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Facebook posts better at predicting diabetes, mental health than demographic info

Language in Facebook posts may help identify conditions such as diabetes, anxiety, depression and psychosis in patients

Language in Facebook posts may help identify conditions such as diabetes, anxiety, depression and psychosis in patients, according to a study from Penn Medicine and Stony Brook University researchers. It's believed that language in posts could be indicators of disease and, with patient consent, could be monitored just like physical symptoms. This study was published in PLOS ONE.

"This work is early, but our hope is that the insights gleaned from these posts could be used to better inform patients and providers about their health," said lead author Raina Merchant, MD, MS, the director of Penn Medicine's Center for Digital Health and an associate professor of Emergency Medicine. "As social media posts are often about someone's lifestyle choices and experiences or how they're feeling, this information could provide additional information about disease management and exacerbation."

Using an automated data collection technique, the researchers analyzed the entire Facebook post history of nearly 1,000 patients who agreed to have their electronic medical record data linked to their profiles. The researchers then built three models to analyze their predictive power for the patients: one model only analyzing the Facebook post language, another that used demographics such as age and sex, and the last that combined the two datasets.

Looking into 21 different conditions, researchers found that all 21were predictable from Facebook alone. In fact, 10 of the conditions were better predicted through the use Facebook data instead of demographic information.

Some of the Facebook data that was found to be more predictive than demographic data seemed intuitive. For example, "drink" and "bottle" were shown to be more predictive of alcohol abuse. However, others weren't as easy. For example, the people that most often mentioned religious language like "God" or "pray" in their posts were 15 times more likely to have diabetes than those who used these terms the least. Additionally, words expressing hostility -- like "dumb" and some expletives-- served as indicators of drug abuse and psychoses.

"Our digital language captures powerful aspects of our lives that are likely quite different from what is captured through traditional medical data," said the study's senior author Andrew Schwartz, PhD, a visiting assistant professor at Penn in Computer and Information Science, and an assistant professor of Computer Science at Stony Brook University. "Many studies have now shown a link between language patterns and specific disease, such as language predictive of depression or language that gives insights into whether someone is living with cancer. However, by looking across many medical conditions, we get a view of how conditions relate to each other, which can enable new applications of AI for medicine."

Last year, many members of this research team were able to show that analysis of Facebook posts could predict a diagnosis of depression as much as three months earlier than a diagnosis in the clinic. This work builds on that study and shows that there may be potential for developing an opt-in system for patients that could analyze their social media posts and provide extra information for clinicians to refine care delivery. Merchant said that it's tough to predict how widespread such a system would be, but it "could be valuable" for patients who use social media frequently.

"For instance, if someone is trying to lose weight and needs help understanding their food choices and exercise regimens, having a healthcare provider review their social media record might give them more insight into their usual patterns in order to help improve them," Merchant said.

Later this year, Merchant will conduct a large trial in which patients will be asked to directly share social media content with their health care provider. This will provide a look into whether managing this data and applying it is feasible, as well as how many patients would actually agree to their accounts being used to supplement active care.

"One challenge with this is that there is so much data and we, as providers, aren't trained to interpret it ourselves -- or make clinical decisions based on it," Merchant explained. "To address this, we will explore how to condense and summarize social media data."

The current study received funding from a Robert Wood Johnson Foundation Pioneer Award.

Other authors on this study include David A. Asch, Patrick Crutchley, Lyle H. Ungar, Sharath C. Guntuku, Johannes Eichstaedt, Shawndra Hill, Kevin Padrez, and Robert J. Smith.

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Most metastatic colorectal cancers have spread before diagnosis, Stanford researchers say

80% of metastatic colorectal cancers likely to have spread far before original tumor is detectable

Up to 80% of metastatic colorectal cancers are likely to have spread to distant locations in the body before the original tumor has exceeded the size of a poppy seed, according to a study of nearly 3,000 patients by researchers at the Stanford University School of Medicine.

Identifying patients with early-stage colorectal tumors that are born to be bad may help doctors determine who should receive early treatments, such as systemic chemotherapy, to kill cancer cells lurking far from the tumor's original location.

