has approved the $1.1 billion bill to provide funding for Zika prevention and research, that we'll be able to do larger-scale studies to evaluate and develop this vaccine for possible human clinical trials in the future."

Additional researchers on this study are Eun Kim, Ph.D., Geza Erdos, Ph.D., Shaohua Huang, Ph.D., and Thomas Kenniston, M.S., all of Pitt.

UPMC and Pitt's Department of Surgery provided funding for this study.

http://bit.ly/2cXSpBy

For women, caffeine could be ally in warding off dementia

2-3 cups of coffee daily associated with 36% reduction in the risk of incident dementia

Among a group of older women, self-reported caffeine consumption of more than 261 mg per day was associated with a 36 percent reduction in the risk of incident dementia over 10 years of follow-up. This level is equivalent to two to three 8-oz cups of coffee per day, five to six 8-oz cups of black tea, or seven to eight 12-ounce cans of cola.

"The mounting evidence of caffeine consumption as a potentially protective factor against cognitive impairment is exciting given that caffeine is also an easily modifiable dietary factor with very few contraindications," said Ira Driscoll, PhD, the study's lead author and a professor of psychology at the University of Wisconsin-Milwaukee. "What is unique about this study is that we had an unprecedented opportunity to examine the relationships between caffeine intake and dementia incidence in a large and well-defined, prospectively-studied cohort of women."

The findings come from participants in the Women's Health Initiative Memory Study, which is funded by the National Heart, Lung, and Blood Institute. Driscoll and her research colleagues used data from 6,467 community-dwelling, postmenopausal women aged 65 and older who reported some level of caffeine consumption. Intake was estimated from questions about coffee, tea, and cola beverage intake, including frequency and serving size.

In 10 years or less of follow-up with annual assessments of cognitive function, 388 of these women received a diagnosis of probable dementia or some form of global cognitive impairment. Those who consumed above the median amount of caffeine for this group (with an average intake of 261 mg per day) were diagnosed at a lower rate than those who fell below the median (with an average intake of 64 mg per day). The researchers adjusted for risk factors such as hormone therapy, age, race, education, body mass index, sleep quality, depression, hypertension, prior cardiovascular disease, diabetes, smoking, and alcohol consumption.

The paper "Relationships Between Caffeine Intake and Risk for Probable Dementia or Global Cognitive Impairment: The Women's Health Initiative Memory Study" is available at: http://biomedgerontology.oxfordjournals.org/content/early/2016/09/20/gerona.glw078

http://bit.ly/2dl9G3B

Study explains how an intestinal microbe protects against other, more dangerous bacteria

Enzyme produced by a common intestinal microbe protects the guts of worms and mammals alike from attack by harmful bacteria

Antibiotics save millions of lives. But their tendency to kill helpful and harmful bacteria alike, coupled with the growing problem of antibiotic resistance, means that they are not without their downside.

Probiotics consisting of beneficial microorganisms, meanwhile, have the potential to deliver the benefits of antibiotics minus the pitfalls. Yet up until now, evidence of their efficacy has been largely anecdotal, their mechanisms of action poorly understood.

Thanks to a pair of papers recently published in Science and Science Immunology by researchers at The Rockefeller University, however, that is beginning to change.

The studies demonstrate that an enzyme produced by a common intestinal microbe can protect the guts of worms and mammals alike from attack by harmful bacteria, and offer important insights into how it does so. Together, their findings could lead to the development of probiotics for use against such dangerous pathogens as Clostridium difficile, a leading cause of hospital-acquired infections.

A bug with therapeutic potential

The researchers set out to investigate the probiotic potential of the microbe Enterococcus faecium in the roundworm Caenorhabditis elegans. Although E. faecium has long been used as a probiotic in livestock, its mode of action has never been clear. And it is far from being an ideal probiotic for use in humans: According to Kavita Rangan, first author of the Science paper and a member of Howard Hang's Laboratory of Chemical Biology and Microbial Pathogenesis, E. faecium readily acquires antibiotic resistance in hospital settings and can lead to dangerous infections in people with compromised immune systems.

Yet in a series of experiments, Rangan and her colleagues demonstrated that when fed E. faecium, C. elegans was better able to resist the harmful effects of infection by Salmonella typhimurium, an intestinal pathogen that in mammals invades the thin layer of epithelial cells lining the gut. "Salmonella was still able to colonize the intestine," says Rangan, "but it didn't cause the same tissue damage to the worms, and it didn't kill them."

What's more, they discovered that a particular enzyme called SagA, which is secreted in abundance by E. faecium, was sufficient to protect both worms and mice from Salmonella. And they showed that SagA worked its magic in mice even when produced by a different microbe called Lactobacillus plantarum--an entirely innocuous bug that is commonly used as a probiotic for human intestinal diseases, and which naturally inhabits environments ranging from sauerkraut to the human gut.

Making good bacteria better

In a series of complementary experiments, Virginia Pedicord--first author of the Science Immunology paper, and a postdoctoral fellow in both the Hang lab and Daniel Mucida's Laboratory of Mucosal Immunology--and colleagues also showed that E. faecium protected mice against S. typhimurium. In addition, they demonstrated that E. faecium prevented the pathogen from passing through the epithelium and invading other organs such as the liver.

Those experiments proved that E. faecium did not protect the mice by attacking S. typhimurium directly or by changing the balance of other microbes in the gut. "It doesn't kill the bacteria, and it doesn't deplete the microbiota, either," Pedicord says. "It just prevents them from causing disease." And it accomplishes this, she explains, by stimulating the production of specialized proteins that prevent pathogens from coming into contact with the epithelial layer in the first place--proteins that are generated by the epithelial cells themselves.

The team confirmed that, as was the case with C. elegans, SagA was by itself sufficient to protect the mice from the ravages of S. typhimurium. And it also identified a clutch of receptors and antimicrobial peptides related to the innate immune system that must be present for the enzyme to do its work.

But perhaps most strikingly, Pedicord and her colleagues showed that, when delivered by L. plantarum, SagA also protected the mice against C. difficile, a pathogen that causes debilitating and sometimes fatal gastroenteritis in human beings.

C. difficile sickens nearly 500,000 people in the United States each year and kills more than 29,000. Long-term antibiotic therapy for other conditions actually heightens the risk of infection, and treatment of C. difficile with antibiotics often leads to relapse.

As a result, the prospect of a benign probiotic that could defend against C. difficile while avoiding the problems associated with antibiotic treatment is welcome news.

"This is something that might really help people," says Pedicord, who is already conducting experiments in mice to see if SagA has an effect on C. difficile recurrence.

http://wb.md/2dK0KX1

Calling It Like It Is: 'Brain Death' Is Death

We are often confused when it comes to the pronouncement of death

Arthur L. Caplan, PhD|October 04, 2016

Hi. I'm Art Caplan at the Division of Medical Ethics at the New York University (NYU) Langone Medical Center.

Death. It's something that we have to talk about with patients and families, and we are often confused when it comes to the pronouncement of death.

There have been a series of cases around the United States in which families who have had a child who has died have been reluctant to accept it because clinicians use the term "brain death." Brain death is something that families often do not understand, and when they learn that their child has brain death, they often do not want to understand it. They want to have hope. They want to believe that something can be done to turn the situation around. When you see situations where a child is dying or you know that death may come for a family you are caring for, a few things are very important to keep in mind.

First, the media commonly confuse people about brain death and coma. I recently did a study[1] with a couple of colleagues of mine at NYU on how brain death is presented in the media. The answer is: very poorly. They mix it up with coma (being unconscious but with the possibility of recovery) and permanent vegetative state (loss of consciousness but not death). Brain death means total and irreversible loss of all organized brain function. Your brain cannot make your heart beat anymore. You cannot breathe anymore—it can only be done artificially. People still see in the media that people allegedly recover from brain death, which is false. They mix it up with things like coma, where people can get better—but that is not brain death. You need to understand that people have biases and they want to hear hope.

When a patient dies or when you are talking to someone about how a loved one may soon die, my recommendation is: Do not use the term "brain death." Say, "They have died." Say the person has "passed away." The reason is because their brain has totally and irreversibly ceased to function. Brain death is one way to die. Cardiopulmonary death is another way to die. But in both instances, they are death. Legally and ethically, they are sufficient. If you use a term like "brain death" with a patient's family, they are going to hear that the brain has died but maybe the rest of the person is still alive. They may hope that somehow the brain can come back. They do not really understand that brain death is death.

We need to be careful in our language. We have to presume that the world of messages about brain death is not accurate, because it's not being well portrayed in movies, television shows, fiction, and other places that people hear about this idea. Death is death. Let's call it that. If someone asks, "How do you know they have died?"—whether it's a child or an adult—you can say, "It's because their heart has stopped" or "Sadly, their brain has ceased to function."

Language matters, and we need to understand this when we come to an area as sensitive as death.

I'm Art Caplan at the Division of Medical Ethics at the NYU Langone Medical Center. Thank you for watching.

Lewis A, Weaver J, Caplan A. Portrayal of brain death in film and television. Am J Transplant. 2016 Sep 19. [Epub ahead of print]

http://bit.ly/2cZOKmI

Archaeogenetics reveals unknown migration in the South Pacific

Archaeogenetic analysis points towards settlers from Melanesia

Only some 3500 years ago people began to colonize the South Pacific archipelagos of Oceania.

An international team of researchers including scientists from the Max Planck Institute for the Science of Human History in Jena now analyzed for the first time, the genomes of the first settlers who lived on the island chains Tonga and Vanuatu 3100-2500 years ago.

The results, published today in Nature contradict common assumptions about the colonization of the region and point to another large and previously unknown migration wave from Melanesia.

A group of people set out from the Solomon Island chain in the southwestern edge of the Pacific Ocean and steered their outrigger canoes toward the horizon more than 3,500 years ago. These people and their descendants were to be the first to cross more than 350 kilometer stretches of open sea into a region known as Remote Oceania.

It was the last great movement of humans to unoccupied but habitable lands.

Now a scientific team led by researchers at Harvard Medical School, University College Dublin, and the Max Planck Institute for the Science of Human History in Jena for the first time have analyzed DNA from people who lived in Tonga and Vanuatu between 2,500 and 3,100 years ago, and were among the first people to live on these islands.

"This is the first genome-wide data on prehistoric humans from the hot tropics, and was made possible by improved methods for preparing skeletal remains" says Ron Pinhasi at University College Dublin, a senior author of the study.

