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A single compound could treat 3 parasitic diseases

Scientists have identified a compound that can kill the parasites responsible for three neglected diseases: Chagas disease, leishmaniasis and sleeping sickness.

These diseases affect millions of people in Latin America, Asia and Africa, but there are few effective treatments available.

A new study, published today in Nature, suggests that a single class of drugs could be used to treat all three. Wellcome-funded researchers at the Genomics Institute of the Novartis Research Foundation (GNF) have identified a chemical that can cure all of these diseases in mice. It also does not harm human cells in laboratory tests, providing a strong starting point for drug development.

Chagas, leishmaniasis and sleeping sickness have different symptoms, but are all caused by parasites called 'kinetoplastids' - a type of single-celled organism. The parasites share similar biology and genetics, which led scientists to think it might be possible to find a single chemical that could destroy all three.

The team at GNF tested over 3 million different chemicals and identified a compound, GNF6702, which was effective against the parasites but did not damage human cells. They refined this starting compound to make it more potent before testing in it mice.

Senior study author Frantisek Supek from GNF said: "We found that these parasites harbour a common weakness. We hope to exploit this weakness to discover and develop a single class of drugs for all three diseases."

Dr Stephen Caddick, Director of Innovation at Wellcome, said: "These three diseases lead to more than 50,000 deaths annually, yet they receive relatively little funding for research and drug development. We hope that our early stage support for this research will provide a basis for the development of new treatments that could reduce suffering for millions of people in the poorest regions of the world."

Existing treatments for the three diseases are expensive, often have side effects and are not very effective. The fact that GNF6702 does not seem to have any adverse effects in mice suggests that it might have fewer side-effects than existing drugs, although this will need to be explored in human studies. GNF6702 is now being tested for toxicity before it can be moved in to clinical trials.

The project was led by Frantisek Supek at GNF, in collaboration with researchers at the Novartis Institute for Tropical Diseases (NITD), University of York, University of Washington and the University of Glasgow. It received funding from the Wellcome Trust and US National Institutes of Health.

Paper reference: Proteasome inhibition for treatment of leishmaniasis, Chagas disease and sleeping sickness, by S Khare et al. Nature DOI: 10.1038/nature19339.

http://www.eurekalert.org/pub_releases/2016-08/uoz-iop080516.php

Impact of prion proteins on the nerves revealed for the first time

Ever since the prion gene was discovered in 1985, its role and biological impact on the neurons has remained a mystery.

Finally, we can ascribe a clear-cut function to prion proteins and reveal that, combined with particular receptor, they are responsible for the long-term integrity of the nerves," says Professor Adriano Aguzzi from the Neuropathological Institute at the University of Zurich and University Hospital Zurich. The present study therefore clears up a question that researchers have been puzzling over for 30 years, but ultimately went unanswered.

Prions are dangerous pathogens that trigger fatal brain degeneration in humans and animals. In the 1990s, they were responsible for the BSE epidemic more commonly known as mad cow disease. In humans, they cause Creutzfeldt-Jakob disease and other neurological disorders that are fatal and untreatable. Meanwhile, we know that infectious prions consist of a defectively folded form of a normal prion protein called PrPC located in the neuron membrane. The infectious prions

multiply by kidnapping PrPC and converting it into other infectious prions.

Absent prion proteins cause nerve diseases

For a long time, it remained unclear why we humans -- like most other organisms -- have a protein in our neurons that does not perform any obvious function, yet can be extremely dangerous. Aguzzi has spent decades researching this issue and examining the theory that animals without the PrPC gene are resistant to prion diseases. But what are the repercussions for the organism if the prion protein is deactivated?

A few years ago, Aguzzi and his team discovered that mice without the PrPC gene suffer from a chronic disease of the peripheral nervous system. The reason: The so-called Schwann cells around the sensitive nerve fibers no longer form an insulating layer to protect the nerves. Due to this insulating myelin deficit, the peripheral nerves become diseased, potentially resulting in motoric disorders in the motion tract and paralysis.

The researchers have now gone one step further in the lab: In a new study, Alexander Küffer and Asvin Lakkaraju clarify exactly why the peripheral nerves become damaged in the absence of the prion protein PrPC. They discovered how the PrPC produced by the neurons docks onto the Schwann cells: namely via a receptor called Gpr126. If the prion protein and the receptor work together, a particular messenger substance (cAMP) which regulates the chemical interaction in the cells and is essential for the integrity of the nerve's protective sheath increases. Gpr126 belongs to the large family of "G-protein-coupled receptors", which are involved in many physiological processes and diseases.

30-year-old research question finally answered

This discovery solves a key question that has long puzzled neuroscientists and points towards future applications in hospitals. "If you want to deactivate the prion protein PrPC fully for potential Creutzfeld-Jakob disease treatments, you need to know the potential side effects on the nerves in the future," explains Aguzzi. Moreover, the present results on the effect of PrPC at molecular level could yield a new approach for peripheral neuropathy. Currently, there are only extremely limited therapeutic options for these chronic debilitating diseases of the nervous system.

Alexander Ku?ffer, Asvin K. K. Lakkaraju, Amit Mogha, Sarah C. Petersen, Kristina Airich, Cédric Doucerain, Rajlakshmi Marpakwar, Pamela Bakirci, Assunta Senatore, Arnaud Monnard, Carmen Schiavi, Mario Nuvolone, Bianka Grosshans, Simone Hornemann, Frederic Bassilana, Kelly R. Monk & Adriano Aguzzi. The prion protein is an agonistic ligand of the G-protein-coupled receptor Gpr1/Adgrg6. Nature, 8 Aug. 2016. doi:10.1038/nature19312

http://bit.ly/2aGtEpq

Triple signal of ‘alien megastructure’ star baffles astronomers

The mystery of the so-called “alien megastructure” star just deepened.

By Shannon Hall

KIC 8462852, as it is more properly known, flickers so erratically that one astronomer has speculated that nothing other than a massive extraterrestrial construction project could explain its weird behaviour. A further look showed it has been fading for a century. Now, fresh analysis suggests the star has also dimmed more rapidly over the past four years – only adding to the enigma.

“It seems that every time someone looks at the star, it gets weirder and weirder,” says Benjamin Montet at the California Institute of Technology, who led the study.

This space oddity was first spotted by NASA’s Kepler space telescope, which continually monitored 100,000 stars from 2009 to 2013. Any dip observed in a star’s light is a sign that an exoplanet has passed in front of it. These dips, which occur regularly, block at most 1 per cent of the star’s light and have revealed thousands of exoplanets.

But KIC 8462852, also known as Tabby’s star after its discoverer Tabetha Boyajian of Yale University, was an outlier. Its light dipped by as much as 20 per cent and didn’t conform to any regular time intervals – so the signature couldn’t have been caused by a planet.

Astronomers came up with an array of potential explanations, from the mundane to the bizarre. The star made headlines when Jason Wright, an astronomer at Pennsylvania State University, announced that an advanced extraterrestrial civilization could be responsible for the signal.

Curiouser and curiouser

But the plot thickened when Bradley Schaefer, at Louisiana State University in Baton Rouge, probed the star's behaviour over the past century by looking at old photographic plates from 1890 to 1989. More than 1200 images revealed that Tabby's star gradually dimmed by as much as 15 per cent over the course of a century.

Schaefer's work was immediately called into question. However, with so few astronomers who have an expertise in these plates, no one seemed able to settle the debate. That is until Montet and his advisor Josh Simon realised that an answer might be hidden within the Kepler data.

They found that for the first 1000 days of the Kepler mission, Tabby's star decreased in brightness at roughly 0.34 per cent a year – twice as fast as measured by Schaefer. What's more, over the next 200 days, the star's brightness dropped another 2.5 per cent before beginning to level out. It was a much more rapid change than before.

That means the star undergoes three types of dimming: the deep dips that first made it famous, the relatively slow decline observed by Schaefer and verified by Montet and Simon, and the intermediate rapid decline that occurred over a few hundred days.

"We can come up with scenarios that explain one or maybe two of these, but there's nothing that nicely explains all three," says Montet.

And the team doesn't want to resort to creating three separate scenarios. "It would be much more satisfying to think of a single physical cause that could be responsible for all of the brightness variations that we observe," says Simon. "But we're still struggling to come up with what that might be."

And Wright couldn't be more thrilled. "I was always worried that the mystery would be solved with some really mundane explanation, like some overlooked instrumental effect, and that it would turn out to be a wild goose chase," he says.

Explanations range from a swarm of comets orbiting the star to an intervening cloud in the interstellar medium – but none fit all the data.

An alien concept

What about that advanced alien megastructure? "Once you're invoking arbitrary advanced aliens doing something with technology far beyond ours, then there isn't very much that can't be explained," says Simon. "But we don't really want to resort to that until we exhaust all of the possible natural explanations we can think of."

Even Wright, the astronomer who postulated the alien megastructure in the first place, admits that it's a last resort.

In the meantime, astronomers will continue to monitor the star. A successful crowdfunding campaign earlier this year raised over $100,000, allowing astronomers to secure time at the Las Cumbres Observatory Global Telescope Network, where they can observe the star for a year.

The hope is that Tabby's star will soon drastically dim and they will be able to swing different ground-based and space-based observatories towards it. Catching a transit in as many wavelengths as possible should help pin down what is interfering with the star – be it a swarm of comets, an alien megastructure, or something else entirely.

Reference: http://arxiv.org/abs/1608.01316

http://www.eurekalert.org/pub_releases/2016-08/miot-sfb080816.php

Study finds brain connections key to reading

Pathways that exist before kids learn to read may determine development of brain's word recognition area

A new study from MIT reveals that a brain region dedicated to reading has connections for that skill even before children learn to read.

By scanning the brains of children before and after they learned to read, the researchers found that they could predict the precise location

where each child's visual word form area (VWFA) would develop, based on the connections of that region to other parts of the brain.

Neuroscientists have long wondered why the brain has a region exclusively dedicated to reading -- a skill that is unique to humans and only developed about 5,400 years ago, which is not enough time for evolution to have reshaped the brain for that specific task. The new study suggests that the VWFA, located in an area that receives visual input, has pre-existing connections to brain regions associated with language processing, making it ideally suited to become devoted to reading.

"Long-range connections that allow this region to talk to other areas of the brain seem to drive function," says Zeynep Saygin, a postdoc at MIT's McGovern Institute for Brain Research. "As far as we can tell, within this larger fusiform region of the brain, only the reading area has these particular sets of connections, and that's how it's distinguished from adjacent cortex."

Saygin is the lead author of the study, which appears in the Aug. 8 issue of Nature Neuroscience. Nancy Kanwisher, the Walter A. Rosenblith Professor of Brain and Cognitive Sciences and a member of the McGovern Institute, is the paper's senior author.

Specialized for reading

The brain's cortex, where most cognitive functions occur, has areas specialized for reading as well as face recognition, language comprehension, and many other tasks. Neuroscientists have hypothesized that the locations of these functions may be determined by prewired connections to other parts of the brain, but they have had few good opportunities to test this hypothesis.

Reading presents a unique opportunity to study this question because it is not learned right away, giving scientists a chance to examine the brain region that will become the VWFA before children know how to read. This region, located in the fusiform gyrus, at the base of the brain, is responsible for recognizing strings of letters.

Children participating in the study were scanned twice -- at 5 years of age, before learning to read, and at 8 years, after they learned to read. In the scans at age 8, the researchers precisely defined the VWFA for each child by using functional magnetic resonance imaging (fMRI) to measure brain activity as the children read. They also used a technique called diffusion-weighted imaging to trace the connections between the VWFA and other parts of the brain.

The researchers saw no indication from fMRI scans that the VWFA was responding to words at age 5. However, the region that would become the VWFA was already different from adjacent cortex in its connectivity patterns. These patterns were so distinctive that they could be used to accurately predict the precise location where each child's VWFA would later develop.

Although the area that will become the VWFA does not respond preferentially to letters at age 5, Saygin says it is likely that the region is involved in some kind of high-level object recognition before it gets taken over for word recognition as a child learns to read. Still unknown is how and why the brain forms those connections early in life.

Pre-existing connections

The MIT team now plans to study whether this kind of brain imaging could help identify children who are at risk of developing dyslexia and other reading difficulties.

"It's really powerful to be able to predict functional development three years ahead of time," Saygin says. "This could be a way to use neuroimaging to try to actually help individuals even before any problems occur."

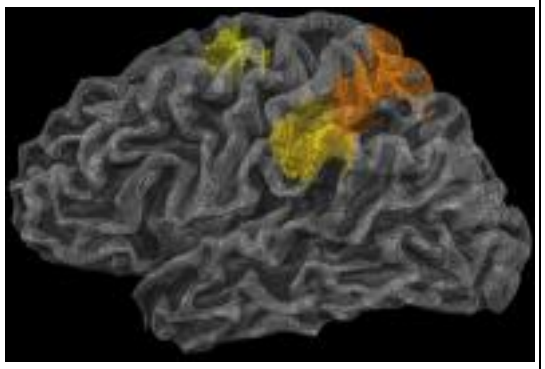
http://www.eurekalert.org/pub_releases/2016-08/jhu-rfb080416.php

Researchers find brain's 'physics engine'

Predicts how world behaves; among 'most important aspects of cognition for survival'

Researchers Find Brain's 'Physics Engine'Predicts how world behaves; among 'most important aspects of cognition for survival'

Whether or not they aced the subject in high school, human beings are physics masters when it comes to understanding and predicting how objects in the world will behave. A Johns Hopkins University cognitive scientist has found the source of that intuition, the brain's "physics engine."