"This finding was quite surprising," said Christina Curtis, PhD, assistant professor of medicine and of genetics at Stanford. "In the majority of metastatic colorectal cancer patients analyzed in this study, the cancer cells had already spread and begun to grow long before the primary tumor was clinically detectable. This indicates that metastatic competence was attained very early after the birth of the cancer. This runs counter to the prevailing assumption that metastasis occurs late in advanced primary tumors and has implications for patient stratification, therapeutic targeting and earlier detection."

Researchers and clinicians have assumed that cancers acquire the ability to metastasize through the gradual accumulation of molecular changes over time. These changes, the thinking goes, confer specific traits that eventually allow cancer cells to escape the surrounding tissue, enter the bloodstream and take up residence in new locations. In this scenario, metastasis, if it occurs, would be a relatively late event in the evolution of the primary cancer.

Curtis, who co-directs the molecular tumor board at the Stanford Cancer Institute, is the senior author of the study, which will be published online June 17 in *Nature Genetics*. Postdoctoral scholar Zheng Hu, PhD, is the lead author.

Second-leading cause of cancer death

Colorectal cancer is the second-leading cause of cancer death in men and women combined in the United States. It metastasizes most often to the liver. Rarely, it metastasizes to the brain, where it is almost always fatal.

The initial changes to the genome that cause cancer are called driver mutations. The driver changes that jumpstart colorectal cancer are well-known, making it a good model to learn more about how and when the disease progresses. Curtis and her colleagues sought to reconstruct when metastasis occurred on a patient-by-patient basis and to identify its drivers by analyzing tumor-genome data.

Studying tumor biopsies, the researchers compared patterns of genetic mutations in the primary tumors of 23 patients with the

patterns in their liver or brain metastases. They looked for similarities or differences between primary and metastatic cancers obtained from the same person. They then used those patterns to create a kind of evolutionary tree of each patient's cancer -- similar to one a biologist might make to trace the evolution of an animal species from a single ancestor.

The trees the researchers pieced together indicated that in 17 of 21 patients (two of the original patients were excluded from the analysis), the metastatic tumors were started by just one cell, or a small group of genetically similar cells, that broke off from the primary tumor early in its development.

"The cells that formed the metastasis were more closely related to the ancestors of the primary tumor than its present-day relatives," Curtis said. "Moreover, the metastasis shared early drivers present in the 'trunk' of the evolutionary tree, but harbored few additional drivers. This suggested that these cancers acquired metastatic competence very early on during their growth."

To further pinpoint when metastasis occurred, Curtis and her team developed a computer program and statistical method to measure the time of metastatic spread relative to the size of the primary tumor in an individual patient. Their analysis provides the first quantitative evidence for early metastatic spread in human colon cancer -- a pattern observed in virtually all cases they examined. However, Curtis noted that not all colorectal tumors will metastasize and that it will be important to also understand cellular processes that keep the cancer from spreading to other organs.

A culprit: Mutated PTPRT

Curtis and her colleagues then took what they had learned and applied it to 938 people with metastatic and 1,813 people with non-metastatic colorectal cancer whose medical histories were known and whose primary tumors had been profiled to identify genetic changes in known cancer-associated genes.

"We found that specific combinations of mutations were highly predictive of metastasis," Curtis said. For example, mutations in a gene called PTPRT, in combination with mutations in classic colorectal cancer driver genes, were almost exclusively found in patients with metastatic cancers.

Previous studies have shown that the loss of PTPRT function increases the activity of a protein called STAT3, which enhances cellular survival. The researchers speculate that inhibiting STAT3 might thwart tumor growth and metastasis.

Curtis and her colleagues are now working to learn whether specific molecular changes tilt the balance of metastasis in colorectal cancers toward the liver or the brain. They are also applying similar analyses to other types of cancers.

"The concept of early systemic spread has been controversial, due in part to the challenge of quantifying this process in the human system and the reliance on animal models," Curtis said. "These data indicate that metastasis can occur early in human colorectal cancer and highlights the critical need for the earlier detection of aggressive disease. New biomarkers based on specific combinations of alterations might enable the identification of potentially lethal colorectal tumors at an earlier stage so that they may be intercepted and appropriately treated, potentially with therapies directed against their specific aberrations."