"DNA gets degrades very quickly in tropical climates, however we found that in the very dense inner ear bone, called the petrous bone, DNA is well preserved even under such adverse environmental conditions for thousands of years," says Cosimo Posth, doctoral student at the Max Planck Institute for the Science of Human History in Jena.

Genetic evidence overturn established colonization model

The result of genetic analysis was a big surprise for the research team: the ancient individuals carried no trace of ancestry from people who settled Papua New Guinea more than 40,000 years ago, in contrast to all present-day Pacific islanders who derive at least one-quarter of their ancestry from Papuans.

Instead, the early islanders resemble genetically people who live in China and Taiwan. This means - contrary to previous assumptions - that the Remote Oceanian pioneers swept past the archipelago that surrounds New Guinea without much mating with local people.

"A major and not previously recognized migration must have spread the Papuan ancestry that is found everywhere in the Pacific today " says David Reich, a senior author at Harvard Medical School and at the Howard Hughes Medical Institute.

"The unexpected results about Oceanian history highlight the power of ancient DNA to overthrow established models of the human past", says Johannes Krause, Director at the Max Planck Institute for the Science of Human History in Jena.

"A particularly striking finding is the different ancestry observed on the X-chromosome, which is inherited mainly from females" says lead author Pontus Skoglund of Harvard Medical School and Stockholm University. "This reveals that the vast majority of the ancestry from these open water pioneers that survives today is derived from females, showing how DNA information can provide insights into cultural processes in ancient societies".

Original publication: Pontus Skoglund, Cosimo Posth, Kendra Sirak, Matthew Spriggs, Frederique Valentin, Stuart Bedford, Geoffrey A. Clark, Christian Reepmeyer, Fiona Petchey, Daniel Fernandes, Qiaomei Fu, Eadaoin Harney, Mark Lipson, Swapan Mallick, Mario Novak, Nadin Rohland, Kristin Stewardson, Syafiq Abdullah, Murray P. Cox, Françoise R. Friedlaender, Jonathan S. Friedlaender, Toomas Kivisild, George Koki, Pradiptajati Kusuma, D. Andrew Merriwether, Francois-X. Ricaut, Joseph T. S. Wee, Nick Patterson, Johannes Krause5, Ron Pinhasi, and David Reich

Ancient genomics and the peopling of the Southwest Pacific Nature, published online, 3 October 2016

http://bit.ly/2dOb2aM

Revising the meaning of 'prion'

A team of Whitehead Institute and Stanford University scientists are redefining what it means to be a prion--a type of protein that can pass heritable traits from cell to cell by its structure instead of by DNA.

CAMBRIDGE, Mass. - Although prions are infamous for causing Creutzfeld-Jakob disease, fatal familial insomnia, and bovine spongiform encephalopathy, commonly known as mad cow's disease, the present study indicates that prions identified in yeast, and possibly in plants, and other organisms may be beneficial.

All prions identified thus far share defining characteristics, including the ability to fold into a self-perpetuating conformation, efficient transmission when the contents of a prion-containing cell are injected into a "naïve" cell (a technique known as cytoplasmic transfer), and the ability to form large aggregates of similarly folded proteins, called amyloids. The biological importance of these molecules is underscored by the presence of cellular machines that evolved to propagate prions. One helper protein, called Hsp104, dices up prion aggregates into smaller "seeds" that are passed from a mother to all or almost all daughter cells and confer dominant traits.

To assess the breadth of such protein-based inheritance, the lab of Whitehead Member Susan Lindquist lab devised an unbiased screen that examines all proteins in yeast for those capable of producing stable phenotypes that are passed from mother to daughter cells for at least 100 generations. The screen and its outcome are described in this week's issue of the journal Cell.

When they scrutinized the results, the team noted that most of the 46 prion prospects lack some conventional characteristics, specifically amyloid formation and the dependence on a helper protein to transform the amyloid into heritable seeds. Nevertheless, their protein-conformation dependent traits are dominantly inherited from mother cells to all daughter cells and could be transmitted via cytoplasmic transfer--two key prion traits. Interestingly, most of the identified "molecular memories" help yeast cells adapt to varied stressful environments.

Unlike canonical prions, which are noted for creating specific structures, these proteins contained large sections that are intrinsically disordered, meaning that those domains lack a fixed three-dimensional architecture. In this way, they are related to human proteins that also have prion-like characteristics. According to Sohini Chakrabortee, lead author of the Cell paper, the physical flexibility of intrinsically disordered proteins could allow them to fulfill a variety of roles in a cell, from an enzyme to a chaperone protein like Hsp70. When the team examined the human cognates of the prion-proteins, the intrinsically disordered domains were conserved over hundreds of millions of years.

"This conservation over millennia could be because these proteins are vastly beneficial in nature," says Chakrabortee, who is currently Research Development Officer for European and International Funding for the University of Birmingham, United Kingdom.

For Chakrabortee, the unbiased screen has called into question the fundamental assumptions surrounding prions.

"We don't know how deep is the ocean," she says about the pool of potential prions. "This opens up new directions, and we're just starting to look into what these proteins do and their impact. This screen just gives us a taste of the breadth of prions and protein-based inheritance."

This work was supported by the National Institutes of Health (NIH grants R00-GM098600, NIH-DP2-GM119140, T32-GM007790, F32-GM109680), the Searle Scholars Program (14-SSP-210), Sidney Kimmel Foundation (SKF-15-154), the David and Lucile Packard Foundation, the Howard Hughes Medical Institute (HHMI), the Harold and Leila Mathers Charitable Foundation, the Eleanor Schwartz Charitable Foundation, the Broodbank Trust, Hughes Hall fellowship (University of Cambridge), the Ford Foundation, Stanford University, and the Stanford Summer Research Program/Amgen Scholars Program.

Susan Lindquist's primary affiliation is with Whitehead Institute for Biomedical Research, where her laboratory is located and all her research is conducted. She is also a Howard Hughes Medical Institute investigator and a professor of biology at Massachusetts Institute of Technology.

Full Citation:"Intrinsically disordered proteins drive emergence and inheritance of biological traits" Cell, October 6, 2016.

Sohini Chakrabortee (1,6,8), James S. Byers (2,6), Sandra Jones (1,9), David M. Garcia (3), Bhupinder Bhullar (1,10), Amelia Chang (4,11), Richard She (3), Laura Lee (4), Brayon Fremin (3,7), Susan Lindquist (1,5), Daniel F. Jarosz (2,3).
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http://bit.ly/2d3w14M

Protein linked to high risk of Alzheimer's can be removed from brain without hindering learning

Protein can be removed from the brains of mice without hindering memory and learning

DALLAS - A protein linked to higher risk of Alzheimer's can be removed from the brains of mice without hindering memory and learning, according to a study that addresses whether potential therapeutics targeting this protein would have detrimental side effects.

The study from the Peter O'Donnell Jr. Brain Institute also showed, however, that the protein's absence in other parts of the body hinders brain function as blood cholesterol levels rise. This result substantiates previous research that indicated cardiovascular health affects the brain.

Researchers focused on the removal of apolipoprotein E (ApoE), which in a certain form can support the buildup of toxic plaques in the brains of Alzheimer's patients. Studies elsewhere have sought to determine whether reducing ApoE could be an effective treatment in preventing the disease, but a lingering question has been whether the protein is necessary for healthy brain function.

The study found that mice can maintain their learning and memory when virtually all ApoE is removed from the brain but kept present in the liver to filter cholesterol. Mice that lacked ApoE in both the brain and liver experienced unhealthy cholesterol levels and lost cognitive function.

More research is needed to determine what causes the cardiovascular issues to affect the brain, said Dr. Joachim Herz, the study's Principal Investigator and Professor of Molecular Genetics, Neuroscience, Neurology and Neurotherapeutics at the O'Donnell Brain Institute at UT Southwestern Medical Center.

But the findings, published in The Journal of Neuroscience, add support to the belief that reducing ApoE in the brain could eventually be a viable therapeutic option for treating Alzheimer's.

"This approach still holds potential," said Dr. Herz, holder of the Thomas O. and Cinda Hicks Family Distinguished Chair in Alzheimer's Disease Research and Director of the Center for Translational Neurodegeneration Research.

ApoE has several roles in the body, including transporting cholesterol and related molecules such as β-amyloid that form plaques in the brains of Alzheimer's patients if not properly filtered or removed.

The type of ApoE produced by the ApoE gene determines how effectively the amyloid is removed from the brain. ApoE2 is the most effective, ApoE3 is in the middle and ApoE4 is the most likely to allow for the buildup of amyloid plaques. People whose genes produce ApoE4 are at high risk of developing Alzheimer's.

Studies are ongoing at UT Southwestern and elsewhere to further understand the various effects that ApoE4 removal has on brain and body function.

The latest study was performed by Courtney Lane-Donovan, a Medical Science Training Program student in her final clinical year with her colleagues and co-authors Wen Mai Wong, Dr. Murat S. Durakoglugil, Dr. Catherine R. Wasser, Dr. Shan Jiang, and Dr. Xunde Xian in the Department of Molecular Genetics and the Center for Translational Neurodegeneration Research.

The research was supported with funding from the National Institutes of Health, the American Health Assistance Foundation, the Consortium for Frontotemporal Dementia Research, the Bright Focus Foundation, the Lupe Murchison Foundation, and the Ted Nash Long Life Foundation.

http://bit.ly/2dVZCOw

Brain study reveals how teens learn differently than adults

Columbia-led research finds adolescents' ability to remember is closely linked to reward-learning behavior

NEW YORK - Scientists have uncovered a unique feature of the adolescent brain that enriches teens' ability to learn and form memories: the coordinated activity of two distinct brain regions. This observation, which stands in contrast to the adult brain, may be related to teens' oft-derided affinity for reward-seeking behavior.

These findings suggest that such behavior is not necessarily detrimental, but instead may be a critical feature of adolescence and the maturing brain.

The results of this research were published today in Neuron.

"Studies of the adolescent brain often focus on the negative effects of teens' reward-seeking behavior. However, we hypothesized that this tendency may be tied to better learning," said Daphna Shohamy, PhD, a principal investigator at Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute and associate professor of psychology at Columbia.

"Using a combination of learning tasks and brain imaging in teens and adults, we identified patterns of brain activity in adolescents that support learning -- serving to guide them successfully into adulthood."

For this study, which involved 41 teens and 31 adults, the authors initially focused on a brain region called the striatum.

Previous research has shown that the striatum coordinates many aspects of higher brain function, from planning to decision making. But it is most well-known for its role in something called reinforcement learning.