The location of the 'physics engine' in the brain is highlighted in color in this illustration. **Jason Fischer/JHU**

This engine, which comes alive when people watch physical events unfold, is not in the brain's vision center, but in a set of regions devoted to planning actions, suggesting the brain performs constant, real-time physics calculations so people are ready to catch, dodge, hoist or take any necessary action, on the fly. The findings, which could help design more nimble robots, are set to be published in the journal Proceedings of the National Academy of Sciences.

"We run physics simulations all the time to prepare us for when we need to act in the world," said lead author Jason Fischer, an assistant professor of psychological and brain sciences in the university's Krieger School of Arts and Sciences. "It is among the most important aspects of cognition for survival. But there has been almost no work done to identify and study the brain regions involved in this capability."

Fischer, along with researchers at Massachusetts Institute of Technology, conducted a series of experiments to find the parts of the brain involved in physical inference. First they had 12 subjects look at videos of Jenga-style block towers. While monitoring their brain activity, the team asked the subjects either to predict where the blocks would land should the tower topple, or guess if the tower had more blue or yellow blocks. Predicting the direction of falling blocks involved physics intuition, while the color question was merely visual.

Next, the team had other subjects watch a video of two dots bouncing around a screen. They asked subjects to predict the next direction the dots would head, based either on physics or social reasoning.

With both the blocks and dots, the team found, when subjects attempted to predict physical outcomes, the most responsive brain regions included the premotor cortex and the supplementary motor area - the brain's action planning areas.

"Our findings suggest that physical intuition and action planning are intimately linked in the brain," Fischer said. "We believe this might be because infants learn physics models of the world as they hone their motor skills, handling objects to learn how they behave. Also, to reach out and grab something in the right place with the right amount of force, we need real-time physical understanding."

In the last part of the experiment, the team asked subjects to look at short movie clips -- just to look; they received no other instructions -- while having their brain activity monitored. Some of the clips had a lot of physics content, others very little. The team found that the more physical content in a clip, the more the key brain regions activated.

"The brain activity reflected the amount of physical content in a movie, even if people weren't consciously paying attention to it," Fischer said. "This suggests that we are making physical inferences all the time, even when we're not even thinking about it."

The findings could offer insight into movement disorders such as apraxia, as it's very possible that people with damage to the motor areas of the brain also have what Fischer calls "a hidden impairment" -- trouble making physical judgments.

A better understanding of how the brain runs physics calculations might also enrich robot design. A robot built with a physics model, constantly running in its programming almost like a video game, could navigate the world more fluidly.

Note: ***Related video here***

Fischer's co-authors are John G. Mikhael, now a student in the Harvard/MIT M.D.-Ph.D. program; and Joshua B. Tenenbaum and Nancy Kanwisher, both professors at the McGovern Institute for Brain Research and the Department of Brain and Cognitive Sciences at the Massachusetts Institute of Technology.

This research was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development Award F32-HD075427, National Eye Institute grant EY13455 and NSF Science and Technology Center for Brains, Minds, and Machines CCF-1231216.

http://bit.ly/2aBlrkv

Ice age fashion showdown: Neanderthal capes versus human hoodies

Early modern humans dressed for ice age success – Neanderthals, not so much.

By Colin Barras

An analysis of animal remains at prehistoric hominin sites across Europe suggests modern humans clad themselves in snug, fur-trimmed clothing, while Neanderthals probably opted for simple capes. Even so, the finding suggests our extinct cousin was far more sophisticated than once thought.

Some researchers argue that Neanderthals didn't bother with clothes at all, others that they dressed in much the same way as early members of our species. Mark Collard at Simon Fraser University in Burnaby, Canada, and his colleagues think the truth lies somewhere in between.

The team examined a database of the mammals that lived between 60,000 and 24,000 years ago in ice age Europe.

Next, they used a database of world cultures to identify those mammals now exploited for clothing by traditional peoples living at mid-to-high latitudes. Finally, they returned to the ice age database to compare the abundance of these animals at Neanderthal and modern human archaeological sites.

The researchers found that such mammals – including species of deer, bison and bear – were common at both sets of sites, consistent with the idea that both Neanderthals and modern humans wore clothes. But, importantly, the animals were generally more common at sites associated with our species.

There are a few ways to explain this finding. One is that modern humans produced complicated garments, each stitched together from several animal skins, so they caught more of these animals to have more material to work with. Neanderthals might have caught fewer of them because they wore much simpler clothes.

"It's a great new perspective on Neanderthal clothing"

"The idea is that [Neanderthals] were making capes of fur," says Collard. Some might simply have worn the skin of a large animal around their shoulders, he says, as Hercules is often depicted.

Modern humans, meanwhile, might have opted for a more practical – if less heroic – look; what Collard calls "close-fitting sewn garments". A collection of 24,000-year-old carved figurines from Siberia suggest what the prevailing style might have been during the ice age, with hoodies in vogue.

A closer look at the databases potentially tells us even more about ice age styles, says Collard. Weasel, wolverine and dog remains are found at sites occupied by modern humans – but not at Neanderthal sites.

The fur of these animals is a mix of long and short hairs, which makes it an ideal as a trim added to sleeves or hoods for extra insulation. Collard thinks ice age humans could have used fur trims in this way. Neanderthals might have been left shivering in their untrimmed capes.

John Stewart at the University of Bournemouth, UK, who performed a similar analysis a decade ago, says it's possible that the data tells us something about ice age clothing, but is cautious about jumping to conclusions.

Bones at an archaeological site might represent the remains of animals hunted for food instead of fur, for instance, or that shared the same living space as hominins but were not actively exploited.

"You need to look at the bones of the animals and find evidence that they were skinned – and you can't do that by studying a database," he says.

Collard, however, says that many of the more interesting species highlighted, including weasels and wolverines, are rarely caught for food today.

Stewart also thinks the database approach can overlook important information.

For instance, the remains of some animals might be absent from Neanderthal sites because those mammals simply weren't present in those areas at the same time as Neanderthals.

But other researchers say the work is important despite such concerns. "I think it's a great new perspective on Neanderthal clothing," says Nathan Wales at the University of Copenhagen, Denmark. In particular, he regards the evidence that Neanderthals didn't add fur trim to their clothing as quite strong.

Ice age style

If modern humans used fur trim early on, did that mean they had already developed a sense of style? Collard says present-day ethnographic data suggests otherwise: fur trim is generally added for function rather than fashion.

"However, I think there is reason to suspect that early modern human clothing had a stylistic dimension," he says. "They produced beads and there appear to be multiple clear regional or stylistic groups."

Ian Gilligan, formerly at the Australian National University in Canberra, says that the fashion probably began with the early modern humans, whereas Neanderthals lived generally fashion-free lives.

"I suspect that it is only with fitted garments – what I call complex clothes – that symbolic and fashion elements become important."

But Neanderthals might not have been completely clueless when it came to personal appearance (see box below).

"We now know that Neanderthals were using coloured ochre – probably for body decoration and perhaps colouring clothes as well," says Gilligan.

Neanderthal chic

Neanderthals living in ice age Europe might have opted for capes instead of elaborate outfits (see main story), but that isn't to say they didn't accessorise.

Feathered ornaments

A collection of 44,000-year-old bird-wing bones found at an Italian cave show evidence of being scraped with stone tools where the flight feathers were once attached. Some researchers think Neanderthals removed the feathers to use as ornaments. Similar finds have turned up in Gibraltar.

Eagle talon necklaces

Some 130,000 years ago, Neanderthals living in a cave in what is now Croatia might have strung eagle talons together and worn them as necklaces – no mean feat considering the difficulty of acquiring the talons. Neanderthals in France also collected the talons.

Colourful pendants

João Zilhão et al. http://www.pnas.org/content/107/3/1023.full

Perforated seashells found in 50,000-year-old deposits in a Spanish cave (pictured above) contain the remnants of pigments, leading to suggestions that they might have been made into pendants. Similar shells have been found at Neanderthal sites in Italy.

Journal reference: Journal of Anthropological Archaeology, DOI: 10.1016/j.jaa.2016.07.010

http://www.eurekalert.org/pub_releases/2016-08/uon-ssr080516.php

Study shows rapid decline in male dog fertility, with potential environmental causes

A study led by researchers at The University of Nottingham has discovered that the fertility of dogs may have suffered a sharp decline over the past three decades.

The research, published in the academic journal Scientific Reports, found that sperm quality in a population of stud dogs studied over a 26-year period had fallen significantly.

The work has highlighted a potential link to environmental contaminants, after they were able to demonstrate that chemicals found in the sperm and testes of adult dogs -- and in some commercially available pet foods -- had a detrimental effect on sperm function at the concentrations detected.

As 'man's best friend' and closest companion animal, the researchers believe that the latest results may offer a new piece of the puzzle over the reported significant decline in human semen quality - a controversial subject which scientists continue to debate.

Dr Richard Lea, Reader in Reproductive Biology in the University's School of Veterinary Medicine and Science, who led the research said: "This is the first time that such a decline in male fertility has been reported in the dog and we believe this is due to environmental contaminants, some of which we have detected in dog food and in the sperm and testes of the animals themselves.

"While further research is needed to conclusively demonstrate a link, the dog may indeed be a sentinel for humans - it shares the same environment, exhibits the same range of diseases, many with the same frequency and responds in a similar way to therapies."

The study centred on samples taken from stud dogs at an assistance dogs breeding centre over the course of 26 years. Professor Gary England, Foundation Dean of the School of Veterinary Medicine and Science and Professor of Comparative Veterinary Reproduction, who oversaw the collection of semen said: "The strength of the study is that all samples were processed and analysed by the same laboratory using the same protocols during that time and consequently the data generated is robust."

The work centred on five specific breeds of dogs - Labrador retriever, golden retriever, curly coat retriever, border collie and German shepherd -- with between 42 and 97 dogs studied every year.

Semen was collected from the dogs and analysed to assess the percentage of sperm that showed a normal forward progressive pattern of motility and that appeared normal under a microscope (morphology).

Over the 26 years of the study, they found a striking decrease in the percentage of normal motile sperm. Between 1988 and 1998, sperm motility declined by 2.5 per cent per year and following a short period when stud dogs of compromised fertility were retired from the study, sperm motility from 2002 to 2014 continued to decline at a rate of 1.2% per year.

In addition, the team discovered that the male pups generated from the stud dogs with declining semen quality, had an increased incidence of cryptorchidism, a condition in which the testes of pups fail to correctly descend into the scrotum.

Sperm collected from the same breeding population of dogs, and testes recovered from dogs undergoing routine castration, were found to contain environmental contaminants at concentrations able to disrupt sperm motility and viability when tested.

The same chemicals that disrupted sperm quality, were also discovered in a range of commercially available dog foods - including brands specifically marketed for puppies.

Dr Lea added: "We looked at other factors which may also play a part, for example, some genetic conditions do have an impact on fertility. However, we discounted that because 26 years is simply too rapid a decline to be associated with a genetic problem."

Over the past 70 years, studies have suggested a significant decline in human semen quality and a cluster of issues called 'testicular

dysgenesis syndrome' that impact on male fertility which also include increased incidence of testicular cancer, the birth defect hypospadias and undescended testes.

However, declining human semen quality remains a controversial issue -- many have criticised the variability of the data of the studies on the basis of changes in laboratory methods, training of laboratory personnel and improved quality control over the years.

Dr Lea added: "The Nottingham study presents a unique set of reliable data from a controlled population which is free from these factors. This raises the tantalising prospect that the decline in canine semen quality has an environmental cause and begs the question whether a similar effect could also be observed in human male fertility."

The paper, Environmental Chemicals Impact Semen Quality in Dogs in Vitro and May be Associated with a Temporal Decline in Quality and Increased Cryptorchidis, is available to view at the website for the journal Scientific Reports after the embargo lifts. An embargoed copy of the paper is available from the contacts below before publication.

http://bit.ly/2bkrI5O

Research reveals patient can have more than one breast cancer, points at treatments

Majority of ER-positive breast cancers are not a single tumor but more like a family of related tumors

HOUSTON - Breast cancer tumors are complex and dynamic. They comprise a population of continuously dividing cells that carry different genetic mutations. On a paper published today in Nature Communications, researchers from Baylor College of Medicine, Washington University School of Medicine, MD Anderson Cancer Center and the Mayo Clinic reveal, for the first time, that treating human estrogen-receptor positive (ER-positive) breast cancer tumors with estrogen-deprivation therapy results in changes in the spectrum of mutations in the tumor population, and point towards the possibility of using this information to improve cancer treatment.