Curtis is a member of the Stanford Cancer Institute and of Stanford Bio-X. Other Stanford co-authors of the study are former senior research scientist Jie Ding, PhD; senior research scientist Zhicheng Ma, MD; instructors Ruping Sun, PhD, and Jose Seoane, PhD; visiting scientist J. Scott Shaffer, PhD; and clinical assistant professor of pathology Carlos Suarez, MD. Researchers from the Medical University of Vienna, the University of Pisa, University of Padua and the University of Southern California also contributed to the study. The research was supported by the National Institutes of Health (grant DP1-CA238296), the American Cancer Society, the Wunderglo Foundation, the Emerson Collective Cancer Research Fund, the Innovative Genomics Initiative and the National Cancer Institute. Curtis is a scientific adviser to Menlo Park-based GRAIL Inc. and holds stock options. She is a consultant for GRAIL and Genentech. Stanford's departments of Medicine and of Genetics also supported the work.

http://bit.ly/2WY2pBN

Underenrollment in clinical trials: Patients not the problem

Enrollment of patients in clinical trials outpaced by increasingly sophistication of cancer treatments

DALLAS - The increasing sophistication of cancer treatments threatens to outpace the ability of health care providers to enroll patients in clinical trials to test those therapies. That's a key finding by researchers in UT Southwestern's new Department of Population and Data Sciences.

The authors of the study published this month in the Journal of Clinical Oncology investigated why many cancer clinical trials fail to enroll enough patients. The researchers sought to identify potential interventions - i.e., solutions - to improve the situation.

Research in the Department of Population and Data Sciences investigates ways to improve health care delivery on a population level. Its studies often involve breaking a problem into its component steps, identifying potential barriers at each step, and developing a list of possible interventions for future study. In this specific project, the researchers approached suboptimal clinical trial enrollment - a significant national concern - as a health care delivery issue.

"Cancer clinical trials are meant to result in treatment advances. However, their potential benefits are diminished by suboptimal trial participation, both by patients and by clinicians and their organizations," said Dr. Celette Sugg Skinner, Chair and Professor of Population and Data Sciences and corresponding author of the study. Dr. Skinner is also a member of the Harold C. Simmons Comprehensive Cancer Center and holds the Parkland Community Medicine Professorship.

Nearly half - 40 percent - of cancer trials fail to reach targets for accrual, the medical term for the number of patients who have completed or will complete the trial. Fewer than 2 percent of adults with cancer enroll in trials, and last year no trials were offered in 36 percent of physician-owned and 14 percent of hospital-owned oncology practices, she said.

In order to help ensure results will reach statistical significance, clinical trials are designed to enroll a calculated number of patients, she explained. "Before we can figure out how to improve accrual in trials, we need to better understand the entire process and challenges along the way."

To gain this understanding, lead author Dr. Simon Craddock Lee, Associate Professor in the Department, conducted in-depth interviews with 10 key oncology physicians, nurses, and research staff in leadership positions across nine states.

"Nationally, we know there are large numbers of cancer patients and relatively few of them are in clinical trials," Dr. Lee said. "Most of the research to date has focused on the idea that the problem must be that patients don't know about clinical trials."

That mindset led to a research emphasis on improving communication so that patients are aware of trials and understand the risks and benefits as well as reaching out to underrepresented populations and ensuring messages are culturally appropriate - all worthy goals. However, this study identifies another group of problems, he explained.

The researchers found that emerging therapies and the changing landscape of oncology have introduced complexity, he continued. Specifically, oncology practices encounter barriers to (1) staying aware of available trials, (2) identifying eligible patients, (3) introducing the idea of trial participation vs. standard treatment to those patients, and (4) enrolling and caring for them throughout clinical trials.

These steps have become more complicated due to emerging discoveries in the realm of precision oncology, which seeks to

determine the best treatment based on patient genetic, environmental, or lifestyle factors. For example, whereas trials in the past would enroll all patients with stage 2 breast cancer, current trials often are designed to enroll only patients with certain biomarkers.

"As eligibility criteria become more numerous and specific, the likelihood of any patient meeting all criteria goes down," Dr. Lee explained. "Because oncology practices are not reimbursed for determining and documenting enrollment, trial accrual is threatened as these tasks become more costly and time-consuming."