"In simplest terms, reinforcement learning is making a guess, being told whether you're right or wrong, and using that information to make a better guess next time," said Juliet Davidow, PhD, the paper's first author, who completed this research while earning her doctorate in psychology at Columbia and is now a postdoctoral fellow at Harvard University.

For example, imagine you are given a series of cards with numbers on them and are asked to guess the next number in the sequence.

"If you guess right, the striatum shows activity that corresponds to that positive feedback, thus reinforcing your choice," Dr. Davidow explained. "Essentially, it is a reward signal that helps the brain learn how to repeat the successful choice again."

Because of teens' inclination toward reward-seeking behavior, the researchers proposed that this age group would outpace adults in terms of reinforcement learning by showing a greater affinity for rewards. This hypothesis was confirmed after asking both groups to perform a series of learning tasks.

To see what was happening in the brain, Dr. Shohamy teamed up with Adriana Galván, PhD. Dr. Galván, who is an associate professor of psychology and faculty member of the Brain Research Institute at the University of California, Los Angeles, is an expert in brain imaging in teenagers.

Together, they scanned the brains of each participant with functional magnetic resonance imaging (fMRI) while they were performing the learning tasks. The authors hypothesized that the teens' superior abilities were due to a hyperactive striatum.

"But surprisingly, when we compared the brains of teens to those of adults, we found no difference in reward-related striatal activity between the two groups," said Dr. Davidow. "We discovered that the difference between adults and teens lay not in the striatum but in a nearby region: the hippocampus."

The hippocampus is the brain's memory headquarters. And while important for storing memories of events, places or individuals, it is not typically related to reinforcement learning. But in this study, the authors' fMRI analysis revealed an uptick in hippocampal activity for teens -- but not adults -- during reinforcement learning. Moreover, that activity seemed to be tightly coordinated with activity in the striatum.

To investigate this connection, the researchers slipped in random and irrelevant pictures of objects into the learning tasks, such as a globe or a pencil.

The images -- which had no bearing on whether the participants guessed right or wrong -- served as a kind of background noise during the tasks.

When asked later on, both adults and teens remembered seeing some of the objects, but not others. However, only in the teens was the memory of the objects associated with reinforcement learning, an observation that was related to connectivity between the hippocampus and striatum in the teen brain.

"What we can take from these results isn't that teens necessarily have better memory, in general, but rather the way in which they remember is different," said Dr. Shohamy, who is also a member of Columbia's Kavli Institute for Brain Science. "By connecting two things that aren't intrinsically connected, the adolescent brain may be trying to build a richer understanding of its surroundings during an important stage in life."

Indeed, studies have shown that adolescence is a pivotal time when powerful memories are formed, which the authors argue could be due to this enhanced connectivity between the hippocampus and striatum.

"Broadly speaking, adolescence is a time when teens begin to develop their independence," said Dr. Shohamy.

"What more could a brain need to do during this period than jump into learning overdrive? It may be that the uniqueness of the teen brain may drive not only how they learn, but how they use information to prime themselves for adulthood."

This paper is titled: "An upside to reward sensitivity: The hippocampus supports enhanced reinforcement learning in adolescence." Additional coauthors include Karin Foerde, PhD, assistant professor of psychology at New York University.

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The authors report no financial or other conflicts of interest.

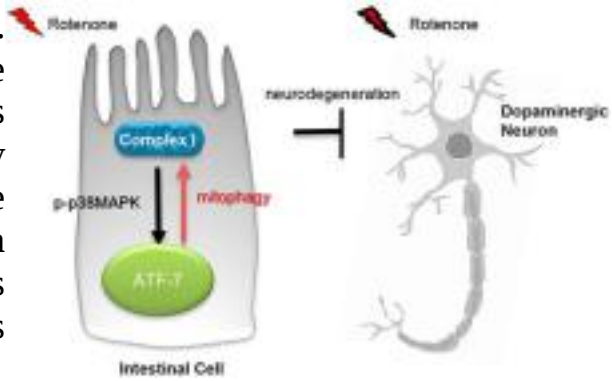
http://bit.ly/2dc3Wvn

Parkinson's disease protection may begin in the gut

University of Iowa researchers find intestinal cells' immune response protects vital neurons

Your gut may play a pivotal role in preventing the onset of Parkinson's disease. And the reason may be its knack for sleuthing.

Researchers at the University of Iowa have found that the gut may be key to preventing Parkinson's disease. Cells located in the intestine spark an immune response that protects nerve cells, or neurons, against damage connected with Parkinson's disease. Acting like detectives, the immune intestinal cells identify damaged machinery within neurons and discard the defective parts. That action ultimately preserves neurons whose impairment or death is known to cause Parkinson's.



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"We think somehow the gut is protecting neurons," says Veena Prahlad, assistant professor in biology at the UI and corresponding author on the paper published Aug. 30 in the journal Cell Reports.

Parkinson's disease is a brain disorder that erodes motor control and balance over time. It affects some 500,000 people in the U.S., according to the National Institutes of Health. The disease occurs when neurons--nerve cells--in the brain that control movement become impaired or die. Normally, these neurons produce dopamine,

and when they are damaged or killed, the resulting dopamine shortage causes the motor-control problems associated with the disease.

Scientists have previously linked Parkinson's to defects in mitochondria, the energy-producing machinery found in every human cell. Why and how mitochondrial defects affect neurons remain a mystery. Some think the impaired mitochondria starve neurons of energy; others believe they produce a neuron-harming molecule. Whatever the answer, damaged mitochondria have been linked to other nervous disorders as well, including ALS and Alzheimer's, and researchers want to understand why.

Prahlad's team exposed roundworms to a poison called rotenone, which researchers know kills neurons whose death is linked to Parkinson's. As expected, the rotenone began damaging the mitochondria in the worms' neurons. To the researchers' surprise, though, the damaged mitochondria did not kill all of the worms' dopamine-producing neurons; in fact, over a series of trials, an average of only seven percent of the worms, roughly 210 out of 3,000, lost dopamine-producing neurons when given the poison. "That seemed intriguing, and we wondered whether there was some innate mechanism to protect the animal from the rotenone," Prahlad says.

It turns out there was. The roundworms' immune defenses, activated when the rotenone was introduced, discarded many of the defected mitochondria, halting a sequence that would've led to the loss of dopamine-producing neurons. Importantly, the immune response originated in the intestine, not the nervous system.

"If we can understand how this is done in the roundworm, we can understand how this may happen in mammals," Prahlad says.

The researchers plan to conduct more experiments, but they've got some interesting hypotheses. One is the intestinal immune cells are, according to Prahlad, "constantly surveilling mitochondria for defects."

Even more, those cellular watchdogs may be keeping their eyes on the mitochondria "because they don't trust them," Prahlad suggests. The reason has to do with the prevailing theory that mitochondria originated independently as a type of bacterium and were only later incorporated into the cells of animal, plants, and fungi as an energy producer.

If that theory is correct, the intestinal immune responders may be especially sensitive to changes in mitochondrial function not only for its potential damaging effects, but because of the mitochondria's ancient and foreign past as well.

"How it's happening is suggestive of the possibility that the innate immune response is constantly checking its mitochondria," Prahlad says, "perhaps because of the bacterial origin of the mitochondria."

The paper is titled, "The Mitochondria-Regulated Immune Pathway Activated in the C. elegans Intestine Is Neuroprotective." The first author is Madhusudana Rao Chikka, who was a postdoctoral researcher at the UI during the study and who helped design and execute the experiments. Contributing authors, all from UI's biology department, include Charumathi Anbalagan, Katherine Dvorak, and Kyle Dombeck.

The nonprofit Ellison Medical Foundation funded the study.

http://bit.ly/2d3SIpx

Humans May Have Reached Maximum Life Span

There may be a limit to how long humans can live, according to a new study.

By Agata Blaszczak-Boxe

The oldest known person was Jeanne Calment, a French woman who died in 1997 at age 122. Calment's longevity record is unlikely to be broken, the researchers said.

"In contrast to previous suggestions that human longevity can be extended ever further, our data strongly suggest that the duration of life is limited," the researchers wrote in their study, published today (Oct. 5) in the journal Nature.

However, the new findings don't mean that researchers know for sure that humans will never live longer than 122 years, said Steven Austad, a professor of biology and aging at the University of Alabama at Birmingham, who was not involved in the study. He said that scientists used to believe that the limit to the human life span was 110

years until somebody lived to be older than that, which shows that it is tough to predict what this limit can be for humans.

In the new study, the researchers looked at the Human Mortality Database, an international database with detailed mortality data that's maintained by researchers at the University of California, Berkeley and the Max Plank Institutes in Germany. The database contains information on how long people have lived in recent decades in many countries.

The researchers found that, in at least 40 countries and territories, the number of people surviving to age 70 and older has increased since 1900. This suggests that people's life expectancy, or the estimate of how long a person may expect to live, has increased.

However, if there is no limit to how long people can live, then the greatest increases in survival rates over time should have occurred among those people who are the oldest, the researchers hypothesized. But the data showed that the greatest increase in survival rates among people in the oldest age groups in most countries peaked around 1980, and has not changed since. This may suggest that, after all, there may be a natural limit to how long people can live, the researchers said.

The scientists also looked to see how old the very oldest people were when they died. They focused on deaths between 1968 and 2006, in France, Japan, the United Kingdom and the United States, which are the four countries with the largest numbers of people who have lived longer than 110 years, according to the International Database on Longevity. The researchers also looked at the maximum reported age at death between 1972 and 2015 reported by another source, called the Gerontology Research Group.

The researchers found that, though the maximum reported age at death did increase until the 1990s, it has actually plateaued, and even slightly decreased since the time Jeanne Calment died. But Austad said that the human life span could likely still be extended. Experiments on mice have shown that these animals live longer if their calorie intake is restricted or if their genes are manipulated, he said. If researchers found medications or lifestyle factors such as special diets that are better than the ones known today, that could allow humans to live longer, too, he said.

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Children with fatal muscle disease walk after drug breakthrough

"TO SEE children who would have been dead sitting and standing is something I never thought I would see."

By Michael Le Page

Francesco Muntoni, at University College London, is talking about videos of children given an experimental drug for treating spinal muscular atrophy. This genetic disorder involves the deterioration of nerves connecting the brain and spinal cord to the body's muscles. Children with the severest form can't sit upright and seldom survive past the age of 2. Yet a few parents have posted videos online showing children given the drug, called nusinersen, who appear to be sitting and even walking with assistance.

The trial of nusinersen was stopped in August when it became clear it was effective, making it unethical not to give the real drug to those on the placebo.