"The majority of ER-positive breast cancers are not a single tumor but more like a family of related tumors referred to as 'sub-clones,'" said senior author Dr. Matthew Ellis, professor and director of the Lester and Sue Smith Breast Center at Baylor. "The tumors are like a large family. A family has the same genetic origin - the same parents - but each family member has distinct genetic characteristics. The brothers and sisters are clearly individuals but they are also related. When we treat the tumor with aromatase inhibitors, an estrogen-deprivation therapy that lowers the levels of estrogen the tumor needs to grow, we are creating a situation where certain members in the tumor family are able to persist and grow while others perish. The surviving members of the tumor family are likely the ones that will cause future problems with recurrence."

Although researchers have extensively studied the genetic heterogeneity in breast cancer in untreated samples, they knew little about how aromatase inhibitors, such as letrozole, anastrozole and exemestane, affect the genetic diversity of the tumor.

"In this study, we present a first answer to this question by studying 22 human breast cancer tumors scheduled for surgery," said Ellis. "To reduce tumor size before surgery, we treated the tumors with estrogen-deprivation therapy for four months. The tumors were then surgically removed. We analyzed in great detail the effect of estrogen-deprivation therapy on the gene mutation patterns of the tumors by studying the entire genomic structure - the whole genome - of each of the tumors on biopsies taken before and after estrogen-deprivation therapy."

"In the post-treatment samples, we found many new mutations or enrichment of mutations present at low levels in the pre-treatment samples," said Ellis. "This means that under the environmental stress of the treatment, the tumors are spawning new sub-clones which subsequently can survive and grow despite therapy, and that is why we are having difficulty treating ER-positive breast cancer. We found this result for a majority of ER-positive breast cancers we studied."

A majority of the breast cancer tumors the researchers studied comprised a number of sub-clones with a common origin - they were all members of the same tumor family. But, the researchers also

discovered that some patients had more than one tumor of different origin.

"Even though each patient in this study was diagnosed only with a single tumor, looking at the cancer genome allowed us to see that in some cases the patient actually had two separate tumors growing closely together. We call these "collision tumors," said first author Dr. Christopher Miller, research faculty at the McDonnell Genome Institute at Washington University in St Louis.

In these cases, the two separate tumors were like "two unrelated families growing so close together they were originally incorrectly identified as a single family," said Ellis.

Undiagnosed collision tumors could explain why sometimes tumors with an initial good prognosis have an unexpected relapse after surgical treatment.

In one of the 22 tumors, the researchers discovered ER-negative tumor cells that were hiding inside a mostly ER-positive tumor. "By the end of four months of therapy - because the treatment had shrunk the ER-positive tumor - we could detect this second ER-negative tumor, and treat it accordingly to its nature before it grew larger," said Ellis. "Without this approach, that ER-negative tumor would have never been diagnosed early and treated."

"If a patient with breast cancer has the tumor surgically removed, it won't be possible to detect the cells with the genetic makeup most likely to be driving relapse," said Ellis. "But, if, on the other hand, we start by treating the tumor with aromatase inhibitors before surgery for a few months, so we can track the behavior of that tumor, we would get a more complete picture of the cancer. We can potentially detect sub-clones that can cause relapse in the future."

"Our results suggest that studying the genetic makeup of a tumor at diagnosis is not enough - periodically scanning the genome in several biopsy samples to understand how it is changing may help us evolve treatment strategies to match," said Miller.

"The results emphasize the importance of proper trial design coupled with sample banking and annotation within clinical trials toward ultimately arriving at a better understanding of the disease and its treatment," said senior author Dr. Elaine R. Mardis, Robert E. and Louise F. Dunn distinguished professor of medicine and co-director of the McDonnell Genome Institute at Washington University School of Medicine.

Treatment with aromatase inhibitors before surgery can have advantages for patients. "Because the treatment shrinks the tumor, patients are more likely to have breast-conserving surgery," said Ellis.

Other contributors to this work include Yevgeniy Gindin, Charles Lu, Obi L. Griffith, Malachi Griffith, Dong Shen, Jeremy Hoog, Tiandao Li, David E. Larson, Mark Watson, Sherri R. Davies, Kelly Hunt, Vera Suman, Jacqueline Snider, Thomas Walsh, Graham A. Colditz, Katherine DeSchryver and Richard K. Wilson from Baylor College of Medicine, Washington University School of Medicine, MD Anderson Cancer Center and Mayo Clinic.

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http://bit.ly/2aIiI99

Study pushes back the origin of HIV-related retroviruses to 60 million years ago

Using phylogenetic analysis, ELVgv are estimated to have invaded an ancestor of today's Dermoptera in the distant past

Lentiviruses cause a variety of chronic diseases in mammals ---ranging from the most notorious example of HIV/AIDS in humans to various neurological disorders in primates----yet little is known of their evolutionary history and origin.

As HIV/AIDS has emerged only recently and so far eluded efforts to outwit it, researchers have been looking at imprints left by related viruses in other animals to better understand their origins. Until

recently, the oldest known lentiviral lineages --- in lemurs, rabbits and ferrets --- have been found to date back to 3-12 million years ago.

Now, a research group led by Daniel Elleder from the Czech Academy of Sciences has used genomic data from the exotic Malayan flying lemur (colugo) to uncover the oldest lentivirus ever identified, whose first emergence may date to as early as 60 million years ago. Three samples of colugo genomic DNA containing lentiviral remnants were sequenced and ancient viral genomes were reconstructed and analyzed.

The findings were published in the advanced online edition of Molecular Biology and Evolution.

"We hope that our findings will allow virologists to better understand how lentiviruses evolved and how their hosts developed defenses against them," said Elleder.

In future studies, the team wants to follow the timeline even deeper into the past by surveying a broad spectrum of animals, hoping to identify more pieces of the puzzle of lentivirus evolution.

http://www.eurekalert.org/pub_releases/2016-08/b-spd080816.php

Study provides details of possible link between Zika and severe joint condition at birth

A study published by The BMJ today provides more details of an association between Zika virus infection in the womb and a condition known as arthrogryposis, which causes joint deformities at birth, particularly in the arms and legs.

Microcephaly (a rare birth defect where a baby is born with an abnormally small head) and other severe fetal brain defects are the main features of congenital Zika virus syndrome. However, little is still known about other potential health problems that Zika virus infection during pregnancy may cause.

Until recently there were no reports of an association between congenital viral infection and arthrogryposis. After the outbreak of microcephaly in Brazil associated with Zika virus, two reports suggested an association, but they did not describe the deformities in detail.

So a research team based in Recife, the Brazilian city at the centre of the Zika epidemic, decided to investigate the possible causes of the joint deformities.

They studied detailed brain and joint images of seven children with arthrogryposis and a diagnosis of congenital infection, presumably caused by Zika virus. All children tested negative for the five other main infectious causes of microcephaly - toxoplasmosis, cytomegalovirus, rubella, syphilis, and HIV.

All children showed signs of brain calcification, a condition in which calcium builds up in the brain. The theory is that the Zika virus destroys brain cells, and forms lesions similar to "scars" on which calcium is deposited.

All the children underwent high definition scanning of the joints and surrounding tissues, but there was no evidence of joint abnormalities.

This led the researchers to say that the arthrogryposis "did not result from abnormalities of the joints themselves, but was likely to be of neurogenic origin" - a process involving motor neurones (cells that control the contraction or relaxation of muscles) - leading to fixed postures in the womb and consequently deformities.

They point out that further research is needed with a larger number of cases to study the neurological abnormalities behind arthrogryposis, but suggest that children should receive orthopaedic follow-up ... "because they could develop musculoskeletal deformities secondary to neurological impairment."

Based on these observations, the researchers conclude that "congenital Zika syndrome should be added to the differential diagnosis of congenital infections and arthrogryposis."

Because this is an observational study, no firm conclusions can be drawn about the effect of the Zika virus on arthrogryposis. Nevertheless, the authors suggest that this condition might be related to the way motor neurons carry signals to the unborn baby's muscles, or to problems with arteries and veins (vascular disorders).

http://www.eurekalert.org/pub_releases/2016-08/uoca-oao080916.php

Outdated assessment of treatment response makes good cancer drugs look bad

Tumor shrinkage is not the only measure of a successful anti-cancer therapy.

A University of Colorado Cancer Center article published in the journal Frontiers in Oncology describes a promising alternative: metabolic imaging. Tumors rush their metabolism to grow and proliferate. By recognizing a drug's ability to stop this energy overuse, doctors may be able to determine a patient's response to a new, targeted therapy far earlier and with far more precision than watching and waiting for a tumor to shrink.

"What we have been using for decades is called RECIST - it measures the dimensions of a tumor and it does a good job of showing a patient's response to chemotherapy and radiation. These therapies (called cytotoxic) kill cells and so if they are working, we see the tumor shrink," says Natalie Serkova, PhD, investigator at the University of Colorado Cancer Center and professor at the University of Colorado School of Medicine.

However, many modern targeted therapies do not immediately kill cancer cells. Instead, they interrupt a cancer cell's ability to grow and proliferate, often by immediate cessation of metabolic rates. Eventually these cells "interrupted" by targeted therapies die, but cell death and tumor shrinkage are not immediate, direct markers of a therapy's usefulness.

Serkova points out that a recent article published in the Journal of Clinical Oncology shows that 15 percent of patients who are taken off clinical trials due to perceived lack of response to a trial medication aren't in fact non-responders - the drug may be working for these people in a way that is not captured by RECIST.

"With this criteria, it doesn't look like the new experimental drug is working. But it may be the criteria and not the drug that is failing in trials of these new targeted therapies," says S. Gail Eckhardt, MD, FASCO, associate director for translational research at CU Cancer Center, the Stapp Harlow Chair in Cancer Research at CU SOM, and the paper's senior author.

One possible solution is to image a tumor's metabolic rate, such as glucose uptake. "Cancer are gluttons for glucose," Eckhardt says, meaning that in order to drive their growth, cancers burn glucose at many times the rate of healthy cells. Drugs including anti-EGFR therapies stop cancer cells' ability to over-use glucose.

"These new therapies stop a cancer cell's glucose uptake within 24 hours after the first dose, but changes in tumor volume happen months later," Eckhardt says. Is the drug working? Watching for changes in a tumor's use of glucose could answer this question months earlier than current RECIST criteria.

Another metabolic aspect that can hint at a medicine's success is a tumor's uptake of "phospholipids". Boundless cell replication is a feature of cancer. This requires building new cell membranes at a breakneck pace. These membranes are made from phospholipids - a drug that slows a tumor's use of phospholipids in building new cell membranes is successful, even before it leads to a reduction in tumor volume.

Finally, new criteria are desperately needed to determine the success of immunotherapies. "With useful immunotherapies like PD1 and PDL1 checkpoint inhibitors, we can actually see an initial increase in tumor size. A successful immune response against a tumor is marked by inflammation which might mimic an increase in tumor dimensions. With RECIST criteria that prioritizes tumor volume, inflammation can make it look like these drugs have made the cancer worse," Serkova says.

"RECIST will remain the gold standard to measure the success of classic, cytotoxic therapies like chemotherapy and radiation - therapies whose singular goal is cell death," Serkova says. "And it remains useful in characterizing the response to these new targeted

therapies after they have had months to eventually result in tumor shrinkage. But new measures are needed to show before months have passed whether these drugs are working."

The immediate danger, say Serkova and Eckhardt, is that patients are missing out on successful treatments because current measures make them seem unsuccessful. In the researchers' opinion, the various forms of metabolic imaging could provide alternative tests of a patient's response to novel targeted therapies.

http://www.eurekalert.org/pub_releases/2016-08/wfbm-rst080916.php

Researchers successfully test modified stun gun with heart monitoring capability

Taser that monitors the heart while continuing to shock!

WINSTON-SALEM, N.C. - Researchers at Wake Forest Baptist Medical Center have successfully tested a prototype conducted electrical weapon (CEW) capable of recording a subject's heart rate and rhythm while still delivering incapacitating electrical charges.

The study is published in the current online edition of the Journal of Forensic and Legal Medicine.

CEWs, best known by the brand name Taser - have proved to be a generally safe and effective way for law-enforcement officers to subdue criminal suspects and threatening individuals in non-lethal situations. Cases of serious injury and death related to the use of these devices are extremely rare and often include other risk factors, including drug use and pre-existing medical conditions. But isolated reports of deaths occurring shortly after the use of CEWs have raised concerns they caused cardiac rhythm disturbances in targeted individuals.

"The basic components of a CEW - probes that penetrate the skin while attached to insulated wires connected to an electronic device - are functionally similar to what is used to obtain an electrocardiogram," said Jason P. Stopyra, M.D., assistant professor of emergency medicine at Wake Forest Baptist and lead author of the study. "We set out to see if we could combine a heart monitoring device with an existing CEW to detect and store cardiac rhythms without impeding the function of the weapon, and we succeeded."

For the study, the research team modified standard law enforcement CEW cartridges to transmit electrocardiogram (EKG) signals then combined a miniaturized EKG recorder with a standard-issue CEW. In tests on human volunteers, the researchers' prototype device successfully produced both incapacitating charges and interpretable EKG signals.

"This serves as proof-of-concept that safety measures such as cardiac biomonitoring can be incorporated into CEWs and possibly other law enforcement devices," said William B. Bozeman, M.D., professor of emergency medicine at Wake Forest Baptist and senior author of the study. "Such devices, when fully developed, could alert law enforcement personnel to potential medical issues in real time and promote the rapid treatment of individuals who may suffer a medical crisis while in custody."