The authors suggest that addressing challenges to trial accrual may involve changes in trial-specific reimbursement, as well as incentives for administrative and infrastructure costs.

"Our next goal must be to enhance logistic, infrastructure, and policy support to translate oncology discoveries into high-quality cancer care," said co-author Dr. David Gerber, a Professor of Internal Medicine and Population and Data Sciences. Dr. Gerber serves as Associate Director for Clinical Research and co-Leader of the Experimental Therapeutics Program in the Simmons Cancer Center.

The researchers will use this study to guide future investigations. Most immediately, they have surveyed more than 1,000 oncology providers, asking in-depth questions about the barriers identified in this study. Findings from that survey will help to identify strategies to ensure that clinical trials enroll the targeted number of patients.

http://bit.ly/2MUt3Xl

We may have helped give our canine pals 'puppy dog eyes'

Study of dog facial anatomy suggests our favoring canines with "puppy dog eyes" may have helped create this expression

By David Grimm

Dog owners know the look: Your pooch stares up at you, eyes wide, and you can't resist giving them a hug or favorite treat. A new study of dog facial anatomy suggests we may have helped create this expression by favoring canines with "puppy dog eyes" over the course of thousands of years of dog evolution.

Sarah Bickel

To conduct the work, researchers dissected the remains of four wolves and six dogs, focusing on their faces. They spotted two striking differences: The levator anguli oculi medialis muscle, which raises the eyebrows, was highly developed in all of the dogs but barely there in wolves. And all dogs except a Siberian husky—an ancient breed—sported a robust retractor anguli oculi lateralis muscle, which widens the eyes by pulling the eyelids towards the ears. This muscle was mostly absent in the wolves.

Combined, the two muscles allow dogs to express the big, sad eyes that melt our hearts, the team reports today in the *Proceedings of the National Academy of Sciences*. And indeed, when the researchers asked strangers to approach a number of shelter dogs and tame wolves, the dogs produced the sad eye look—known scientifically as "the AU101 movement"—on average five times more often and with far more intensity than the wolves did.

The team suspects that early in dog evolution humans were more likely to care for canines with this look, perhaps because it reminded them of the big eyes of human infants. Those dogs had more pups, and so the muscles that power big eyes spread through dog populations. Even today, shelter dogs that rock the look are more likely to find a home. The next question: whether other domestic animals like cats have hit on the same strategy.

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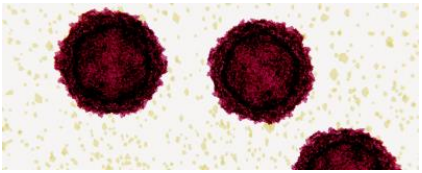
Enterovirus Might Be Behind Kids' Paralysis: Preprint

Researchers identify a possible driver of acute flaccid myelitis, a polio-like disease diagnosed in more than 500 children over the last few years.

Catherine Offord

A mysterious, polio-like condition that leads to paralysis in children likely involves an enterovirus, according to research published last week (June 10) as a preprint in *bioRxiv*.



Researchers report that acute flaccid myelitis may be caused by an enterovirus, the viral family that contains pathogens such as poliovirus (pictured).* © ISTOCK.COM, *SELVANEGRA

Researchers linked acute flaccid myelitis (AFM), a rare disease that's been on the rise in the US since 2014, to a virus called EV-D68 and related pathogens, although it's not clear whether this group of viruses is the sole cause.

"It is a very good paper," Stephen Elledge, a Harvard Medical School geneticist who was not involved in the work but helped develop the method off which it was based, tells *STAT*. The study "demonstrates clearly and convincingly what others had some data for that were not conclusive, that AFM is likely to be caused by enteroviruses."

AFM has been diagnosed in more than 500 children in the last five years. The pattern of cases is similar to that typical of enterovirus infections—that is, alternating between high and low incidence from one year to the next. According to *STAT*, there were 22 cases in 2015, 149 in 2016, 35 in 2017, and 232 in 2018.