The full results haven't yet been published, but what has been revealed so far of this "antisense" therapy suggests we have overcome the biggest obstacle – how to deliver such therapies – at least in disorders that affect the nervous system. The breakthrough could open the floodgates for similar treatments for neurological conditions such as Huntington's, motor neurone disease and possibly even Alzheimer's.

Antisense drugs are essentially pieces of DNA that bind to specific RNAs – the recipe that cells use to make proteins. By binding to RNAs, they can block the production of proteins, or alter their form.

These drugs have the potential to prevent or cure many diseases. But there's been a huge snag: if naked DNA is injected into people, it doesn't last long, let alone get into cells. So biologists have spent

decades trying to create synthetic forms that can survive in the body. They have strengthened the DNA backbone, for example, to prevent these drugs being broken down and also made them bind more strongly to RNA. They have also made tweaks that help them enter nerve cells.

Nusinersen is one such modified antisense drug. Reports of its success have created great excitement among parents of children with spinal muscular atrophy, but we need to be cautious about individual reports, says neuroscientist James Sleigh at the University of Oxford.

Even if the final results show nusinersen doesn't work as well as hoped, there is still cause for optimism. Animal studies, and postmortems of children who died despite being given nusinersen, show widespread distribution of the antisense molecule in the brain and spinal cord, says Muntoni, who has helped develop and test therapies such as nusinersen.

These findings, and others, show it is possible to get antisense molecules into nerve cells, meaning improved versions should soon become available. "It became clear that the drug was effective, meaning it was unethical to keep giving the placebo"

"I think it will happen surprisingly quickly," says Edward Wild at University College London's Huntington's Disease Centre, who is part of a team testing an antisense drug for Huntington's disease.

This inherited condition remains untreatable despite decades of attempts to develop therapies. With the delivery problem seemingly cracked, Wild thinks that will soon change. The Huntington's antisense drug that Wild's team is trialling has passed initial safety tests with flying colours.

Such therapies could be used to treat a range of disorders, possibly including Alzheimer's. There is no single mutation that causes Alzheimer's, says Wild, but we know of several gene variations that increase the risk of the disease. In theory, blocking the production of proteins encoded by these genes could delay or prevent people becoming ill.

The downside of antisense treatments is that repeat doses are required at least every few months, and often for life. The drugs have to be injected directly into the cerebrospinal fluid, which flows around the brain and spine. This procedure, called a lumbar puncture, can cause side effects including headaches and back pain.

But Muntoni and colleagues may have found a way to modify the antisense molecules so they can cross the blood-brain barrier, meaning they can be injected into the bloodstream. Animal studies published last month suggest this approach works well, Sleigh says, but it has not yet been tested in people.

The advent of therapies for genetic conditions considered untreatable could change the way we approach them. If treatments become available for childhood disorders such as spinal muscular atrophy, it will mean children should be tested for the condition at birth so they can begin therapy as soon as possible.

It could also change the way adults approach genetic sequencing of their own genes. At present, most people who have their genome sequenced opt not to find out if they have inherited diseases such as Huntington's, preferring not to know their fate. But if it becomes treatable and perhaps even preventable, they may wish to start therapies early. "As soon as we have something that works, people will want to get tested," says Wild.

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We're All a Little Biased, Even if We Don't Know It

Researchers in the growing field of implicit bias say all of us have biases that are hidden even to ourselves.

Emily Badger OCT. 5, 2016

One of the newest chew toys in the presidential campaign is "implicit bias," a term Mike Pence repeatedly took exception to in the vice-presidential debate on Tuesday.

Police officers hear all this badmouthing, said Mr. Pence, Donald J. Trump's running mate, in response to a question about whether society demands too much of law enforcement. They hear politicians

painting them with one broad brush, with disdain, with automatic cries of implicit bias. He criticized Hillary Clinton for saying, in the first presidential debate, that everyone experiences implicit bias. He suggested a black police officer who shoots a black civilian could not logically experience such bias.

"Senator, please," Mr. Pence said, addressing his Democratic opponent, Tim Kaine, "enough of this seeking every opportunity to demean law enforcement broadly by making the accusation of implicit bias every time tragedy occurs."

The concept, in his words, came across as an insult, a put-down on par with branding police as racists. Many Americans may hear it as academic code for "racist." But that connotation does not line up with scientific research on what implicit bias is and how it really operates.

Researchers in this growing field say it isn't just white police officers, but all of us, who have biases that are subconscious, hidden even to ourselves.

Implicit bias is the mind's way of making uncontrolled and automatic associations between two concepts very quickly. In many forms, implicit bias is a healthy human adaptation — it's among the mental tools that help you mindlessly navigate your commute each morning. It crops up in contexts far beyond policing and race (if you make the rote assumption that fruit stands have fresher produce, that's implicit bias). But the same process can also take the form of unconsciously associating certain identities, like African-American, with undesirable attributes, like violence.

The science of how this submerged bias affects your actions is still a work in progress; studies have found a link between the biases and specific actions in some situations but not others. But because this bias is a function of universal human psychology, researchers say, we all experience it — and you can't exactly get "rid" of it.

Well-intentioned people may also hold implicit biases that run counter to their stated values. That's why it's hard to square Mr. Pence's description with the science. To broach implicit bias isn't to impugn someone's values; it's to recognize that our values compete on an unconscious level with all the stereotypes we absorb from the world around us. And even black police officers aren't immune to internalizing them.

"These types of cultural biases are like smog in the air," Jennifer Richeson, a Yale psychologist, wrote in an email, citing an analogy often used by a former president of Spelman College, Beverly Daniel Tatum. "To live and grow up in our culture, then, is to 'take in' these cultural messages and biases and do so largely unconsciously."

In the context of race, implicit bias is considered a particularly important idea because it acknowledges forces beyond bigotry that perpetuate inequality. If we talk less about it, as Mr. Pence suggested — this "really has got to stop," he said Tuesday night — we lose vocabulary that allows us to confront racial disparities without focusing on the character of individual people.

"You're removing the language that allows you talk about the mechanism of inequality," said Phillip Atiba Goff, the president of the Center for Policing Equity at John Jay College of Criminal Justice and a professor there. "If you take away that language, what that means is inequality gets stronger and justice gets weaker. It really gets that serious."

Mr. Goff said he hears objections similar to Mr. Pence's every time he gives presentations or leads training sessions with police departments. "Someone will say, 'I'm tired of being called a racist,' " he said. To which he explains that racism and implicit bias aren't interchangeable.

"That wrong formulation is so ingrained," Mr. Goff said. "That's what's dangerous. It's so easy to call it a slight, and if that metastasizes in our political discourse, we really have lost out on an incredible opportunity to take great strides forward."

He fears that implicit bias could become a political trope, dismissed as an insult and not as science, or worse, tugged into the realm of political correctness. He acknowledges that the left mistreats the topic,

too, citing implicit bias as a catchall to explain all the forces of racial unfairness in society that aren't bigotry.

In fact, implicit bias is just one of many psychological processes that shape how we interact with one another. We also tend to be better at remembering the faces of people in our own racial group, or to subconsciously favor people in our group. The fear of being stereotyped psychologically weighs on people, too. In police training, Mr. Goff has watched officers using other kinds of mental shortcuts in which they assume "active shooters" must be men. He now talks more broadly about "identity traps" that encompass implicit biases and much more.

The challenge, he argues, isn't to eliminate biases, but to try to interrupt them so we can act more often in ways that line up with our values. Researchers, though, still have a lot to learn about how to do that. And it would be unfortunate, Mr. Goff argued, if implicit bias became politically unmentionable right at the moment when science was trying to uncover the answer.

For now, laboratory simulations don't easily translate to the real world, and it's hard to convert beliefs into behaviors. It's unclear how well nascent police training programs work. And police officers are not the only ones facing implicit-bias training — this fall, the home-sharing company Airbnb announced it planned to offer such a program to its hosts. It's not clear that will work, either.

Tony Greenwald, a professor of psychology at the University of Washington, said training can even backfire, as a result of another tendency we have: People who attend programs like these may falsely believe they've rooted out their biases and so don't need to worry about them any more.

"Just wanting to eliminate implicit bias is not sufficient," Mr. Greenwald said. "You can't unlearn implicit biases. We live in a society and culture where the influences that create these are so strong and pervasive, that we're not going to get rid of those influences in any short period."

http://bit.ly/2e1fuAx

Protein-like structures from the primordial soup

Primordial lifelike structures could well have been proteinaceous aggregates, or amyloids

The story starts at least four billion years ago, when there was no living matter on the planet. Sometime around then, smaller chemical compounds formed into larger organised structures capable of self-reproduction. And so the early precursors of life were born. Exactly which molecules were involved, and what they were made of, is the biggest puzzle in evolutionary history.

However, ETH Professor Roland Riek and his senior scientist Jason Greenwald have a compelling idea: these primordial lifelike structures could well have been proteinaceous aggregates, or amyloids. The latest results of their laboratory research now lend weight to their hypothesis.

The scientists performed an experiment to demonstrate that it is remarkably easy for such amyloid structures to assemble spontaneously from building blocks that existed on the prebiotic Earth, and under reaction conditions that also seem plausible for the primeval era. The scientists used four simple amino acids as starting materials: glycine, alanine, aspartate and valine. In addition, they used carbonyl sulphide as a catalyst for the reaction. This volcanic gas is also likely to have existed in the atmosphere billions of years ago.

Long sheet structures

In the laboratory experiment, the amino acid molecules spontaneously assembled, with the help the carbonyl sulphide, into short chains (peptides) comprising between 5 and 14 building blocks. These chains in turn arranged themselves in parallel into amyloid structures known as beta sheets. In the experiment, these sheet structures took the form of fibres and typically comprised thousands of adjoining peptide chains which the scientists were able to identify using an electron microscope.

To make sure the amino acid molecules formed into sufficiently long peptide chains, the scientists had to use a clever trick. "Simply mixing amino acids with carbonyl sulphide in a test tube only produces very short peptide chains which do not assemble into a sheet structure", Greenwald explains. The scientists therefore slowly dripped amino acid molecules activated with carbonyl sulphide into a test tube in a procedure lasting several hours. "It is conceivable that an equally slow process - possibly taking several years - with a steady flow of new chemical compounds may well have taken place in the Earth's primeval history", says Greenwald.

Catalytic effect

Scientists have already proposed amyloids as candidates for the very first lifelike structures on Earth, as even simple amyloids are capable of performing certain chemical functions. Last year, for example, Professor Riek and his team discovered amyloid structures able to split esters.