Support for the project was provided by grants 2004-IJ-CX-K047 and 2006-DE-BX-K002 from the National Institute of Justice. Phase 3 of this project was supported by an investigator-initiated grant from the Medtronic Corporation.

Co-authors are Samuel I. Ritter, M.D., Jennifer Beatty, M.D., James C. Johnson, M.P.A.S., James E. Winslow III, M.D., and Alison R. Gardner, M.D., of Wake Forest Baptist and Douglas M. Kleiner, Ph.D., of Tactical Medics International, Jacksonville Beach, Fla.

http://www.eurekalert.org/pub_releases/2016-08/fos--tso080816.php

Textbook story of how humans populated America is 'biologically unviable,' study finds

The established theory about the route by which Ice Age peoples first reached the present-day United States has been challenged by an unprecedented study which concludes that their supposed entry route was "biologically unviable".

The first people to reach the Americas crossed via an ancient land bridge between Siberia and Alaska but then, according to conventional wisdom, had to wait until two huge ice sheets that covered what is

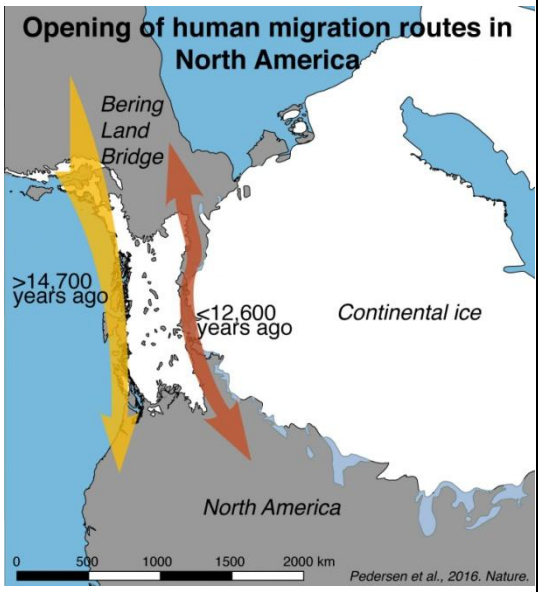
now Canada started to recede, creating the so-called "ice-free corridor" which enabled them to move south.

In a new study published in the journal Nature, however, an international team of researchers used ancient DNA extracted from a crucial pinch-point within this corridor to investigate how its ecosystem evolved as the glaciers began to retreat. They created a comprehensive picture showing how and when different flora and fauna emerged and the once ice-covered landscape became a viable passageway. No prehistoric reconstruction project like it has ever been attempted before.

The researchers conclude that while people may well have travelled this corridor after about 12,600 years ago, it would have been impassable earlier than that, as the corridor lacked crucial resources, such as wood for fuel and tools, and game animals which were essential to the hunter-gatherer lifestyle.

If this is true, then it means that the first Americans, who were present south of the ice sheets long before 12,600 years ago, must have made the journey south by another route.

The study's authors suggest that they probably migrated along the Pacific coast.



Map outlining the opening of the human migration routes in North America revealed by the results presented in this study. **Mikkel Winther Pedersen**

Who these people were is still widely disputed. Archaeologists agree, however, that early inhabitants of the modern-day contiguous United States included the so-called "Clovis" culture, which first appear in the archaeological record over 13,000 years ago. And the new study argues that the ice-free corridor would have been completely impassable at that time.

The research was led by Professor Eske Willerslev, an evolutionary geneticist from Centre for GeoGenetics, University of Copenhagen and University of Cambridge, who also hold posts at St John's College and the Wellcome Sanger Institute.

"The bottom line is that even though the physical corridor was open by 13,000 years ago, it was several hundred years before it was possible to use it," Willerslev said.

"That means that the first people entering what is now the US, Central and South America must have taken a different route. Whether you believe these people were Clovis, or someone else, they simply could not have come through the corridor, as long claimed."

Mikkel Winther Pedersen, a PhD student at the Centre for GeoGenetics, University of Copenhagen, who conducted the molecular analysis, added: "The ice-free corridor was long considered the principal entry route for the first Americans. Our results reveal that it simply opened up too late for that to have been possible."

The corridor is thought to have been about 1,500 kilometres long, and emerged east of the Rocky Mountains 13,000 years ago in present-day western Canada, as two great ice sheets - the Cordilleran and Laurentide, retreated.

On paper, this fits well with the argument that Clovis people were the first to disperse across the Americas. The first evidence for this culture, which is named after distinctive stone tools found near Clovis, New Mexico, also dates from roughly the same time, although many archaeologists now believe that other people arrived earlier.

"What nobody has looked at is when the corridor became biologically viable," Willerslev said. "When could they actually have survived the long and difficult journey through it?"

The conclusion reached by Willerslev and his colleagues is that the journey would have been impossible until about 12,600 years ago. Their research focused on a "bottleneck", one of the last parts of the

corridor to become ice-free, and now partly covered by Charlie Lake in British Columbia, and Spring Lake, Alberta - both part of Canada's Peace River drainage basin.

The team gathered evidence including radiocarbon dates, pollen, macrofossils and DNA taken from lake sediment cores, which they obtained standing on the frozen lake surface during the winter season. Willerslev's own PhD, 13 years ago, demonstrated that it is possible to extract ancient plant and mammalian DNA from sediments, as it contains preserved molecular fossils from substances such as tissue, urine, and faeces.

Having acquired the DNA, the group then applied a technique termed "shotgun sequencing". "Instead of looking for specific pieces of DNA from individual species, we basically sequenced everything in there, from bacteria to animals," Willerslev said. "It's amazing what you can get out of this. We found evidence of fish, eagles, mammals and plants. It shows how effective this approach can be to reconstruct past environments."

This approach allowed the team to see, with remarkable precision, how the bottleneck's ecosystem developed. Crucially, it showed that before about 12,600 years ago, there were no plants, nor animals, in the corridor, meaning that humans passing through it would not have had resources vital to survive.

Around 12,600 years ago, steppe vegetation started to appear, followed quickly by animals such as bison, woolly mammoth, jackrabbits and voles. Importantly 11,500 years ago, the researchers identified a transition to a "parkland ecosystem" - a landscape densely populated by trees, as well as moose, elk and bald-headed eagles, which would have offered crucial resources for migrating humans.

Somewhere in between, the lakes in the area were populated by fish, including several identifiable species such as pike and perch. Finally, about 10,000 years ago, the area transitioned again, this time into boreal forest, characterised by spruce and pine.

The fact that Clovis was clearly present south of the corridor before 12,600 years ago means that they could not have travelled through it. David Meltzer, an archaeologist at Southern Methodist University and a co-author on the study, said: "There is compelling evidence that Clovis was preceded by an earlier and possibly separate population, but either way, the first people to reach the Americas in Ice Age times would have found the corridor itself impassable."

"Most likely, you would say that the evidence points to their having travelled down the Pacific Coast," Willerslev added. "That now seems the most likely scenario."

The paper Postglacial viability and colonization in North America's ice-free corridor is published in the journal Nature on 10. August 2016. DOI: 10.1038/nature19085

http://www.eurekalert.org/pub_releases/2016-08/sumc-srd080816.php

Stanford researchers devise method for bone marrow transplants without using chemotherapy

Blood stem cell transplantation, widely known as bone marrow transplantation, is a powerful technique that potentially can provide a lifelong cure for a variety of diseases.

But the procedure is so toxic that it is currently used to treat only the most critical cases.

Now, researchers at the Stanford University School of Medicine have come up with a way of conducting the therapy that, in mice, dramatically lowers its toxicity. If the method eventually proves safe and effective for humans, it potentially could be used to cure autoimmune diseases like lupus, juvenile diabetes and multiple sclerosis; fix congenital metabolic disorders like "bubble boy" disease; and treat many more kinds of cancer, as well as make organ transplants safer and more successful.

"There is almost no category of disease or organ transplant that is not impacted by this research," said Irving Weissman, MD, a co-author of the research and professor of pathology and of developmental biology at Stanford. A paper describing the technique will be published Aug.

10 in Science Translational Medicine. The paper's senior author is Judith Shizuru, MD, PhD, professor of medicine. The lead authors are research associate Akanksha Chhabra, PhD, and former graduate students Aaron Ring, MD, PhD, and Kipp Weiskopf, MD, PhD.

Noxious treatment

To successfully transplant blood stem cells, a patient's own population of blood stem cells must be killed. Currently, this is done using chemotherapy or radiotherapy, treatments that are toxic enough to damage a variety of organs and even result in death. "The chemotherapy and radiation used for transplant damage DNA and can cause both immediate problems and long-term damage to many tissues in the body," Shizuru said. "Among the many known toxic side effects, these treatments can cause damage to the liver, reproductive organs and brain, potentially causing seizures and impairing neurological development and growth in children." For these reasons, blood stem cell transplantation is used only when the risks of serious disease outweigh the complications from the transplant.

To avoid these terrible side effects, the Stanford researchers composed a symphony of biological instruments that clear the way for blood stem cell transplantation without the use of chemotherapy or radiotherapy.

Using antibodies

The scientists started with an antibody against a cell surface protein called c-kit, which is a primary marker of blood stem cells. Attaching the antibody to c-kit resulted in depletion of blood stem cells in immune-deficient mice. "However, this antibody alone would not be effective in immune-competent recipients, who represent a majority of potential bone marrow transplant recipients," Chhabra said. The researchers sought to enhance the effectiveness by combining it with antibodies or with biologic agents that block another cell surface protein called CD47. Blocking CD47 liberated macrophages to "eat" target cells covered with c-kit antibody, Chhabra said.

With the CD47 marker blocked and the antibody attached to c-kit proteins, the immune system effectively depleted the animals' blood-forming stem cells, clearing the way for transplanted blood stem cells from a donor to take up residence in the bone marrow and generate a whole new blood and immune system.

Comparing blood stem cell transplants to planting a new field of crops, Shizuru noted that the researchers not only found a safer way to clear the field for planting, but "we also used safer techniques to seed the new blood-generating cells."

Currently, bone marrow transplants involve a mix of cells that includes blood stem cells as well as various immune cells from the donor, which can attack the tissue of the transplant recipient. This immune attack results in what is called graft-versus-host disease, which can damage tissues and even kill patients.

Building on knowledge gained from previous research, the team purified the donor tissue so that it contained only blood stem cells and not the other immune cells that cause graft-versus-host disease.

The success of these techniques in mice raises hopes that similar techniques will succeed in human patients. "If it works in humans like it did in mice, we would expect that the risk of death from blood stem cell transplant would drop from 20 percent to effectively zero," Shizuru says.

'New era in disease treatment'

"If and when this is accomplished, it will be a whole new era in disease treatment and regenerative medicine," said Weissman, who is director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, as well as the director of the Ludwig Center for Cancer Stem Cell Research and Medicine.

Once a patient's blood and immune system can safely be replaced, any disease caused by the patient's own blood and immune cells could potentially be cured by a one-time application of blood stem cell transplantation, they said. Safely replacing a patient's blood and

immune cells will get rid of the cells that attack their own tissues and produce disease like rheumatoid arthritis and Type 1 diabetes.

A method of safely doing blood stem cell transplants would also potentially make organ transplantation safer and easier, the researchers said. Currently, people who get an organ transplant must for the rest of their lives stay on drugs that keep their immune systems from attacking the transplanted organ.

"Even if you are on immunosuppressants, most organ transplants diminish in function or fail over time, and the immunosuppressive drugs themselves make the patient more susceptible to life-threatening infections or newly forming cancers," Weissman said.

But if blood and immune stem cells from the organ donor can be transplanted at the same time as the organ, the new immune system will recognize the donated organ and not attack it, the researchers said. "The transplanted cells, the donated organ and the patient's own tissues all learn to coexist," Shizuru said. "The donor blood stem cells re-educate the immune system of the patient, and the transplanted organ doesn't get kicked out."

Blood and immune stem cell transplants may also be critical to making the new era of regenerative medicine a success. If stem cells for organs or tissues like heart or liver are grown for general transplantation -- that is, not designed specifically for one patient -- the patient will require immune conditioning through blood stem cell transplantation so that the stem cells are not rejected as foreign bodies, the researchers said.

Other Stanford-affiliated co-authors of the work are graduate student Sydney Gordon; research assistant Alan Le; research associate Hye-Sook Kwon, PhD; former medical fellow Nan Guo Ring, MD; Jens-Peter Volkmer, MD, an instructor at the Institute for Stem Cell Biology and Regenerative Medicine; former research assistants Serena Tseng and Peter John Schnorr; and Po Yi Ho.

Support for this research came from the Virginia and D.K. Ludwig Fund for Cancer Research, the California Institute for Regenerative Medicine, the National Institutes of Health (grants R01CA86065 and R01HL058770), the Stanford Medical Science Training Program, the Tom and Stacy Siebel Foundation, the Stinehart-Reed Foundation, the Gunn/Olivier Research Fund, and the HL Snyder Medical Foundation.

http://bit.ly/2aXppaE

A spoonful of fat makes the medicine go down

By-passing the 'first past metabolism' barrier

For years scientists and dieticians have argued over the health benefits of dietary fat. Research published this week, however, shows that piggybacking onto natural fat absorption pathways can dramatically enhance the utility of some drugs.