The disease attacks gray matter in the spinal cord, so neurologist Michael Wilson of the University of California, San Francisco, and colleagues at the Centers for Disease Control and Prevention (CDC) wanted to investigate whether an enterovirus might be present in that part of the body in affected children.

To identify evidence of any past viral infections in AFM patients, the researchers adapted a method developed by Elledge that uses bacteriophages to collect antibodies present in a sample, in this case, the patients' spinal fluid.

The test identified signs of infection by EV-D68 as well as other enteroviruses in a group of more than 40 children with AFM. "Finding evidence of antibodies in spinal fluid in response to the virus is an important first step toward a diagnostic test for AFM and a path toward treatment," the CDC says in a statement to *STAT*.

"While continued vigilance for other possible etiologies of AFM is warranted, together, our combined [results support] the notion that EV infection likely underlies the majority of AFM cases tested in this study," the authors write in their paper, which has yet to undergo peer review. "These results offer a roadmap for rapid development of enteroviral cerebrospinal fluid antibody assays to enable efficient clinical diagnosis of enterovirus-associated AFM in the future."

http://bit.ly/2IZHmor

Fossil teeth reveal ancient hyenas in the Arctic

Ice age hyenas may have hunted herds of caribou and horses, or scavenged carcasses of mammoths on a vast steppe-tundra

BUFFALO, N.Y. -- Modern hyenas are known as hunters and scavengers in Asian and African ecosystems such as the savanna.

But in ancient times, these powerful carnivores also roamed a very different landscape, inhabiting the frigid Arctic during the last ice age, according to a new study led by the University at Buffalo.

The research, which will be published on June 18 in the journal Open Quaternary, reports on the first known fossils of hyenas from the Arctic. The study and all information in this press release are embargoed until 6 a.m. U.S. Eastern Time on Tuesday, June 18.

The study reveals that two ice age fossil teeth discovered in Yukon Territory in Canada belonged to the so-called "running hyena" Chasmaporthetes. The specimens, recovered in the 1970s, were tentatively thought to be from hyenas by previous paleontologists, but the new paper is the first to confirm the fossils' identity and report on them in detail, assigning them a genus based on comparisons to a global sample of hyena fossils.

The findings fill an important gap in scientists' knowledge of how hyenas reached North America. Previously, Chasmaporthetes fossils had been found as far north as Mongolia in Asia and the southern United States in North America, with no sites in between.

"Fossils of this genus of hyenas had been found in Africa, Europe and Asia, and also in the southern United States. But where and how did these animals get to North America? The teeth we studied, even though they were just two teeth, start to answer those questions," says paleontologist Jack Tseng, PhD, the paper's first author and an assistant professor of pathology and anatomical sciences in the Jacobs School of Medicine and Biomedical Sciences at UB.

How hyenas got to North America

Ancient hyenas likely entered North America via Beringia, an area, including Alaska and Yukon Territory, that connects Asia with North America during periods of low sea levels. From there, the animals made their way south all the way to Mexico, scientists say.

The newly described fossils are important in part because they provide the first proof of ancient hyenas living in Beringia.

"It is amazing to imagine hyenas thriving in the harsh conditions above the Arctic Circle during the ice age," says study co-author Grant Zazula, PhD, Government of Yukon paleontologist. "Chasmaporthetes probably hunted herds of ice age caribou and horses or scavenged carcasses of mammoths on the vast steppe-tundra that stretched from Siberia to Yukon Territory."

"Our previous understanding of where these far-ranging hyenas lived was based on fossil records in southern North America on one hand, and Asia, Europe and Africa on the other," Tseng says. "These rare records of hyenas in the Arctic fill in a massive gap in a location where we expected evidence of their crossing between continents, but had no proof until now."

The fossil teeth are most likely between about 1.4 million and 850,000 years old, with ages more likely closer to the older figure, according to the researchers' analysis. But the first hyenas crossed into North America long before that, as the earliest known hyena fossils on the continent date back about 5 million years, Tseng says.

Enigmatic fossil teeth identified

The fossil teeth were collected in the 1970s during paleontological expeditions in the remote Old Crow River region in northern Yukon Territory. One tooth was discovered by Richard "Dick" Harington, Gerry Fitzgerald and Charlie Thomas, and the other by Brenda Beebe and William Irving.