The ETH scientists stress, however, that there is still an important piece of the puzzle missing from their argument in support of the "amyloid hypothesis": Are amyloids also capable of self-replication, just like RNA molecules? This is conceivable, claim Riek and Greenwald, but there is still no experimental evidence to support it. The professor and his team are working on it.

Amyloids more likely than exclusively RNA

Even so, the researchers already describe their hypothesis as being much more plausible than the decades-old scientific assumption that the precursors of life were made up solely of RNA molecules. The scientists' main contention: RNA molecules with a biological function are comparatively large and complex. "They are so big that it would have been difficult for them to form spontaneously. Even with far simpler structures, amyloids exhibit certain chemical functions", says Greenwald. On top of that, the building blocks of RNA are more complex than those of amyloids and proteins. Furthermore, the latter are more stable even under harsh environmental conditions. "All this makes it plausible that the first functional molecules were amyloids", concludes Professor Riek.

http://bit.ly/2do8sVc

Researchers activate repair program for nerve fibers

Releasing molecular brake allowed damaged neurons to regenerate

Human nerve cells are interconnected in a network that extends to all parts of the body. In this way control signals are transmitted from head to toe, while sensory inputs flow in the opposite direction. For this to happen, impulses are passed from neuron to neuron, not unlike a relay race. Damages to this wiring system can have drastic consequences - particularly if they affect the brain or the spinal cord. This is because the cells of the central nervous system are connected by long projections. When severed, these projections, which are called "axons", are unable to regrow.

Reawakening a lost talent

Neural pathways that have been injured can only regenerate if new connections arise between the affected cells. In a sense, the neurons have to stretch out their arms, i.e. the axons have to grow. In fact, this happens in the early stages of embryonic development. However, this ability disappears in the adult. Can it be reactivated? This was the question Professor Bradke and co-workers asked themselves. "We started from the hypothesis that neurons actively down-regulate their growth program once they have reached other cells, so that they don't overshoot the mark. This means, there should be a braking mechanism that is triggered as soon as a neuron connects to others," says Dr. Andrea Tedeschi, a member of the Bradke Lab and first author of the current publication.

Searching through the genome

In mice and cell cultures, the scientists started an extensive search for genes that regulate the growth of neurons. "That was like looking for the proverbial needle in the haystack. There are hundreds of active genes in every nerve cell, depending on its stage of development. To analyze the large data set we heavily relied on bioinformatics. To this

end, we cooperated closely with colleagues at the University of Bonn," says Bradke. "Ultimately, we were able to identify a promising candidate. This gene, known as Cacna2d2, plays an important role in synapse formation and function, in other words in bridging the final gap between nerve cells." During further experiments, the researchers modified the gene's activity, e.g. by deactivating it. In this way, they were able to prove that Cacna2d2 does actually influence axonal growth and the regeneration of nerve fibers.

Pregabalin triggered neuronal growth

Cacna2d2 encodes the blueprint of a protein that is part of a larger molecular complex. The protein anchors ion channels in the cell membrane that regulate the flow of calcium particles into the cell. Calcium levels affect cellular processes such as the release of neurotransmitters. These ion channels are therefore essential for the communication between neurons.

In further investigations, the researchers used Pregabalin (PGB), a drug that had long been known to bind to the molecular anchors of calcium channels. Over a period of several weeks, they administered PGB to mice with spinal cord injuries. As it turned out, this treatment caused new nerve connections to grow.

"Our study shows that synapse formation acts as a powerful switch that restrains axonal growth. A clinically-relevant drug can manipulate this effect," says Bradke. In fact, PGB is already being used to treat lesions of the spinal cord, albeit it is applied as a pain killer and relatively late after the injury has occurred. "PGB might have a regenerative effect in patients, if it is given soon enough. In the long term this could lead to a new treatment approach. However, we don't know yet."

A new mechanism?

In previous studies, the DZNE researchers showed that certain cancer drugs can also cause damaged nerve connections to regrow. The main protagonists in this process are the "microtubules", long protein complexes that stabilize the cell body. When the microtubules grow, axons do as well. Is there a connection between the different findings? "We don't know whether these mechanisms are independent or whether they are somehow related," says Bradke. "This is something we want to examine more closely in the future."

Original Publication

„The Calcium Channel Subunit Alpha2delta2 Suppresses Axon Regeneration in the Adult CNS", Andrea Tedeschi, Sebastian Dupraz, Claudia J. Laskowski, Jia Xue, Thomas Ulas, Marc Beyer, Joachim L. Schultze, Frank Bradke, Neuron, DOI: 10.1016/j.neuron.2016.09.026

http://bit.ly/2do9hqK

Human neurons continue to migrate after birth, research finds

UCSF study reveals previously unrecognized stage of brain development

Researchers at UC San Francisco have discovered a previously unknown mass migration of inhibitory neurons into the brain's frontal cortex during the first few months after birth, revealing a stage of brain development that had previously gone unrecognized. The authors hypothesize that this late-stage migration may play a role in establishing fundamentally human cognitive abilities and that its disruption could underlie a number of neurodevelopmental diseases.

Most neurons of the cerebral cortex - the outermost layer of the brain responsible for advanced cognition - migrate outward from their birthplaces deep in the brain to take up their positions within the cortex. Developmental neuroscientists have long thought that most neural migration ends well before an infant is born, but the new paper -- published October 6, 2016 in Science -- suggests for the first time that many neurons continue to migrate and integrate into neural circuits well into infancy.

"The dogma among developmental neuroscientists was that after birth all that was left was the fine wiring and pruning," said Mercedes Paredes, MD, PhD, an assistant professor of neurology at UCSF and leader of the new study. "These results suggest there's a whole new phase of human brain development that we had never noticed before."

Study of donated brain tissue unveils massive neural migration after birth

The new study was a collaboration between the labs of co-senior authors Arturo Alvarez-Buylla, PhD, a UCSF professor of neurological surgery who specializes in understanding the migration of immature neurons in the developing brain, and in whose lab Paredes is a postdoctoral researcher, and Eric J. Huang, MD, PhD, a professor of pathology and director of the Pediatric Brain Tissue Bank at the UCSF Newborn Brain Research Institute.

Several recent studies - including work by Alvarez-Buylla and Huang - identified small populations of immature neurons deep in the front of the brain that migrate after birth into the orbito-frontal cortex -- a small region of the frontal cortex just above the eyes. Given that the entire frontal cortex continues to expand massively after birth, the researchers sought to discover whether neural migration continues after birth in the rest of the frontal cortex.

The team examined brain tissue from the Pediatric Brain Tissue Bank using histological stains for migratory neurons. These studies revealed clusters of immature, migratory neurons widely distributed deep within the frontal lobe of the newborn brain, above the fluid-filled lateral ventricles. MRI imaging of the three-dimensional structure of these clusters revealed a long arc of migratory neurons sitting like a cap in front and on top of the ventricles and stretching from deep behind the eyebrows all the way to the top of the head.

"Several labs had observed that there seemed to be many young neurons around birth along the ventricles, but no one knew what they were doing there," said Paredes. "As soon as we looked closely, we were shocked to discover how massive this population was and to find that they were still actively migrating for weeks and weeks after birth."

To determine whether these immature neurons - which the researchers dubbed "the Arc" - actively migrate in the newborn brain, researchers used viruses to label immature neurons in tissue samples collected immediately after death and observed that Arc cells move inch-worm style through the brain, much as neurons migrate in the fetal brain.

Further histological studies of the cingulate cortex, a portion of the brain's frontal lobe, show that Arc neurons migrate outward from the ventricles into the cortex primarily within the first three months of life, where they differentiate into multiple different subtypes of inhibitory neurons.

"It is impressive that these cells can find their way to precise positions within the cortex," said Alvarez-Buylla. "Earlier in fetal development the brain is much smaller and the tissue far less complicated, but at this later stage it is quite a long and treacherous journey."

Late migration of inhibitory neurons could play a role in human cognitive abilities, neurological disease

Inhibitory neurons, which use the neurotransmitter GABA, make up about 20 percent of the neurons in the cerebral cortex and play a vital role in balancing the brain's need for stability with its ability to learn and change. Imbalanced excitation and inhibition -- particularly in circuits of the frontal lobe of the brain, which are involved in executive control -- have been implicated in many neurological disorders, from autism to schizophrenia.

The new research suggests that inhibitory circuits in humans develop significantly later than previously realized. This postnatal migration is much larger than what is seen in mice and other mammals, the authors say, suggesting that it may be an important developmental factor behind the uniqueness of the human brain.

The first months of life, when an infant first begins to interact with its environment, is a crucial time for brain development, Huang said. "The timing of this migration corresponds very well with the development of more complex cognitive functions in infants. It suggests that the arrival of these cells could play a role in setting up the basis for complex human cognition."

The researchers plan to follow up their study by exploring whether this migration of inhibitory neurons from the Arc to the cortex might

be affected in the brains of children with neurological disorders such as autism, which has previously been associated with abnormal inhibitory circuitry in the frontal cortex.

"Trying to understand what makes human brain development so unique was what drove me to tackle this research," said Paredes, who works with patients with epilepsy in her clinical practice. "If we don't understand how our brains are built, we won't be able to understand what is going wrong when people suffer from neurological disease."

Other UCSF authors on the paper are David James, Hosung Kim, PhD, Jennifer A. Cotter, MD, Carissa Ng, PhD, Kadellyn Sandoval, David Rowitch, MD, PhD, and Patrick S. McQuillen, MD, PhD.

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Alvarez-Buylla is on the scientific advisory board and is co-founder of Neurona Therapeutics, which is developing stem cell technology for human clinical trials.

http://bit.ly/2dCNc3u

'Martian Gardens' Help Scientists Find the Best Veggies to Grow on Mars

Simulated "Martian gardens" are helping NASA scientists learn which plants astronauts might be able to grow on the Red Planet.

By Susan Matthews | October 6, 2016 05:15pm ET

A human round-trip journey to Mars may take as long as two and a half years, and one major challenge for these kinds of extended missions is determining how to pack enough food for those astronauts. As such, scientists are studying ways for astronauts to grow their own crops and extend their food supply, because seeds take up less room and have a longer shelf life on spacecraft than full-grown plants do.

Simulated "Martian gardens," developed at NASA's Kennedy Space Center and the Florida Tech Buzz Aldrin Space Institute, are helping researchers overcome food production challenges associated with Mars' barren landscape.

Simulated "Martian gardens" allow NASA scientists to test which plants can be grown on Mars. This photo shows the results of a preliminary study on lettuce plants. From left to right: lettuce seeds grown in potting soil, Martian simulant with added nutrients, and simulant without nutrients. **NASA/Dimitri Gerondidakis**

Farming on Mars is much different from farming on Earth. Martian soil consists of crushed volcanic rock with no organic material, making it nearly impossible for plant life to survive, according to a statement from NASA.