One of the key goals of drug development has long been to produce a therapy that can be taken orally (therefore cheap and easy to deliver) and is absorbed as directly and quickly into the blood stream as possible.

Many medications, however, are broken down in the liver before even making it into the blood stream. This is called "first past metabolism" whereby the drugs we swallow go via the gut and the liver (where breakdown occurs) before even entering the blood.

Scientists have long tried to bypass this process since it can prevent enough drug getting to the site of action to be useful.

Researchers at the ARC Centre of Excellence in Convergent Bio-Nano Science (CBNS) in Melbourne, Australia, have published a patented technology that allows orally administered drugs to by-pass the liver. This technology makes use of a natural nano-scale lipid transport system that delivers drug from the gut through the lymphatic system, and straight into the blood stream.

The publication, in the prestigious European journal, Angewandte Chemie International Edition, has been tested on testosterone in animal models, but, according to Professor Chris Porter, from CBNS, the technology has the potential to be used for a range of drugs that struggle to get through the liver and into the circulation, as well as for drugs targeted to the lymphatic system.

According to Professor Porter, the liver is a marvelous organ for filtering and protecting the body from materials it regards as foreign and breaking them down before they can be toxic. While this is a great advantage when protecting the body from dangerous toxins, it can

severely limit the amount of a drug that reaches the site of action after oral administration. "No matter how good the drug is, it needs to be absorbed (into the bloodstream) and to avoid this first pass metabolism in order to get to the general circulation where it acts," he said.

Professor Porter and his team from the CBNS at the Monash Institute of Pharmaceutical Sciences, have been fine tuning what is called a pro-drug technology. Aimed specifically at targeting drug absorption to the lymphatic system (rather than the hepatic portal blood) this technology modifies drugs so that they chemically mimic dietary lipids. Unlike most nutrients, after absorption lipids are assembled into nano-sized lipid droplets or lipoproteins and transported to the circulation via the lymph.

According to Professor Porter the pro-drug technology has two main benefits. "Firstly, the lymphatics drain directly into the blood and do not pass through the liver. This can dramatically enhance the efficiency of drugs with first pass metabolism problems like testosterone," he said.

"Second, the lymphatic system is a key part of the immune system and helps fight disease and regulates the immune response to infection. Drug delivery directly into the lymph may therefore enhance the utility of drugs that are designed to stimulate the immune system to eg fight cancer, or to suppress the immune system to fight autoimmune diseases such as Crohn's Disease".

Using testosterone, as a test drug, the researchers have found that their new delivery system boosts uptake of the drug into the intestinal lymphatics and in the case of testosterone leads to blood levels up to 90 times higher than that possible with the current commercial product.

"The advantage of our system is that drugs are shielded from degradation in the liver but are ultimately released when they reach their site of action, ensuring that the drug given to the patient goes where it is supposed to," Professor Porter said.

http://www.eurekalert.org/pub_releases/2016-08/vu-tno081016.php

Total number of neurons -- not enlarged prefrontal region -- hallmark of human brain

A new scientific study puts the final nail in the coffin of a long-standing theory to explain human's remarkable cognitive abilities: that human evolution involved the selective expansion of the brain's prefrontal cortex.

It does so by determining that the prefrontal region of the brain which orchestrates abstract thinking, complex planning and decision making contains the same proportion of neurons and fills the same relative volume in non-human primates as it does in humans.

"People need to drop the idea that the human brain is exceptional," said Vanderbilt University neuroscientist Suzana Herculano-Houzel, who directed the study. "Our brain is basically a primate brain. Because it is the largest primate brain, it does have one distinctive feature: It has the highest number of cortical neurons of any primate. Humans have 16 billion compared with 9 billion in gorillas and orangutans and six-to-seven billion in chimpanzees. It is remarkable, but it is not exceptional."

In her popular science book The Human Advantage: A New Understanding of How Our Brain Became Remarkable (MIT Press: March 2016), Herculano-Houzel explains how human brains grew so large, even larger than the brains of gorillas and orangutans, whose bodies are larger than ours. Her answer is surprisingly simple. It is the invention of cooking.

Cooking allowed early humans to overcome the energetic barrier that limits the size of the brains of other primates, she has determined. However, when the human brains grew larger they maintained the basic structure of the primate brain, including the size of the prefrontal cortex, her latest study has found. The comparison of the relative size of the prefrontal region in primate brains is described in a paper titled "No relative expansion of the number of prefrontal neurons in primate and human evolution" by Herculano-Houzel and postdoctoral fellow

Mariana Gabi published online this week in the Proceedings of the National Academy of Sciences early edition.

The researchers compared the brains of seven non-human primates of varying sizes - pig-tailed and crab-eating macaques, baboon, marmoset, galago, owl monkey and capuchin - with the human brain. They found that both the human and non-human primates devote about 8 percent of their neurons to the prefrontal region of the cortex. In addition, they determined that volumes of human prefrontal gray and white matter match the expected volumes for the number of neurons and other cells in the white matter when compared to other primates.

Cooking allowed us to overcome an energetic barrier that restricts the size of the brains of other primates.""Our big brains are very costly. They use 25 percent of all the energy the body needs each day," Herculano-Houzel said. "Cooking allowed us to overcome an energetic barrier that restricts the size of the brains of other primates."

Take the case of the gorilla. It must spend at least eight hours per day foraging and eating to support its body and brain. The human brain is three times larger than that of the gorilla. If a gorilla had a brain the size of a human, it would have to spend an additional one and a half hours a day finding food. So there simply aren't enough hours in the day for the gorilla to support a bigger brain. Likewise, if humans ate like any other primate, we would have to spend nine and a half hours per day eating - every single day.

That's where cooking comes in. "By cooking, I mean cutting, dicing, smashing-all types of food preparation," Herculano-Houzel said. "Take a single carrot. If you eat it raw, it will take 10 to 15 minutes of vigorous chewing and your digestive system will only capture about one third of the calories. But, if you cut the carrot up and cook it for a few minutes, it takes only a few minutes to consume and your body gets 100 percent of the calories."

The origin of cooking, as Herculano-Houzel defines it, dates back about 2.5 million years ago with the development of the first stone tools. Among other things, these stone tools were man's first food processors, allowing our ancestors to slice and dice and mash their food. Evidence for the controlled use of fire appears about 400,000 years ago.

"Those early tool makers had brains about the same size as gorillas. But, beginning about 1.8 million years ago, the brains of our ancestors began growing steadily, tripling in size over the next 1.5 million years," said Herculano-Houzel.

"It's amazing that something we now take for granted, cooking, was such a transformational technology which gave us the big brains that have made us the only species to study ourselves and to generate knowledge that transcends what was observed firsthand; to tamper with itself, fixing imperfections with the likes of glasses, implants and surgery and thus changing the odds of natural selection; and to modify its environment so extensively (for better and for worse), extending its habitat to improbable locations."

Jon Kaas, the Gertrude Conaway Vanderbilt Distinguished Professor of Psychology, and Kleber Neves, Carolinne Masseron, Pedro Ribeiro, Lissa Ventura-Antunes, Laila Torres and Bruno Mota from the Federal University of Rio De Janeiro were co-authors on the paper.

The research was supported by grants from the James S. McDonnell Foundation and the Mathers Foundation.

http://www.eurekalert.org/pub_releases/2016-08/uoaa-ngp081016.php

New guidelines published for physicians treating patients with kidney stones

A new guideline for the surgical management of patients with kidney and/or ureteral stones has been released by the American Urologic Association.

BIRMINGHAM, Ala. - Chair of the panel, Dean Assimos, M.D., worked with a team of kidney stone experts to develop one of the largest guidelines documents that the AUA has ever produced, highlighting more than 50 statements on best practices when treating patients with kidney and ureteral stones.

"The most pertinent change is that decision-making for treatment and therapy for patients with kidney and ureteral stones should be shared between physician and patient," said Assimos, chair of the University of Alabama at Birmingham Department of Urology.

Kidney stones affect more than 8.8 percent of the population in the United States, with direct and indirect treatment costs estimated to be several billion dollars per year, making it a common and costly disease.

The guidelines further outline expert recommendations in relation to treatment of renal stones, small hard mineral deposits formed inside the kidneys, and ureteral stones, stones that have moved from the kidney to the ureter.

These include:

imaging and pre-operative testing
treatment of adult patients with ureteral stones
treatment of adult patients with renal stones
treatment for pediatric patients with ureteral or renal stones
treatment for pregnant patients with ureteral or renal stones
treatment for all patients with ureteral or renal stones

The guidelines provide instruction on the evaluation of patients with renal and/or ureteral stones and highlight the lab and imaging studies that should be used prior to intervention for such patients.

The technical aspects of ureteroscopic removal of stones are addressed more extensively in the guidelines. The previous guidelines discussed medical expulsive therapy via the utilization of alpha blockers to facilitate the passage of stones in all segments of the ureter. However, the recent guidelines recommend this therapy only for stones in the distal ureter, which is located in the lower part of the kidney. Ureteroscopic removal of ureteral stones may potentially render a patient stone-free in one procedure. In this process, a ureteroscope is used to either extract an intact stone or break it up using a laser with subsequent removal of the generated fragments.

The guidelines further discuss the use of stents in the ureter after a ureteroscopic procedure. Clinicians may omit ureteral stenting in patients meeting all of the following criteria:

no ureteral injury during ureteroscopy
no anatomic obstruction, hindrance or obstacle to stone fragment clearance
normal function in the opposite kidney and normal renal function
no plans for secondary ureteroscopic procedure

"In the past, there was a portfolio of guidelines for physicians discussing prevention and treatment in various types of patients with kidney stones," Assimos said. "Evidence has changed over time, prompting an update and the need for more comprehensive guidelines. The panel developed this set of guidelines based on evidence from past clinical trials and studies published in the peer reviewed literature, as well as expert consensus of the physician panelists."

http://nyti.ms/2aTI17R

Obama Administration Set to Remove Barrier to Marijuana Research

Removing major roadblock to marijuana research could potentially spur broad scientific study of a drug

By CATHERINE SAINT LOUIS and MATT APUZZO AUG. 10, 2016

The Obama administration is planning to remove a major roadblock to marijuana research, officials said Wednesday, potentially spurring broad scientific study of a drug that is being used to treat dozens of diseases in states across the nation despite little rigorous evidence of its effectiveness.

The new policy is expected to sharply increase the supply of marijuana available to researchers.

And in taking this step, the Obama administration is further relaxing the nation’s stance on marijuana. President Obama has said he views it as no more dangerous than alcohol, and the Justice Department has not stood in the way of states that have legalized the drug.

For years, the University of Mississippi has been the only institution authorized to grow the drug for use in medical studies. This restriction has so limited the supply of marijuana federally approved for research purposes that scientists said it could often take years to obtain it and in some cases it was impossible to get. But soon the Drug Enforcement Administration will allow other universities to apply to grow marijuana, three government officials said.

While 25 states have approved the medical use of marijuana for a growing list of conditions, including Parkinson's, Crohn's disease, Tourette's syndrome, Alzheimer's, lupus and rheumatoid arthritis, the research to back up many of those treatments is thin. The new policy could begin to change that.

"It will create a supply of research-grade marijuana that is diverse, but more importantly, it will be competitive and you will have growers motivated to meet the demand of researchers," said John Hudak, a senior fellow at the Brookings Institution.

The new policy will be published as soon as Thursday in the federal register, according to the three officials, who have seen the policy but spoke on condition of anonymity because they were not authorized to discuss it.

It is unclear how many additional universities would receive licenses to grow marijuana, but the new policy does not set a cap on the number who could qualify. Any institution that has an approved research protocol and the security measures needed to store dangerous drugs can apply.

Researchers will still have to receive approval from federal agencies to conduct medical studies of marijuana, including from the D.E.A. and the Food and Drug Administration. Those whose projects are funded by the National Institute on Drug Abuse will also need its consent.

But drug policy advocates, experts and researchers predicted that increasing the number of institutions growing marijuana will have a significant practical effect. The University of Mississippi's monopoly on that role has been a barrier.

"It's clear that this was a significant hurdle in limiting the quantity of clinical research taking place in the U.S.," said Paul Armentano, the deputy director of the National Organization for the Reform of Marijuana Laws.

Researchers often had difficulty getting some kinds of marijuana, including ones with large amounts of THC, the main ingredient in the drug that gets people high. Under the University of Mississippi monopoly, Mr. Hudak of Brookings said: "If you were a researcher who thought a product with high THC would help someone with a painful cancer, you were out of luck. You couldn't access high THC marijuana in the same way you could buy it in a market in Colorado," where it is legal.

As recently as June, Dr. Steven W. Gust, a special assistant to the director of National Institute on Drug Abuse, had disagreed with critics who say the monopoly has stifled research. "In the past, NIDA has been able to provide marijuana for every federally qualified research project," he said recently in an emailed response to questions.

Earlier this year, the D.E.A. had suggested that it would possibly remove marijuana from the list of the most restricted and dangerous drugs by end of June. But this week, the agency did not take such a step.