The specimens -- tucked away in the collections of the Canadian Museum of Nature in the Ottawa, Ontario area -- are among 50,000 other fossils recovered from the area over the last century.

The identity of the fossil teeth remained an enigma until they captured Tseng's attention, sparked by the re-discovery of decades-old notes by study co-author Lars Werdelin, paleontologist in the Swedish Museum of Natural History.

Tseng drove to Ottawa from Buffalo in February 2019 to view the specimens. As an expert on the evolution and fossil record of hyenas, he was able to identify the teeth as belonging to the genus Chasmaporthetes.

Though there are only four living species of hyena today (three bone-crushing species, plus the ant-eating aardwolf), ancient hyenas had a diverse family history, with many dozens of species found in localities spanning the Northern Hemisphere.

Hyenas disappeared from North America before the first people arrived. Although the reasons for this extinction between 1 and 0.5 million years ago remain unclear, it is possible that the animals' bone-crushing, scavenging niche was replaced by the impressive short-faced bear Arctodus simus, which lived across North America until the end of the ice age about 12,000 years ago.

http://bit.ly/2WQD7R6

Why Global Population Growth Will Grind to a Halt by 2100

Global population growth will nearly grind to a stop by the end of the century, a new analysis by the Pew Research Center suggests.

By Yasemin Saplakoglu, Staff Writer

Right now, the world's population is over 7.7 billion people, and it has been growing between 1% and 2% every year since 1950, according to the Pew Research Center. By 2100, the center projects the population will reach around 10.9 billion people and grow by less than 0.1% a year, the center wrote.

This is mostly due to a decreasing number of children born worldwide, the analysis said, based on data from the United Nation's report "World Population Prospects 2019."

The U.N.'s report found that global fertility rates will be less than the "replacement fertility rate," or the number of births per woman that would keep the population the same size, replacing people as they die. The current replacement fertility rate is 2.1 births per woman, which is less than the current global fertility rate of 2.5 births per woman. By 2100, the global fertility rate is expected to dip to 1.9 births per woman.

What's more, the U.N. report found that the global median age to which people live will increase from 31 to 42 by 2100. Between 2020 and 2100, people 80 and over will increase from the current 146 million to 881 million. Latin America and the Caribbean will have the oldest people in the world by 2100.

Only Africa is expected to have a strong population growth by the end of the century, increasing from 1.3 billion people in 2020 to 4.3 billion people in 2100. Meanwhile, Europe's population is expected to peak in 2021, and both Europe and Latin America will be declining in population by 2100. Asia will increase in population by 2055, then decline and North America's population will continue to increase, mostly because of migration to the area, according to the U.N. report.

http://bit.ly/2ZKURzh

A prebiotic route to DNA

DNA may have appeared on Earth earlier than has hitherto been assumed. LMU chemists led by Oliver Trapp show that a simple reaction pathway could have given rise to DNA subunits on the early Earth.

by Ludwig Maximilian University of Munich

How were the building-blocks of life first formed on the early Earth? As yet, only partially satisfactory answers to this question are available. However, one thing is clear: The process of biological evolution that has given rise to the diversity of life on our planet must have been preceded by a phase of chemical evolution. During this 'prebiotic' stage, the first polymeric molecules capable of storing information and reproducing themselves were randomly assembled from organic precursors that were available on the early Earth. The most efficient replicators subsequently evolved into the macromolecular informational nucleic acids—DNA and RNA—that became the basis for all forms of life on our planet.

For billions of years, DNA has been the primary carrier of hereditary information in biological organisms. DNA strands are made up of four types of chemical subunits, and the genetic information it contains is encoded in the linear sequence of these 'nucleosides'. Moreover, the four subunits comprise two complementary pairs. Interactions between two strands with

complementary sequences are responsible for the formation of the famous double helix, and play a crucial role in DNA replication. RNA also has vital functions in the replication of DNA and in the translation of nucleotide sequences into proteins.