"We are using advances in science to learn about increasing plant production to supplement astronauts' diets," Trent Smith, project manager for the Vegetable Production System (Veggie) experiment at NASA's Kennedy Space Center, said in the statement. The Veggie experiment has allowed astronauts to garden in space and conduct experiments on plant biology on the International Space Station.

The soil being used in the "Martian garden" was collected from Hawaii and chosen because it simulates the kind of soil found on Mars. Using this Hawaiian soil, the researchers tested how much soil should be used, and which nutrients should be added to the soil, for the various crops to achieve optimal growth.

For example, the researchers tested how lettuce grows in the Mars-like soil simulant. They compared their results to lettuce plants grown in the soil simulant with added nutrients, as well as lettuce planted in normal potting soil. This experiment revealed that the lettuce grown in the Mars-like soil simulant with no added nutrients tasted the same but had weaker roots and a slower germination rate (in other words, they took longer to grow), according to the NASA statement.

In the future, the researchers plan to test how crops such as radishes, Swiss chard, kale, Chinese cabbage, snow peas, dwarf peppers and tomatoes fare in the Martian soil simulant.

"Discoveries made in these Earth-based 'Martian gardens' will pave the way for future studies and technology development in terms of reliable, efficient food production a long way from the home planet," Ralph Fritsche, senior project manager for food production at Kennedy Space Center, said in the statement. "We're right at the cutting edge of this research."

http://bit.ly/2dQUTBj

Chimps, bonobos and orangutans grasp how others view the world

Apes may be even more like us than we thought.

By Emily Benson

They appear to anticipate that a person's actions will follow his or her beliefs, even when they know the person is wrong – an ability never before demonstrated in non-human primates.

The capacity to infer what others might be thinking, known as theory of mind, is central to what makes us human, and is reflected in the ways we cooperate and communicate, says Christopher Krupenye at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Humans, for example, possess an awareness of false beliefs held by other individuals, recognising that the thoughts of others don't necessarily reflect reality.

To see whether apes have this same type of awareness, Krupenye, Fumihiro Kano at Kyoto University in Japan, and their colleagues filmed scenarios designed to stimulate apes. The videos involve conflict between pairs of human actors, one of whom is dressed in a King Kong costume. "The apes are curious; they want to know what's going on," says Krupenye.

King Kong in a haystack

In one video, the fake ape hits a person, and then hides in one of two haystacks while the person watches. After the human leaves the scene, "King Kong" exits the haystack and runs off screen. The person then reappears, apparently looking for the attacker.

Because humans and other animals will look at a location where they anticipate action, the haystack that the apes glanced at first when they watched the video might indicate the one they expected the human to approach.

The researchers used a camera to track the eyes of 40 apes, including chimpanzees, bonobos and orangutans. Of the 30 apes that focused on the haystacks, two-thirds looked first at the one where the human falsely believed the character was hiding.

The scientists also tested the apes with a similar scenario, in which the King Kong character hides a stone in one of two boxes as a person watches, but then steals it when they leave. When the person returns to look for the stone, about three-quarters of apes that paid attention to the boxes glanced first at the one that the human should open.

To test that the apes weren't just looking at the last place where they saw an object or character, the researchers filmed different versions of the videos. In these, King Kong briefly hides in the other haystack after the person leaves before dashing away, or transfers the stone to the other box without a person watching.

"They can anticipate that an individual will search for an object where they last saw it, even though the apes know that it's no longer there," Krupenye says. "That is a really important human skill that has never been shown before in apes."

This means that one of our most sophisticated and significant skills – reading the minds of others – is not unique to us, but also possessed by some of our evolutionary relatives, says Kano. Just like us, he says, great apes have complex social lives bolstered by mutual understanding.

Infant-like understanding

Although the study demonstrates an exciting new method for testing apes' understanding, it raises more questions than it answers, says Laurie Santos at Yale University.

"We don't yet have a reason why primates fail other false-belief studies while succeeding on this," says Santos.

One possibility is that earlier studies tested for conscious understanding, whereas the new one demonstrates implicit knowledge similar to the kind that human infants display, says Alia Martin at Victoria University of Wellington in New Zealand.

Krupenye agrees that the study doesn't necessarily mean apes are explicitly aware of others' false beliefs – but points out that even an implicit awareness implies a high level of social understanding.

Martin says the case might be strengthened by a comparison of a situation in which, for example, apes need to anticipate how someone who is aware of the true situation might behave. If apes are able to understand what others are thinking, she says, we should see signs of them using that skill.

"Can we find any evidence of it in their behaviour?" asks Martin.

The answer is yes, according to Richard William Byrne at the University of St Andrews in the UK. For decades, researchers have watched apes demonstrate behaviours that suggest complex social understanding, such as deceiving their peers, he says. "To me, this is another nice block slotting into place where it should," says Byrne.

This paper adds to the growing body of evidence that great apes – which are endangered in the wild – are deeply similar to humans, Krupenye says.

Conservation measures to combat habitat destruction and direct killing of apes are sorely needed, says Byrne. "They are too much like us to be treated just as animals," he adds.

The findings suggest that an ability to recognise false beliefs in others has existed in the primate family tree for at least 13 to 18 million years, and was present in the last common ancestor of great apes and humans.

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http://bit.ly/2dFpz6S

Weethinking the role of bacteria in incontinence

Researchers look at the role of bacteria in incontinence

We all know that feeling of suddenly needing to pee, and the agonizing worry that we might not find a toilet in time or make it that far. Sadly, for many people this is a regular occurrence and wetting themselves uncontrollably is an inevitable consequence.

Almost 1 in 5 women over the age of 44 suffer from what is known as Urgency Urinary Incontinence (UUI): experiencing a strong sensation of an urgent need to pee, followed by immediate leakage of a large volume of urine. It can severely adversely affect someone's life, contributing to anxiety, depression and social isolation.

In spite of its impact, the causes of the complaint are still relatively unknown. The condition is often attributed to abnormal signalling prompting the bladder muscles to contract involuntarily, but this seems to account for only about three fifths of cases. Scientists are searching for other possible causes of the condition. Some think that understanding the bacteria that live within us may hold the key.

The urinary tract has long been thought to be a sterile environment: a place where no bacteria can grow. A new study from Oregon Health and Science University that was published in Frontiers in Cellular and Infection Microbiology, suggests that this assumption might be far from the truth. Furthermore, their research suggests that the variety

and type of bacteria that are present in the tract may have a role in general health and conditions like urgent urinary incontinence.

The main reason why the urinary tract has been assumed to be inhospitable for bacteria is that scientists have been unable to grow bacteria from urine samples in the laboratory and so believed that there was nothing living within those samples. However, the Oregon team has taken a different approach, looking for the tell-tale signs of bacterial DNA within urine.

Nearly every woman from whom they collected urine, regardless of whether or not she suffered from urinary incontinence, had a wide variety of bacteria present, though the women with UUI seemed to have fewer different types of bacteria. Rahel Nardos, one of the scientists behind the study, hopes that "the scientific community can learn to understand how these bacteria behave under normal and diseased conditions".

In some cases, the bacteria present in the urine of women suffering from UUI are the same kinds that cause urinary tract infections. This suggests that a persistent low grade infection by bacteria that are not commonly detected by routine cultures could potentially be responsible for the irritative symptoms of UUI, at least for some individuals. Rahel hopes "that future work in this area of research will lead to more accurate diagnoses and better targets for treatments."

Furthermore, it seems that the fewer different kinds of bacteria that are present in the urinary tract, the more severe are the symptoms experienced by the patient. Dr Lisa Karstens, one of the scientists in this project thinks that "much larger studies will need to be completed in order to understand the variability of these bacterial communities in healthy individuals and to determine if there are specific patterns that emerge from this variability that indicate normal and abnormal states."

Medicine is increasingly acknowledging that our bodies are host to an entire ecosystem of bacteria and other microbes that hitchhike upon us and that the health of that network can affect our wellbeing. Decreased microbial diversity of other body sites has also been associated with a variety of clinical conditions such as obesity, irritable bowel syndrome and inflammatory bowel disease. As Rahel says, "It turns out, diversity is a good thing to have in all aspects of life". Understanding the complexities of bacteria in the urinary tract could lead to valuable progress in this area.

http://bit.ly/2d2b7HW

Why 'Hoppy' Beer May Be Better for Your Liver

The hops found in beer not only add flavor, but also may lessen the damaging effects of alcohol on the liver, a new study in mice suggests.

By Rachael Rettner, Senior Writer | October 7, 2016 07:03 am ET

In the study, the researchers gave mice regular beer with hops, a special beer without hops, or plain ethanol (alcohol). After 12 hours, the mice that were given the beer with hops showed less buildup of fat in their livers than the mice that were given ethanol. In contrast, the mice that were given beer without hops had about the same level of fat accumulation in their livers as the mice that were given ethanol.

"Our data suggest that hops content in beer is at least in part responsible for the less damaging effects of beer on the liver," over the short-term in mice, the researchers from Friedrich Schiller University Jena in Germany wrote in their study, published online Sept. 22 in the journal Alcohol and Alcoholism.

The researchers said their new findings may help explain why some earlier studies in people suggested that drinking hard liquor is more strongly associated with death from liver disease than drinking beer. Also, the researchers who worked on the new study had found in earlier work that mice accumulated less fat in their livers when they were given beer versus ethanol.

Hops refers to the flowers of the hops plant, Humulus lupulus. They are a main ingredient in beer, and are used to add flavor and act as a preservative. [Raise Your Glass: 10 Intoxicating Beer Facts]

The new study also suggested that hops may lower the formation of compounds called reactive oxygen species, which are highly reactive

and can cause damage to cells in the liver. However, future studies are needed to see if the same effects are found in people, and if these effects last for long periods, the researchers said. They noted that their study received funding from the German brewing industry.

William Kerr, a senior scientist at the Alcohol Research Group, part of the nonprofit Public Health Institute in Emeryville, California, said that, in some countries, consumption of hard liquor is more strongly linked to death from liver disease, compared to beer consumption.

But "beer does cause liver damage," added Kerr, who was not involved in the new study.

The reason for the weaker association between beer consumption and death from liver disease is not known. It's possible that people who drink spirits are more likely to be heavy drinkers than those who drink beer. It's also possible that something about beer, like the ingredient hops, is protective against liver damage, Kerr said.