Dr. Orrin Devinsky of the Comprehensive Epilepsy Center at New York University Langone Medical Center called it "deeply disappointing" that the agency had not done so. He said the scientific data overwhelmingly indicated it should not be listed as such a dangerous drug.

The federal government still classifies marijuana as a highly addictive drug without medical value, as it has for 46 years. The D.E.A. did not say when it will answer two petitions demanding a change of that policy, filed separately in 2009 and 2011.

Others were relieved that the D.E.A. had moved to allow more institutions to grow marijuana for research, but not taken it off the list of the most dangerous drugs.

“They’re looking at the science, taking a nuanced view,” said Kevin A. Sabet, a former Obama administration drug-policy adviser and president of the group Smart Approaches to Marijuana. “It’s a good day for science.”

http://www.eurekalert.org/pub_releases/2016-08/uom-tof080916.php

Treatment option for Alzheimer's disease possible

A research project has shown that an experimental model of Alzheimer's disease can be successfully treated with a commonly used anti-inflammatory drug.

A team led by Dr David Brough from The University of Manchester found that the anti-inflammatory drug completely reversed memory loss and brain inflammation in mice.

Nearly everybody will at some point in their lives take non-steroidal anti-inflammatory drugs; mefenamic acid, a common Non-Steroidal Anti Inflammatory Drug (NSAID), is routinely used for period pain.

The findings are published today in a paper authored by Dr Brough and colleagues, in the respected journal Nature Communications. Dr Brough and Dr Catherine Lawrence supervised PhD student Mike Daniels, and postdoc Dr Jack Rivers-Auty who conducted most of the experiments.

Though this is the first time a drug has been shown to target this inflammatory pathway, highlighting its importance in the disease model, Dr Brough cautions that more research is needed to identify its impact on humans, and the long-term implications of its use.

The research, funded by the Medical Research Council and the Alzheimer's Society, paves the way for human trials which the team hope to conduct in the future.

Around 500,000 people in the UK have Alzheimer's disease which gets worse over time, affecting many aspects of their lives, including the ability to remember, think and make decisions.

In the study transgenic mice that develop symptoms of Alzheimer's disease were used. One group of 10 mice was treated with mefenamic acid, and 10 mice were treated in the same way with a placebo.

The mice were treated at a time when they had developed memory problems and the drug was given to them by a mini-pump implanted under the skin for one month.

Memory loss was completely reversed back to the levels seen in mice without the disease.

Dr Brough said: "There is experimental evidence now to strongly suggest that inflammation in the brain makes Alzheimer's disease worse.

"Our research shows for the first time that mefenamic acid, a simple Non-Steroidal Anti Inflammatory Drug can target an important inflammatory pathway called the NLRP3 inflammasome , which damages brain cells."

He added: "Until now, no drug has been available to target this pathway, so we are very excited by this result.

"However, much more work needs to be done until we can say with certainty that it will tackle the disease in humans as mouse models don't always faithfully replicate the human disease.

"Because this drug is already available and the toxicity and pharmacokinetics of the drug is known, the time for it to reach patients should, in theory, be shorter than if we were developing completely new drugs.

"We are now preparing applications to perform early phase II trials to determine a proof-of-concept that the molecules have an effect on neuroinflammation in humans."

Dr Doug Brown, Director of Research and Development at Alzheimer's Society, said: "Testing drugs already in use for other conditions is a priority for Alzheimer's Society - it could allow us to shortcut the fifteen years or so needed to develop a new dementia drug from scratch.

"These promising lab results identify a class of existing drugs that have potential to treat Alzheimer's disease by blocking a particular part of the immune response. However, these drugs are not without side effects and should not be taken for Alzheimer's disease at this stage - studies in people are needed first."

Fenamate NSAIDs inhibit the NLRP3 inflammasome and 2 protect against Alzheimer's disease in rodent models, published in the journal Nature Communications.

http://bit.ly/2b5lhp6

Long-term health effects of Hiroshima and Nagasaki atomic bombs not as dire as perceived

Article highlights mismatch between public perception and decades of research on nearly 200,000 survivors and their children

The detonation of atomic bombs over the Japanese cities of Hiroshima and Nagasaki in August 1945 resulted in horrific casualties and devastation. The long-term effects of radiation exposure also increased cancer rates in the survivors. But public perception of the rates of cancer and birth defects among survivors and their children is in fact greatly exaggerated when compared to the reality revealed by comprehensive follow-up studies. The reasons for this mismatch and its implications are discussed in a Perspectives review of the Hiroshima/Nagasaki survivor studies published in the August issue of the journal GENETICS, a publication of the Genetics Society of America.

"Most people, including many scientists, are under the impression that the survivors faced debilitating health effects and very high rates of cancer, and that their children had high rates of genetic disease," says Bertrand Jordan, an author and a molecular biologist at UMR 7268 ADÉS, Aix-Marseille Université/EFS/CNRS, in France. "There's an enormous gap between that belief and what has actually been found by researchers."

Dr. Jordan's article contains no new data, but summarizes over 60 years of medical research on the Hiroshima/Nagasaki survivors and their children and discusses reasons for the persistent misconceptions. The studies have clearly demonstrated that radiation exposure increases cancer risk, but also show that the average lifespan of survivors was reduced by only a few months compared to those not exposed to radiation. No health effects of any sort have so far been detected in children of the survivors.

Approximately 200,000 people died in the bombings and their immediate aftermath, mainly from the explosive blast, the firestorm it sparked, and from acute radiation poisoning. Around half of the those who survived subsequently took part in studies tracking their health over their entire lifespan. These studies began in 1947 and are now conducted by a dedicated agency, the Radiation Effects Research Foundation (RERF), with funding from the Japanese and U.S. governments. The project has followed approximately 100,000 survivors, 77,000 of their children, plus 20,000 people who were not exposed to radiation.

This massive data set has been uniquely useful for quantifying the risks of radiation because the bombs served as a single, well-defined exposure source, and because the relative exposure of each individual can be reliably estimated using the person's distance from the detonation site. The data has been particularly invaluable in setting acceptable radiation exposure limits for nuclear industry workers and the general public.

Cancer rates among survivors was higher compared to rates in those who had been out of town at the time. The relative risk increased according to how close the person was to the detonation site, their age (younger people faced a greater lifetime risk), and their sex (greater risk for women than men). However, most survivors did not develop cancer. Incidence of solid cancers between 1958 and 1998 among the survivors were 10% higher, which corresponds to approximately 848 additional cases among 44,635 survivors in this part of the study. However, most of the survivors received a relatively modest dose of radiation. In contrast, those exposed to a higher radiation dose of 1

Gray (approximately 1000 times higher than current safety limits for the general public) bore a 44% greater risk of cancer over the same time span (1958-1998). Taking into consideration all causes of death, this relatively high dose reduced average lifespan by approximately 1.3 years.

Although no differences in health or mutations rates have yet been detected among children of survivors, Jordan suggests that subtle effects might one day become evident, perhaps through more detailed sequencing analysis of their genomes. But it is now clear that even if the children of survivors do in fact face additional health risks, those risks must be very small.

Jordan attributes the difference between the results of these studies and public perception of the long-term effects of the bombs to a variety of possible factors, including historical context.

"People are always more afraid of new dangers than familiar ones," says Jordan. "For example, people tend to disregard the dangers of coal, both to people who mine it, and to the public exposed to atmospheric pollution. Radiation is also much easier to detect than many chemical hazards. With a hand-held Geiger counter, you can sensitively detect tiny amounts of radiation that pose no health risk at all."

Jordan cautions that the results should not be used to foster complacency about the effects of nuclear accidents or the threat of nuclear war. "I used to support nuclear power until Fukushima happened," he says. "Fukushima showed disasters can occur even in a country like Japan that has strict regulations. However, I think it's important that the debate be rational, and I would prefer that people look at the scientific data, rather than gross exaggerations of the danger."

The Hiroshima/Nagasaki survivor studies: discrepancies between results and general perception Bertrand R. Jordan GENETICS, August 2016, Vol. 203, 1505-1512; doi: 10.1534/genetics.116.191759

http://bit.ly/2bh3WKy

Paraplegics regain some feeling, movement after using brain-machine interfaces

People paralyzed from spinal cord injuries for years have regained partial sensation and muscle control after training with brain-controlled robotics

Eight people who have spent years paralyzed from spinal cord injuries have regained partial sensation and muscle control in their lower limbs after training with brain-controlled robotics, according to a study published Aug. 11 in Scientific Reports.

The patients used brain-machine interfaces, including a virtual reality system that used their own brain activity to simulate full control of their legs. Videos accompanying the study illustrate their progress.

The research -- led by Duke University neuroscientist Miguel Nicolelis, M.D., Ph.D., as part of the Walk Again Project in São Paulo, Brazil -- offers promise for people with spinal cord injury, stroke and other conditions to regain strength, mobility and independence.

"We couldn't have predicted this surprising clinical outcome when we began the project," said Nicolelis, co-director of the Duke Center for Neuroengineering who is originally from Brazil.

"What we're showing in this paper is that patients who used a brain-machine interface for a long period of time experienced improvements in motor behavior, tactile sensations and visceral functions below the level of the spinal cord injury," he said. "Until now, nobody has seen recovery of these functions in a patient so many years after being diagnosed with complete paralysis."

Several patients saw changes after seven months of training. After a year, four patients' sensation and muscle control changed significantly enough that doctors upgraded their diagnoses from complete to partial paralysis.

Most patients saw improvements in their bladder control and bowel function, reducing their reliance on laxatives and catheters, he said. These changes reduce patients' risk of infections, which are common

in patients with chronic paralysis and are a leading cause of death, Nicolelis said.

Brain-machine systems establish direct communication between the brain and computers or often prosthetics, such as robotic limbs. For nearly two decades, Nicolelis has worked to build and hone systems that record hundreds of simultaneous signals from neurons in the brain, extracting motor commands from those signals and translating them into movement.

Nicolelis and colleagues believe with weekly training, the rehab patients re-engaged spinal cord nerves that survived the impact of the car crashes, falls and other trauma that paralyzed their lower limbs. At the beginning of rehabilitation, five participants had been paralyzed at least five years; two had been paralyzed for more than a decade.

One participant, "Patient 1," was a 32-year-old woman paralyzed for 13 years at the time of the trial who experienced perhaps the most dramatic changes. Early in training, she was unable to stand using braces, but over the course of the study, she walked using a walker, braces and a therapist's help. At 13 months, she was able to move her legs voluntarily while her body weight was supported in a harness, as seen in a video recorded at the Alberto Santos Dumont Association for Research Support where the neurorehabilitation lab is located.

"One previous study has shown that a large percentage of patients who are diagnosed as having complete paraplegia may still have some spinal nerves left intact," Nicolelis said. "These nerves may go quiet for many years because there is no signal from the cortex to the muscles. Over time, training with the brain-machine interface could have rekindled these nerves. It may be a small number of fibers that remain, but this may be enough to convey signals from the motor cortical area of the brain to the spinal cord."

Building a foundation at Duke

Since the 1990s, Nicolelis has investigated how populations of brain cells represent sensory and motor information and how they generate behavior, including movements of upper and lower limbs.

In one early experiment carried out with fellow neuroscientist John K. Chapin, Ph.D., Nicolelis used brain-implanted microelectrodes to record the brain activity of rats trained to pull a robotic lever to get a sip of water. Through a brain-machine interface, the rats learned to control the lever using only their brain activity.

"They simply produced the correct brain activity and the robotic arm would bring water to the rat's mouth without them having to move a muscle," Nicolelis said. "With training, animals stopped producing overt behavior and started relying on brain activity."

In later endeavors, Nicolelis trained rhesus monkeys to use brain-machine interfaces to control robotic limbs, and later, the 3-D movements of an avatar -- animated versions of themselves on a digital screen. The animals soon learned they could control the movements by mentally conceiving them; there was no need to physically move.

The rhesus monkeys later learned to walk on a treadmill with robotic legs controlled by their brains. They also learned they could use thought to propel a small electric wheelchair toward a bowl of grapes.

The Duke experiments with rats and primates built a foundation for the work in human patients, including a 2004 article with Duke neurosurgeon Dennis Turner, M.D., that established a model for recording brain activity in patients when they used a hand to grip a ball with varied force.

"It's important to understand how the brain codes for movement," Nicolelis said. "We discovered principles of how the brain operates that we wouldn't have discovered without getting inside the brain."

Still, Nicolelis said, the goal of these studies was to open doors for better prosthetics and brain-controlled devices for the severely disabled.

"Nobody expected we would see what we have found, which is partial neurological recovery of sensorimotor and visceral functions," he said.

International collaboration

The Walk Again Project has brought together more than 100 scientists from 25 countries, who first made news at the 2014 World Cup in São Paulo when Julian Pinto, a young paraplegic man, using a brain-controlled robotic exoskeleton, was able to kick a soccer ball during the opening ceremony.

The Walk Again Project also launched the neuro-rehabilitation study in São Paulo that year. The eight patients spent at least two hours a week using brain-machine interfaces, or devices controlled through their brain signals. All began the program by learning how to operate their own avatar, or digital likeness, in a virtual reality environment.

The patients wore fitted caps lined with 11 non-invasive electrodes to record their brain activity through EEG. Initially, when participants were asked to imagine walking in the virtual environment, scientists didn't observe the expected signals in the areas associated with motor control of their legs.

"If you said, use your hands, there was modulation of brain activity," Nicolelis said. "But the brain had almost completely erased the representation of their lower limbs."

After months of training, scientists began to observe the brain activity they expected to see when the patients' thought about moving their legs. "Basically, the training reinserted the representation of lower limbs into the patients' brains," Nicolelis said.

As they progressed, patients graduated from virtual reality to more challenging equipment that required more control over their posture, balance and ability to use their upper limbs, including two commercially available walking devices used in some physical therapy centers in the U.S.: the ZeroG and the Lokomat. Both use overhead harnesses to support a patient's weight as they build strength and proper gait after paralysis due to injury or neurological conditions such as stroke.

The patients rotated through other training systems that applied robotics, including the exoskeleton Pinto wore at the 2014 World Cup. During most of their training, the participants also wore a sleeve equipped with touch-technology called haptic feedback to enrich the experience and train their brains, Nicolelis said. Haptics use varied vibrations to offer tactile feedback, much like the buzzing jolts or kickbacks gamers feel through a handheld controller.

Each sensation is unique. So when the avatar walked on sand, the patient felt a different pressure wave on the forearm than when they walked on grass or asphalt, Nicolelis said.

"The tactile feedback is synchronized and the patient's brain creates a feeling that they are walking by themselves, not with the assistance of devices," Nicolelis said. "It induces an illusion that they are feeling and moving their legs. Our theory is that by doing this, we induced plasticity not only at the cortical level, but also at the spinal cord."

Next steps

Nearly all of the patients described in the study have continued their rehabilitation, now exceeding two years of training, Nicolelis said. He and colleagues plan to publish additional data about participants' continued progress. They also plan to create a new trial with patients who suffered more recent spinal cord injuries to see whether quicker treatment can lead to faster or better results.

The team also continues efforts to adapt technologies that are accessible for patients around the world who don't have access to physical therapy centers with the latest equipment. Perhaps the best answer is haptic sleeves, which by comparison are affordable and something a patient could use at home, Nicolelis said.

Scientific Reports will make the manuscript available for download after the embargo lifts.

In addition to Nicolelis, study authors include Ana R. C. Donati; Solaiman Shokur; Edgard Morya; Debora S. F. Campos; Renan C. Moioli; Claudia M. Gitti; Patricia B. Augusto; Sandra Tripodi; Cristhiane G. Pires; Gislaine A. Pereira; Fabricio L. Brasil; Simone Gallo; Anthony A. Lin; Angelo K. Takigami; Maria A. Aratanha; Sanjay Joshi; Hannes Bleuler; Gordon Cheng; and Alan Rudolph.

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http://bit.ly/2brSIBh

Intermediate HDL cholesterol levels may be best for longevity

Large study associates low and high HDL cholesterol levels with higher risks of dying prematurely compared with intermediate levels

Washington, DC - A new study indicates that maintaining an intermediate level of high density lipoprotein cholesterol (HDL-C) may help people live longer. The study, which appears in an upcoming issue of the Clinical Journal of the American Society of Nephrology (CJASN), found that both low and high HDL-C levels were linked with a higher risk of premature death. Also, intermediate HDL-C levels were associated with a lower risk of death across all levels of kidney function.

Patients with kidney disease often have reduced levels of HDL-C, which may partly explain their higher risk of dying prematurely; however, the relationship between HDL-C and premature death in patients with kidney disease is unclear. To investigate, a team led by Benjamin Bowe, MPH and Ziyad Al-Aly, MD, FASN (Washington University School of Medicine and VA Saint Louis Health Care System) retrospectively studied 1,764,986 US male veterans with at least one measurement of kidney function and one measure of HDL-C between October 2003 and September 2004. Participants were followed until September 2013.

The researchers found that both low and high HDL-C levels were associated with higher risks of dying during follow-up compared with intermediate HDL-C levels, forming a U-shaped relationship between HDL-C and mortality risk. The beneficial properties of intermediate levels of HDL-C were attenuated, but remained significant, in the presence of kidney disease.

"The finding that high HDL-C was also associated with higher risk of death was not expected and has not been reported previously in large epidemiologic studies such as the Framingham Heart Study and others," said Dr. Al-Aly. "Prior epidemiologic studies significantly advanced our understanding of the relationship between cholesterol parameters and clinical outcomes; however, these studies are limited in that the number of patients in these cohorts is relatively small compared with the current Big Data approach." He noted that a Big Data approach allows a more nuanced examination of the relationship between HDL-C and risk of death across the full spectrum of HDL-C levels.

"Our findings may explain why clinical trials aimed at increasing HDL-C levels have failed to show improvement of clinical outcomes," noted Bowe.

Study co-authors include Yan Xie, MPH, Hong Xian, PhD, Sumitra Balasubramanian, MS, and Mohamed Zayed MD, PhD.

Disclosures: The authors reported no financial disclosures.

The article, entitled "High Density Lipoprotein Cholesterol and the Risk of All-cause Mortality among U.S. Veterans," will appear online at http://cjasn.asnjournals.org/ on August 11, 2016, doi: 10.2215/CJN.00730116.

http://www.bbc.com/news/business-37055471

McDonald's pressured to serve up global antibiotics ban

A new online campaign is putting pressure on fast food giant McDonald's to impose a global ban on products from animals treated with antibiotics.

Scientists warn that treating livestock with antibiotics is leading to a rise in drug-resistant superbugs. The charity ShareAction has called on consumers to email McDonald's chief executive Steve Easterbrook. Last week, the fast food chain stopped using poultry treated with antibiotics - but only in its US restaurants. ShareAction has called on McDonald's - which operates in more than 100 countries - to stop using chicken, beef, pork and dairy products that have been given antibiotics in all of its 30,000 stores globally.

'Superbugs'

Medical experts warn that the routine use of antibiotics to promote growth and prevent - rather than treat - illness in farm animals contributes to the rise of drug-resistant "superbug" infections. They

are said to kill at least 23,000 Americans a year and represent a significant threat to global public health.

Scientists have warned the world is on the cusp of the "post-antibiotic era" after discovering in China in November 2015 bacteria resistant to the antibiotic colistin - the medication used when all others have failed. It appeared to develop in farm animals before also being detected in hospital patients.

Fast food restaurants have become a focal point for change in the food industry by forcing suppliers to change their practices. According to ShareAction, more than 70% of all antibiotics used in the US are given to livestock.

'Supersize their ambition'

In the UK, that figure stands at more than 50% according to the group. "We hope this action will encourage McDonald's to supersize their ambition," said ShareAction chief executive Catherine Howarth.

McDonald's told the Reuters news agency that it was too early to set a timeline for phasing out the use of all meat and milk products from animals treated with antibiotics. The company cited varying practices and regulations around the world as one of the difficulties, but added that it "continues to regularly review this issue".

Rival fast food groups are also under pressure to take action. On Thursday KFC was the target of a petition from consumer groups that called on the chicken chain to stop using poultry products treated with antibiotics. KFC has already said it will limit the use of human antibiotics in its chicken by next year. However, critics claim the policy still allows for routine use of antibiotics by its chicken suppliers.

US burger chain Wendy's plans to stop using chickens raised with antibiotics by 2017 and also plans to set similar goals for pork and beef.

Antibiotics - what you need to know

- ***Some infections are becoming almost impossible to treat because of the excessive use of antibiotics.***
- ***More than half of the antibiotics used around the world are used in animals, often to make them grow more quickly.***
- ***Scientists warned the world was on the cusp of the "post-antibiotic era" after discovering in China in November 2015 bacteria resistant to the antibiotic colistin - the medication used when all others have failed.***
- ***It appeared to develop in farm animals before also being detected in hospital patients.***
- ***In some cases, antibiotics are used in agriculture to treat infections - but most are used prophylactically in healthy animals to prevent infection or, controversially, as a way of boosting weight gain.***
- ***Using antibiotics as growth promoters was banned in the EU in 2006.***
- ***Such uses are more common in intensive farming conditions.***
- ***Antibiotics are most useful in cramped dirty conditions where infections are easier to spread, so more spacious and hygienic living conditions are one way to reduce the need for antibiotics.***
- ***There are also calls for greater investment in research for vaccines and for tests that can diagnose specific infections and a call for countries to agree on a banned list of antibiotics that would never be used in animals, because of their importance to human health.***

http://nyti.ms/2bsjRDo

2 Polio Paralysis Cases in Nigeria Set Back Eradication Effort

In a serious setback to the drive to eradicate polio from the world, two cases of paralysis caused by the virus have been detected in northeast Nigeria, the World Health Organization announced Thursday.

By DONALD G. McNEIL Jr. AUG. 11, 2016

The discovery dashed the hopes of global health authorities to be able to declare the continent polio-free soon. Nigeria's last case of wild polio virus was reported in July 2014. The continent's last was reported in Somalia a month after that. The W.H.O. requires three years with no confirmed cases before declaring a region polio-free.

"We are deeply saddened by the news," said Dr. Matshidiso Moeti, the W.H.O. regional director for Africa. "The overriding priority now is to immunize all children around the affected area."

Polio paralyzes only about one child of every 200 infected, and in dangerous or remote regions, many cases of paralysis are never detected, so health authorities assume the virus is far more widespread than two cases would suggest.

Until Thursday, the last known cases of paralysis caused by "wild" virus were all in Pakistan and Afghanistan. (Vaccination in many countries is still done with oral drops containing weakened live virus, which sometimes mutates to become more dangerous and start outbreaks of "vaccine-derived polio," which also can paralyze. While alarming, those outbreaks can usually be brought under control quickly with further vaccination.)

As recently as 2012, Nigeria accounted for more than half of all polio cases worldwide. Interrupting polio transmission in Africa was considered a major public health triumph. Only two diseases — smallpox and rinderpest, a veterinary disease — have ever been eradicated from the earth, and in both of them the last cases were found in Africa. The last few hundred cases of Guinea worm, or dracunculiasis, the only other disease as close to eradication as polio is, are also confined to Africa.

Genetic sequencing of the Nigerian virus suggests that the new cases were caused by a wild strain last detected in Borno State, Nigeria, in 2011, which implies that it circulated for five years without being detected. Raids by Boko Haram, the Islamic fundamentalist militia — including the kidnapping of 200 schoolgirls in Chibok two years ago — as well as fighting between Boko Haram and the Nigerian Army have made many areas off limits for vaccinators and surveillance specialists.

Massacres and fighting have driven thousands from their home villages. "That fluid movement of population complicates understanding of exactly where they've ended up," said John F. Vertefeuille, director of polio eradication for the Centers for Disease Control and Prevention in Atlanta.

"This is a setback, but we need to double our effort to make sure we interrupt transmission," he added.

Advances by the Nigerian Army this year have opened up new areas in Borno that were formerly off limits, and a case of paralysis caused by mutant polio vaccine was detected in March, prompting the increased surveillance that led to the discovery of the newest cases, Dr. Vertefeuille said.

The Bill and Melinda Gates Foundation has taken over much of the cost of the polio eradication drive from Rotary International, which began it in 1988. The cost has recently been over $1 billion a year. In a statement, the foundation said it was "deeply concerned" about the Nigeria cases but "remained strongly committed to supporting partners, governments and communities until the job is done."

http://bit.ly/2b5JiMK

Incidence of most fatal type of stroke decreasing -- thanks to a decrease in smoking?

A new study indicates that Finland's national tobacco policies seem to be radically reducing the incidence of subarachnoid haemorrhage, the most fatal form of stroke.

Previously it was thought that in Finland approximately a thousand people suffer subarachnoid haemorrhage (SAH) every year - most of them adults of working age. Up to half of those afflicted die within a year. Subarachnoid haemorrhage is typically caused by a ruptured cerebral aneurysm, which leads to a sudden increase in the intracranial pressure. Smoking is a key risk factor for SAH.

A Finnish study published in the journal Neurology looked at changes in the incidence of subarachnoid haemorrhage over a period of 15 years (1998-2012), and these were contrasted with changes in the prevalence of smoking. The results indicated that the number of people afflicted with SAH was nearly half of the previously assumed figure and that the number was in rapid decline, a trend which was particularly apparent in younger generations.

Within fifteen years, the prevalence of SAH had decreased by 45% among women, and 38% among men, under 50. During the same period, the prevalence of SAH decreased by 16% among women, and 26% among men, over 50. Smoking among Finns aged 15-64 decreased by 30% during the monitoring period.

"It is extraordinary for the incidence of any cardiovascular disease to decrease so rapidly at the population level in such a short time," says Professor Jaakko Kaprio from the University of Helsinki, one of the primary authors of the study and director of the Institute for Molecular Medicine Finland. "Even though we cannot demonstrate a direct causation in nation-wide studies, it is highly likely that the national tobacco policies in Finland have contributed to the decline in the incidence of this type of severe brain haemorrhage."

Cerebral aneurysms are fairly common - they are present in up to more than 10% of people over the age of 70 - but most of them never rupture. For decades, researchers have been searching for factors which could be used to identify persons at high risk of aneurysm ruptures and who should consequently be treated.