Still, Kerr said that the amount of hops in beer can vary quite a bit. The study tested only a single beer, a type of German pilsner, so it's not clear what level of hops in beer is needed to have the effect seen in the study.

http://bit.ly/2devsbD

'Game-changing' immunotherapy doubles head and neck cancer survival

An immunotherapy drug has been hailed as a potential 'game changer' after being found to greatly improve survival for patients with relapsed head and neck cancer - a disease which is notoriously difficult to treat.

Nivolumab became the first treatment to extend survival in a phase III clinical trial for patients with head and neck cancer in whom chemotherapy had failed - and it did so with fewer side-effects than existing therapeutic options. More than double the number of patients taking nivolumab were alive after one year as those treated with chemotherapy, reported the major international trial, published today (Sunday) in the New England Journal of Medicine.

There are currently no other treatment options that improve the survival of patients with cisplatin-resistant relapsed or metastatic head and neck cancers. This group of patients are expected to live less than six months.

The trial was led in the UK by Professor Kevin Harrington of The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, and involved 20 research organisations from around the world. It was funded by Bristol Myers Squibb.

Of the 361 patients in the trial, 240 with relapsed or metastatic head and neck cancer were allocated to receive nivolumab and 121 to one of three different chemotherapies. UK patients received the chemotherapy drug docetaxel, which is the only treatment approved for advanced head and neck cancer by NICE.

After one year of the study, 36 per cent of patients treated with nivolumab were still alive compared with 17 per cent for the comparator arm. Median survival for patients on nivolumab was 7.5 months, compared with 5.1 months for chemotherapy.

The survival benefit was more pronounced in patients whose tumours had tested positive for human papillomavirus (HPV). These patients survived an average of 9.1 months with nivolumab and 4.4 months with chemotherapy. HPV-negative patients survived an average of 7.5 months with nivolumab and 5.8 with chemotherapy.

Importantly, fewer patients experienced serious side-effects from taking nivolumab than with conventional treatment - only 13 per cent compared with 35 per cent of patients who received chemotherapy.

Patients given chemotherapy reported feeling physically, socially and emotionally worse off, whereas those who were given nivolumab remained stable during the course of treatment.

Professor Harrington will be presenting some of the findings at the European Society for Medical Oncology 2016 Congress in Copenhagen, simultaneously with publication. Nivolumab will still have to go through approval by the European Medicines Agency and

NICE before it is available for head and neck cancer patients on the NHS.

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

"Nivolumab could be a real game-changer for patients with advanced head and neck cancer. This trial found that it can greatly extend life among a group of patients who have no existing treatment options, without worsening quality of life.

"Once it has relapsed or spread, head and neck cancer is extremely difficult to treat. So it's great news that these results indicate we now have a new treatment that can significantly extend life, and I'm keen to see it enter the clinic as soon as possible."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"Nivolumab is one of a new wave of immunotherapies that are beginning to have an impact across cancer treatment. This phase III clinical trial expands the repertoire of nivolumab even further, showing that it is the first treatment to have significant benefits in relapsed head and neck cancer. "We hope regulators can work with the manufacturer to avoid delays in getting this drug to patients who have no effective treatment options left to them."

Some of the data was presented at 16:25 CEST today (Sunday) at the European Society for Medical Oncology 2016 Congress in Copenhagen.

http://bit.ly/2eiPrI0

Altering the 'flavor' of humans could help fight malaria

Novel study identifies an area of the mosquito brain that mixes taste and smell

A new study by Johns Hopkins researchers suggests that a specialized area of the mosquito brain mixes tastes with smells to create unique and preferred flavors. The findings advance the possibility, they say, of identifying a substance that makes "human flavor" repulsive to the malaria-bearing species of the mosquitoes, so instead of feasting on us, they keep the disease to themselves, potentially saving an estimated 450,000 lives a year worldwide.

A report on the research appeared online on Oct. 3 in the journal Nature Communications. Malaria is an infectious parasite disease of humans and animals transmitted by the bite of the female Anopheles gambiae mosquito. In 2015, experts estimate it affected 214 million people, mostly in Africa, despite decades of mosquito eradication and control efforts. There is no malaria vaccine, and although the disease is curable in early stages, treatment is costly and difficult to deliver in places where it is endemic.

"All mosquitoes, including the one that transmits malaria, use their sense of smell to find a host for a blood meal. Our goal is to let the mosquitoes tell us what smells they find repulsive and use those to keep them from biting us," says Christopher Potter, Ph.D., assistant professor of neuroscience at the Johns Hopkins University School of Medicine.

Because smell is essential to mosquito survival, each mosquito has three pairs of "noses" for sensing odors: two antennae, two maxillary palps and two labella. The maxillary palps are thick, fuzzy appendages that protrude from the lower region of the mosquito's head, more or less parallel to its proboscis, the long, flexible sheath that keeps its "feeding needle" under wraps until needed. At the very tip of the proboscis are the labella, two small regions that contain both "gustatory" neurons that pick up tastes and olfactory neurons for recognizing odorants.

To better understand how An. gambiae mosquitoes that cause malaria receive and process olfactory information from so many sensory regions, Potter's team wanted to see where olfactory neurons from those regions go to in the brain.

They used a powerful genetic technique -- never before accomplished in mosquitoes, according to Potter -- to make certain neurons "glow" green. The green glowing label was designed to appear specifically in neurons that receive complex odors through proteins called odorant

receptors (ORs), since OR neurons are known to help distinguish humans from other warm-blooded animals in Aedes aegypti mosquitoes, which carry the Zika virus.

"This is the first time researchers managed to specifically target sensory neurons in mosquitoes. Previously, we had to use flies as a proxy for all insects, but now we can directly study the sense of smell in the insects that spread malaria," says Olena Riabinina, Ph.D., the lead author of the study and a postdoctoral fellow now at the Imperial College London. "We were pleasantly surprised by how well our genetic technique worked and how easy it is now to see the smell-detecting neurons. The ease of identification will definitely simplify our task of studying these neurons in the future."

As expected, Potter says, the OR neurons from the antennae and maxillary palps went to symmetrical areas of the brain called antennal lobes, just as they do in flies. But Potter was quite surprised when he saw that the OR neurons from the labella went to the so-called subesophageal zone, which, he says, had never before been associated with the sense of smell in any fly or insect; it had only been associated with the sense of taste.

"That finding suggests that perhaps mosquitoes don't just like our smell, but also our flavor," says Potter. "It's likely that the odorants coming off our skin are picked up by the labella and influence the preferred taste of our skin, especially when the mosquito is looking for a place to bite."

Potter says the finding potentially offers researchers one more way to repel mosquitoes. The antennae and maxillary palps are more specialized for picking up long-range signals, while the labella come into direct contact with our skin. In fact, Potter says, before injecting their needlelike proboscis, mosquitoes use the labella to probe about on a victim's skin. "We don't really know why they do that, but we suspect that they're looking for sensory cues that hint at easy access to a blood vessel," he says. "This suggests that a combination of repellants could keep mosquitoes from biting us in two ways. One could target the antennal neurons and reduce the likelihood that they come too close, while another could target the labellar neurons and make the mosquitoes turn away in disgust -- before sucking our blood -- if they got close enough to land on us."

The two-part genetic system Potter devised to generate the glowing neurons will make it much easier for his and other laboratories to mix and match genetically altered mosquitoes to generate new traits, he says. His group has already created a strain of An. gambiae mosquitoes whose OR neurons glow green upon activation. Scientists can thus see which neurons light up in response to a specific smell.

"Using this method, we hope to find an odorant that is safe and pleasant-smelling for us but strongly repellant to mosquitoes at very low concentrations," says Potter.

His group was also able to compare the brains of male and female mosquitoes. Since only females use their sense of smell to find humans and males feed only on nectar, it was previously thought that males had just a rudimentary sense of smell. The Potter group found instead that males have the same level of complexity in their brains to detect odors as females but have fewer olfactory neurons. "It appears that males might just have a scaled-down version of a female's sense of smell. So they can still smell everything a female smells, just not as well," Potter says.

His group plans to study other types of neurons to better understand how signals from the mosquitoes' three types of olfactory receptors interact to influence their behavior. For example, why is lactic acid not attractive on its own but highly attractive when mixed with carbon dioxide? "We'd like to figure out what regions and neurons in the brain lead to this combined effect," says Potter. "If we can identify them, perhaps we could also stop them from working."

Other authors of the report include Darya Task, Elizabeth Marr and Chun-Chieh Lin of the Johns Hopkins University School of Medicine; and Robert Alford and David O' Brochta of the University of Maryland, College Park.

This work was supported by grants from the Johns Hopkins Medicine Discovery Fund, the Johns Hopkins Malaria Research Institute, and the National Institute of Allergy and Infectious Diseases (R01AI099060).

http://bit.ly/2d6Pi5k

Stem cells from jaw bone help repair damaged cartilage

Columbia College of Dental Medicine researchers have identified stem cells that can make new cartilage and repair damaged joints.

NEW YORK, NY - The cells reside within the temporomandibular joint (TMJ), which articulates the jaw bone to the skull. When the stem cells were manipulated in animals with TMJ degeneration, the cells repaired cartilage in the joint. A single cell transplanted in a mouse spontaneously generated cartilage and bone and even began to form a bone marrow niche. The findings were published on October 10 in Nature Communications.

"This is very exciting for the field because patients who have problems with their jaws and TMJs are very limited in terms of clinical treatments available," said Mildred C. Embree, DMD, PhD, assistant professor of dental medicine at Columbia University Medical Center (CUMC) and the lead author of the study. Dr. Embree's team, the TMJ Biology and Regenerative Medicine Lab, conducted the research with colleagues including Jeremy Mao, DDS, PhD, the Edwin S. Robinson Professor of Dentistry (in Orthopedic Surgery) at CUMC.

Up to 10 million people in the United States, primarily women, have TMJ disorders, according to the National Institutes of Health. Options for treatment currently include either surgery or palliative care, which addresses symptoms but can't regenerate the damaged tissue. Dr. Embree's findings suggest that stem cells already present in the joint could be manipulated to repair it.

Cartilage helps to cushion the joints and allows them to move smoothly. The type of cartilage within the TMJ is fibrocartilage, which is also found in the knee meniscus and in the discs between the vertebrae. Because fibrocartilage cannot regrow or heal, injury or disease that damages this tissue can lead to permanent disability.

Medical researchers have been working to use stem cells, immature cells that can develop into various types of tissue, to regenerate cartilage. Given the challenges of transplanting donor stem cells, such as the possibility of rejection by the recipient, researchers are especially interested in finding ways to use stem cells already living in the body.