"Previous studies have indicated that smoking is one of the most important susceptibility factors for rupturing aneurysms, so in that sense the now established connection between a decrease in smoking and a decrease in SAH is not surprising," says the other primary author of the new study, Miikka Korja, a neurosurgeon at Helsinki University Hospital.

Unreliable Incidence Statistics For Sah

Dr. Miikka Korja points out that in most countries the incidence of SAH is unknown, as patients who immediately die of a haemorrhage outside of hospital are often erroneously classified as having succumbed to heart failure. In Finland, autopsies are conducted in most cases where a death occurs outside of hospital, confirming the cause of death.

"According to the research, approximately one fourth of people with subarachnoid haemorrhages have died outside of hospital or in the emergency room. All Nordic countries include deaths outside of hospitals in their incidence statistics for SAH, and have reached largely similar estimates. Nevertheless, assumptions of an extraordinarily high prevalence of SAH in Finland have been repeatedly stated, even in top medical journals, leading to Finnish SAH and aneurysm studies being disregarded in general surveys and recommendations. However, research does not back this assumption," Korja states.

http://bit.ly/2bjiM0c

Sugar addiction: Discovery of a brain sugar switch

Cell types like astrocytes regulate metabolic processes

Researchers at Technical University of Munich discovered that our brain actively takes sugar from the blood. Prior to this, researchers around the world had assumed that this was a purely passive process. An international team led by diabetes expert Matthias Tschöp reported in the journal 'Cell' that transportation of sugar into the brain is regulated by so-called glia cells that react to hormones such as insulin or leptin; previously it was thought that this was only possible for neurons.

The rapid rise in obesity and the associated spread of type 2 diabetes represent an enormous challenge for our society. No efficient and safe medicines to prevent or stop this development are available. The failure to develop adequate treatments is thought to be primarily due to the fact that the molecular machinery controlling systemic metabolism still remains mostly unknown.

Metabolic Control: Fuel for the headquarters

Matthias Tschöp of the Chair for Metabolic Diseases at TUM and Director of the Division of Metabolic Diseases and also of the Helmholtz Diabetes Center (HDC) at Helmholtz Zentrum München, is investigating how control centers in the brain remotely control our metabolism in order to adjust optimally to our environment. The brain has the highest sugar consumption of all organs and also controls for example hunger feelings. "We therefore suspected that a process as

important as providing the brain with sufficient sugar was unlikely to be completely random," so Dr. Cristina García-Cáceres, neurobiologist at the HDC and the study's lead author. "We were misled by the fact that nerve cells apparently did not control this process and therefore first thought it to occur passively. Then we had the idea that glia cells such as astrocytes*, which had long been misunderstood as less important 'support cells', might have something to do with transporting sugar into the brain."

The scientists therefore first examined the activity of insulin receptors on the surface of astrocytes, molecular structures which respond to insulin to influence cell metabolism. Here they found that if this receptor was missing on certain astrocytes the result was less activity in neurons that curb food uptake (proopiomelanocortin neurons).

At the same time, adaption of metabolism to challenges like sugar intake became impaired. With the help of advanced imaging technologies such as positron emission tomography, the scientists were able to show that hormones such as insulin and leptin act specifically on 'support' glia cells to regulate sugar intake into the brain, like a 'sugar switch'. Without insulin receptors, astrocytes became less efficient in transporting glucose into the brain, particularly in the area of the satiety centers, which are located in the hypothalamus.

A paradigm shift

"Our results showed for the first time that essential metabolic and behavioral processes are not regulated via neuronal cells alone and that other cell types in the brain, such as astrocytes, play a crucial role," explains study leader Matthias Tschöp, who also heads the drug discovery division at the German Center for Diabetes Research (DZD). "This represents a paradigm shift and could help explain why it has been so difficult to find sufficiently efficient and save medicines for diabetes and obesity until now."

According to the scientists, numerous new studies will now be necessary to adjust the old model of purely neural control of food intake and metabolism with a concept where astrocytes and possibly even immune cells in the brain also play a crucial role. Once there is a better understanding of the interaction between these various cells, the idea is to find ways and substances that modulate pathways on multiple cell types to curb sugar addiction and ultimately provide better treatment to the growing number of obese and diabetic individuals. "We have a lot of work ahead of us," states García-Cáceres, "but at least now we have a better idea where to look."

Background:

Astrocytes are the most common cells in the brain. One of their jobs is to form the blood-brain barrier by enclosing the blood vessels that run in the brain and selectively allowing only certain substances through to the nerve cells.

Just recently the scientists had already shown that astrocytes react to leptin, a metabolic hormone (Kim et al., 2014). This is an important factor for satiety. Because now both leptin and insulin have been shown to influence astrocytes, the researchers propose to develop a new model which, in addition to the neurons, also takes into account the astrocytes as the adjustors of the metabolism and the feeling of hunger. They hope that the more detailed view this produces will provide new perspectives for drug development.

Original Publication:

Caceres, C. et al. (2016): Astrocytic insulin signaling couples brain glucose uptake with nutrient availability, Cell, DOI: 10.1016/j.cell.2016.07.028

http://bit.ly/2bjiVRl

Large human brain evolved as a result of 'sizing each other up'

Experts suggest that complex decisions of whether to help someone or not could have led to the disproportionately large human brain

Humans have evolved a disproportionately large brain as a result of sizing each other up in large cooperative social groups, researchers have proposed.

A team led by computer scientists at Cardiff University suggest that the challenge of judging a person's relative standing and deciding whether or not to cooperate with them has promoted the rapid expansion of human brain size over the last 2 million years.

In a study published in Scientific Reports today, the team, which also includes leading evolutionary psychologist Professor Robin Dunbar from the University of Oxford, specifically found that evolution

favours those who prefer to help out others who are at least as successful as themselves.

Lead author of the study Professor Roger Whitaker, from Cardiff University's School of Computer Science and Informatics, said: "Our results suggest that the evolution of cooperation, which is key to a prosperous society, is intrinsically linked to the idea of social comparison - constantly sizing each up and making decisions as to whether we want to help them or not.

"We've shown that over time, evolution favours strategies to help those who are at least as successful as themselves."

In their study, the team used computer modelling to run hundreds of thousands of simulations, or 'donation games', to unravel the complexities of decision-making strategies for simplified humans and to establish why certain types of behaviour among individuals begins to strengthen over time.

In each round of the donation game, two simulated players were randomly selected from the population. The first player then made a decision on whether or not they wanted to donate to the other player, based on how they judged their reputation. If the player chose to donate, they incurred a cost and the receiver was given a benefit. Each player's reputation was then updated in light of their action, and another game was initiated.

Compared to other species, including our closest relatives, chimpanzees, the brain takes up much more body weight in human beings. Humans also have the largest cerebral cortex of all mammals, relative to the size of their brains. This area houses the cerebral hemispheres, which are responsible for higher functions like memory, communication and thinking.

The research team propose that making relative judgements through helping others has been influential for human survival, and that the complexity of constantly assessing individuals has been a sufficiently difficult task to promote the expansion of the brain over many generations of human reproduction.

Professor Robin Dunbar, who previously proposed the social brain hypothesis, said: "According to the social brain hypothesis, the disproportionately large brain size in humans exists as a consequence of humans evolving in large and complex social groups.

"Our new research reinforces this hypothesis and offers an insight into the way cooperation and reward may have been instrumental in driving brain evolution, suggesting that the challenge of assessing others could have contributed to the large brain size in humans."

According to the team, the research could also have future implications in engineering, specifically where intelligent and autonomous machines need to decide how generous they should be towards each other during one-off interactions.

"The models we use can be executed as short algorithms called heuristics, allowing devices to make quick decisions about their cooperative behaviour," Professor Whitaker said.

"New autonomous technologies, such as distributed wireless networks or driverless cars, will need to self-manage their behaviour but at the same time cooperate with others in their environment."

http://www.medscape.com/viewarticle/867204

Butter and Health: What Does the Evidence Say?

What impact does butter have on health?

Boris Hansel, MD|August 12, 2016

Editor's Note:

The following is an edited commentary by endocrinologist-nutritionist Boris Hansel, MD, an obesity management specialist who practices in Paris, France. This commentary has been translated from French.

Butter and Health

This is a sensitive and frequently debated topic in France, where butter is a staple in culinary tradition and very important to the industry. In the background is the issue of the relationship between consuming saturated fatty acids and cardiovascular (CV) health.

Traditionally, the recommendation has been to limit saturated fatty acid intake in favor of unsaturated fatty acids. Because butter is one of

the foods highest in saturated fat, the advice often given by practitioners has been to limit butter consumption.

Is Butter Harmful?

Does eating butter increase the risk of developing CV disease? Admittedly, at present, no study formally answers this question. A meta-analysis recently published in PLOS One[1] even questions the hypothesis that butter has a harmful effect. Its authors, who compiled nine observational studies carried out in 15 countries, came to a clear conclusion—that eating butter is not associated with an increase in CV risk. Nor did they find a dose/effect relationship.

In addition to these neutral CV findings, the meta-analysis yielded the following:

Consuming butter is associated with a lower risk for diabetes; and

Consuming butter is associated with a discrete but significant increase in overall mortality.

How Should These Results Be Interpreted?

The mainstream media quickly picked up on this study to extol the virtues of butter, claiming that this wrongly accused food is even beneficial to our health. Such restating of the findings of the PLOS One study is inappropriate and, in my opinion, poses a risk to public health.

The meta-analysis included only observational studies, with all of the biases inherent in this type of study. Furthermore, most of these studies involved healthy persons—not people at high CV risk.

Finally, in nutrition, eating more of one thing means eating less of another.

The authors of the meta-analysis said, "People who eat butter probably eat fewer sweets and processed foods, such as refined, processed grain products. Therefore, butter is perhaps better than certain processed foods, but it can't be concluded that it is, in itself, a healthy food. Bear in mind that butter is the fat with the highest fatty acid content: 10 g of butter contains 5 g of saturated fat. By comparison, 10 g of olive oil contains 1.5 g of saturated fat."

Butter and Cholesterol Levels

What is not debated is butter's cholesterol-raising effect. Butter increases the blood low-density lipoprotein cholesterol level, even when consumed in moderate amounts.

As for saturated fat intake and the incidence of CV disease, what emerges overall is the potential benefit of replacing saturated with unsaturated fats, especially when the latter are provided by vegetable oils. This is the conclusion of a very recent analysis of cohorts of US health professionals published in JAMA Internal Medicine.[2]

We sometimes hear butter consumption being promoted because of its high vitamin A content. Admittedly, 100 g of butter contains a large amount of vitamin A, but this benefit is of no great value, because butter is eaten in moderate amounts.

In fact, one would have to eat 100 g of butter daily to get the recommended dietary allowance of vitamin A. The best way to achieve the recommended allowance is to eat certain fruits and vegetables containing vitamin A precursors.

In short, when talking about butter, we need to have a balanced discussion that is in line with current knowledge:

First, butter is not necessary for maintaining good health. It is not a "health food" per se.

Second, butter is one of the foods with the highest saturated fat content, and consuming it on a regular basis promotes an increase in blood cholesterol levels.

Third, butter is not a poison. There is, therefore, no justification for stigmatizing butter. It should be considered a pleasure food for those who are fond of it, provided that it is consumed in moderate amounts and not consumed in addition to other foods that are high in saturated fatty acids.

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Organ transplants: Hundreds helped by former cancer patients

Hundreds of people in the UK have received an organ transplant from someone with a history of cancer, despite many believing you cannot donate if you have had the disease.

A total of 272 organ donors across the UK in the past five years had a history of cancer, according to data obtained by the Press Association. Their donations resulted in 675 people receiving a transplant.

Eye donation is one key area where such donors have been able to help. The figures from NHS Blood and Transplant also showed that 1,033 people who had suffered from some types of cancer went on to donate their eyes - but not other organs.

Officials say there is a "common misconception" that people cannot be organ donors if they have had cancer, but there are some circumstances where it is possible.

The Advisory Committee on the Safety of Blood, Tissues and Organs has said the "risks of cancer transmission must be balanced against the risks of dying without transplantation". "Organs from deceased donors with some cancers may be safely used for transplantation." The risk of donor-transmitted cancer in the UK is currently assessed as 0.06%.

Minimise the risks

Prof John Forsythe, associate medical director for organ donation and transplantation at NHS Blood and Transplant, said people should not let a health condition or previous illness stop them from registering as a donor. "We are very keen that everyone, regardless of their health status, registers a decision to donate and tells their family they want to donate. "We work hard to minimise the risks to recipients by carefully evaluating all potential organ and tissue donors."

About 70 cornea donations a week are needed to meet the demand for sight-saving transplants. But one in 10 people on the NHS Organ Donor Register do not want to donate their eyes.

Successful procedure

Aspiring midwife Alison Cooney died in 2010 aged 28, only six weeks after she was diagnosed with bowel and liver cancer. Her mother, Ann Cooney, from Alkrington, Greater Manchester, agreed to the donation of her corneas, which helped save the sight of two people. "Her major organs could not be donated, because of the aggressive nature of her illness, but her eyes could be used," she said. "Apparently not many people donate their eyes, although it is one of the most successful procedures. "Even though initially it was very difficult to accept what was about to happen, it wasn't about us, and we had to focus on something good being achieved from something bad."