"The implications of these findings are broad," said Dr. Mao, "including for clinical therapies. They suggest that molecular signals that govern stem cells may have therapeutic applications for cartilage and bone regeneration. Cartilage and certain bone defects are notoriously difficult to heal." Dr. Mao is co-director of the Center for Craniofacial Regeneration at Columbia. His own research with stem cells has regenerated teeth and the meniscus, the pad of cartilage within the knee joint, and the TMJ in 2003.

In a series of experiments described in the new report, Dr. Embree, Dr. Mao, and their colleagues isolated fibrocartilage stem cells (FCSCs) from the joint and showed that the cells can form cartilage and bone, both in the laboratory and when implanted into animals. "I didn't have to add any reagents to the cells," Dr. Embree said. "They were programmed to do this." And while some approaches to regenerating injured tissue require growth factors or biomaterials for the cells to grow on, she noted, the FCSCs grew and matured spontaneously.

Dr. Embree and her team also identified a molecular signal, Wnt, that depletes FCSCs and causes cartilage degeneration. Injecting a Wnt-blocking molecule called sclerostin into degenerated TMJs in animals stimulated cartilage growth and healing of the joint.

She and her colleagues are now searching for other small molecules that could be used to inhibit Wnt and promote FCSC growth. The idea, according to Dr. Embree, will be to find a drug with minimal side effects that could be injected right into the joint.

Children with juvenile idiopathic arthritis can have stunted jaw growth that can't be treated with existing drugs, Dr. Embree noted. Since the TMJ is a growth center for the jaw, the new research may offer strategies for treating these children, and lead to a better understanding of how the jaw grows and develops. While

orthodontists currently rely on clunky technologies like headgear to modify jaw growth, she added, the findings could point towards ways to modulate growth on the cellular level.

Ultimately, Dr. Embree and her team say, the findings could lead to strategies for repairing fibrocartilage in other joints, including the knees and vertebral discs. "Those types of cartilage have different cellular constituents, so we would have to really investigate the molecular underpinnings regarding how these cells are regulated," the researcher said.

The study is titled, "Exploiting endogenous fibrocartilage stem cells to regenerate cartilage and repair joint injury."

Authors included Mildred C. Embree (Columbia University Medical Center, New York, NY), Mo Chen (CUMC), Serhiy Pylawka (CUMC), Danielle Kong (CUMC), George M. Iwaoka (CUMC), Ivo Kalajzic (University of Connecticut, Farmington CT), Hai Yao (Clemson University, Charleston, SC), Chancheng Shi (Chinese Academy of Sciences, Chongqing, China), Dongming Sun (Rutgers University, Piscataway, NJ), Tzong-Jen Sheu (University of Rochester Medical Center, Rochester, NY), David A. Koslovsky (Metropolitan Oral Associates, New York, NY), Alia Koch (CUMC), and Jeremy J. Mao (CUMC).

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The authors declare no competing financial interests.

http://bit.ly/2dFiIOj

Mars-bound astronauts face chronic dementia risk from galactic cosmic ray exposure

UCI study raises questions about long-term brain health after extended spaceflights

Irvine, Calif. -- Will astronauts traveling to Mars remember much of it? That's the question concerning University of California, Irvine scientists probing a phenomenon called "space brain."

UCI's Charles Limoli and colleagues found that exposure to highly energetic charged particles - much like those found in the galactic cosmic rays that will bombard astronauts during extended spaceflights - causes significant long-term brain damage in test rodents, resulting in cognitive impairments and dementia.

Their study appears today in Nature's Scientific Reports. It follows one last year showing somewhat shorter-term brain effects of galactic cosmic rays. The current findings, Limoli said, raise much greater alarm. (Link to study available Oct. 10: http://www.nature.com/articles/srep34774)

"This is not positive news for astronauts deployed on a two-to-three-year round trip to Mars," said the professor of radiation oncology in UCI's School of Medicine. "The space environment poses unique hazards to astronauts. Exposure to these particles can lead to a range of potential central nervous system complications that can occur during and persist long after actual space travel - such as various performance decrements, memory deficits, anxiety, depression and impaired decision-making. Many of these adverse consequences to cognition may continue and progress throughout life."

For the study, rodents were subjected to charged particle irradiation (fully ionized oxygen and titanium) at the NASA Space Radiation Laboratory at New York's Brookhaven National Laboratory and then sent to Limoli's UCI lab.

Six months after exposure, the researchers still found significant levels of brain inflammation and damage to neurons. Imaging revealed that the brain's neural network was impaired through the reduction of dendrites and spines on these neurons, which disrupts the transmission of signals among brain cells. These deficiencies were parallel to poor performance on behavioral tasks designed to test learning and memory.

In addition, the Limoli team discovered that the radiation affected "fear extinction," an active process in which the brain suppresses prior unpleasant and stressful associations, as when someone who nearly drowned learns to enjoy water again.

"Deficits in fear extinction could make you prone to anxiety," Limoli said, "which could become problematic over the course of a three-year trip to and from Mars."

Most notably, he said, these six-month results mirror the six-week post-irradiation findings of a 2015 study he conducted that appeared in the May issue of Science Advances.

Similar types of more severe cognitive dysfunction are common in brain cancer patients who have received high-dose, photon-based radiation treatments. In other research, Limoli examines the impact of chemotherapy and cranial irradiation on cognition.

While dementia-like deficits in astronauts would take months to manifest, he said, the time required for a mission to Mars is sufficient for such impairments to develop. People working for extended periods on the International Space Station, however, do not face the same level of bombardment with galactic cosmic rays because they are still within the Earth's protective magnetosphere.

Limoli's work is part of NASA's Human Research Program. Investigating how space radiation affects astronauts and learning ways to mitigate those effects are critical to further human exploration of space, and NASA needs to consider these risks as it plans for missions to Mars and beyond.

Partial solutions are being explored, Limoli noted. Spacecraft could be designed to include areas of increased shielding, such as those used for rest and sleep. However, these highly energetic charged particles will traverse the ship nonetheless, he added, "and there is really no escaping them."

Preventive treatments offer some hope. Limoli's group is working on pharmacological strategies involving compounds that scavenge free radicals and protect neurotransmission.

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http://nyti.ms/2d2niF0

I'm a Doctor. If I Drop Food on the Kitchen Floor, I Still Eat It.

Why are we so worried about the floor? So many other things are more dangerous than that.

Aaron E. Carroll

You may have read or heard about the study debunking the five-second rule. It said that no matter how fast you pick up food that falls on the floor, you will pick up bacteria with it.

Our continued focus on this threat has long baffled me. Why are we so worried about the floor? So many other things are more dangerous than that.

I first became interested in the five-second rule years ago, when I was a co-author of a book on medical myths. We cited a number of studies showing that food that touched household surfaces — even for brief periods of time — could pick up bacteria or other harmful substances.

This most recent study was similar in that it tested a variety of foods, a variety of substances, for various periods. And, like those other studies, this one found that food touching the floor, even for a very short amount of time, could pick up bacteria.

There's no magic period of time that prevents transmission. But even though I know bacteria can accumulate in less than five seconds, I will still eat food that has fallen on my kitchen floor. Why? Because my kitchen floor isn't really that dirty.

Our metric shouldn't be whether there are more than zero bacteria on the floor. It should be how many bacteria are on the floor compared with other household surfaces. And in that respect, there are so many places in your house that pose more of a concern than the floor.

Perhaps no one in the United States has spent more time investigating the occurrence of bacteria on public surfaces than Charles Gerba. He's a professor of microbiology and environmental sciences at the University of Arizona, and he has published many papers on the subject.

In 1998, he and his colleagues investigated how well cleaning products could reduce coliform bacteria counts on household surfaces. As part of that research, they measured various locations in the house before any cleaning.

They found that the kitchen floor was likely to harbor, on average, about three colonies per square inch of coliform bacteria (2.75 to be exact). So there are some. But here's the thing — that's cleaner than both the refrigerator handle (5.37 colonies per square inch) and the kitchen counter (5.75 colonies per square inch).

We spend so much time worrying about what food might have picked up from the floor, but we don't worry about touching the refrigerator. We also don't seem as worried about food that touches the counter. But the counter is just as dirty, if not dirtier.

The same thing happens in the bathroom. I know a lot of people who are worried about the toilet seat, but it's cleaner than all the things in the kitchen I just mentioned (0.68 colonies per square inch). What's dirtier in the bathroom? Almost everything. The flush handle (34.65 colonies per square inch), the sink faucet (15.84 colonies per square inch) and the counter (1.32 colonies per square inch).

Things get dirty when lots of hands touch them and when we don't think about it. We worry about the floor and the toilet seat, so we clean them more. We don't think about the refrigerator handle or the faucet handle as much.

If we carry this logic out further, there are things we handle a lot and never really clean. One study, for instance, found that about 95 percent of mobile phones carried by health care workers were contaminated with nosocomial bacteria. More than half were contaminated with staph aureus, and almost 40 percent were contaminated with methicillin resistant bacteria (MRSA).

Think about how many people have handled the money in your wallet. A study of one-dollar bills found that 94 percent were colonized by bacteria, 7 percent of which were pathogenic to healthy people and 87 percent of which were pathogenic to people who were hospitalized or who had compromised immune systems. Where do you keep your money? In a wallet or purse? When did you last clean it? It's probably filthy.

I see people pay for food every day and then eat what they're handed with no concern that the food might have been contaminated. And the money and the hands that just held it could be much dirtier than the floor.

There are so many studies out there showing that things we touch every day are so, so dirty. Gas pump handles. A.T.M. buttons. Remote controls. Light switches. Computer keyboards.

The dirtiest thing in your kitchen, by far, is likely to be the sponge you keep near the sink. Most people almost never wash or disinfect those sponges. Mr. Gerba found they had, on average, more than 20 million colonies per square inch.

All of this should remind you that it's always a good idea to wash your hands before you eat. Hand-washing is still one of the best ways to prevent illness.

People react to news like this in one of two ways. One is to become paranoid about everything. Such people start to clean compulsively, worry about all the things they're touching, and use hand sanitizer obsessively.

The alternative is to realize that for most of us, our immune systems are pretty hardy. We've all been touching this dirty stuff for a long time, without knowing it, and doing just fine.

I clearly fall into the latter group. If I drop food on the floor, I still eat it. I do that because the harm I might get from the floor is not worth my concern compared with many, many other things. You may feel differently. Either way, make an informed judgment based on relative risks, not on any arbitrary span of time that one thing has been touching another.