Which of these two types of nucleic acid came first? The unanimous answer to that question up to now was RNA. Plausible models that explain how RNA molecules could have been synthesized from precursor compounds in prebiotic settings were first proposed decades ago, and have since received substantial experimental support. Moreover, its conformational versatility allows RNA both to store information and to act as a catalyst. These insights have led to the idea of an 'RNA world' that preceded the emergence of DNA, which is now well established among specialists. How then were the first DNA subunits synthesized? The generally accepted view is that this process was catalyzed by an enzyme—a comparatively complex biomolecule whose emergence would have required millions of years of evolution.

But now a team of chemists led by LMU's Professor Oliver Trapp has proposed a much more direct mechanism for the synthesis of DNA subunits from organic compounds that would have been present in a prebiotic environment. "The reaction pathway is relatively simple," says Trapp, which suggests it could well have been realized in a prebiotic setting. For example, it does not require variations in reaction parameters, such as temperature. In Trapp's experiments, the necessary ingredients are water, a mildly alkaline pH and temperatures of between 40 and 70°C. Under such conditions, adequately high reaction rates and product yields are achieved, with high selectivity and correct stereochemistry.

Each of the nucleoside subunits found in DNA is made up of a nitrogen-containing base and a sugar called deoxyribose. Up to now, it was thought that deoxynucleosides could only be synthesized under prebiotic conditions by directly coupling these two—preformed—components together. But no plausible non-enzymatic mechanism for such a step had ever been proposed. The essential feature of the new pathway, as Trapp explains, is that the sugar is not linked to the base in a single step. Instead, it is built up on the preformed base by a short sequence of reaction steps involving simple organic molecules such as acetaldehyde and glyceraldehyde. In addition, the LMU researchers have identified a second family of possible precursors of DNA in which the deoxyribose moiety is replaced by a different sugar.

According to the authors of the study, these results suggest that the earliest DNA molecules could have appeared in parallel with RNA—some 4 billion years ago. This would mean that DNA molecules emerged around 400 million years earlier than previously thought.

More information: ***Oliver Trapp et al. Direct Prebiotic Pathway to DNA Nucleosides, Angewandte Chemie International Edition (2019). DOI: 10.1002/anie.201903400***

http://bit.ly/2L7PTZf

Artificial muscles powered by glucose

Artificial muscles made from polymers can now be powered by energy from glucose and oxygen, just like biological muscles.

This advance may be a step on the way to implantable artificial muscles or autonomous microrobots powered by biomolecules in their surroundings. Researchers at Linköping University, Sweden, have presented their results in the journal *Advanced Materials*.

The motion of our muscles is powered by energy that is released when glucose and oxygen take part in biochemical reactions. In a similar way, manufactured actuators can convert energy to motion, but the energy in this case comes from other sources, such as electricity. Scientists at Linköping University, Sweden, wanted to develop artificial muscles that act more like biological muscles. They have now demonstrated the principle using artificial muscles powered by the same glucose and oxygen as our bodies use.

The researchers have used an electroactive polymer, polypyrrole, which changes volume when an electrical current is passed. The artificial muscle, known as a "polymer actuator", consists of three layers: a thin membrane layer between two layers of electroactive polymer. This design has been used in the field for many years. It works by the material on one side of the membrane acquiring a positive electrical charge and ions being expelled, causing it to shrink. At the same time, the material on the other side acquires a negative electrical charge and ions are inserted, which causes the material to expand. The changes in volume cause the actuator to bend in one direction, in the same way that a muscle contracts.

The electrons that cause motion in artificial muscles normally come from an external source, such as a battery. But batteries suffer from several obvious drawbacks: they are usually heavy, and need to be charged regularly. The scientists behind the study decided instead to use the technology behind bioelectrodes, which can convert chemical energy into electrical energy with the aid of enzymes. They have used naturally occurring enzymes, integrating them into the polymer.

"These enzymes convert glucose and oxygen, in the same way as in the body, to produce the electrons required to power motion in an artificial muscle made from an electroactive polymer. No source of voltage is required: it's enough simply to immerse the actuator into a solution of glucose in water", says Edwin Jager, senior lecturer in Sensor and Actuator Systems, in the Department of Physics, Chemistry and Biology at Linköping University. Together with Anthony Turner, professor emeritus, he has led the study.

Just as in biological muscles, the glucose is directly converted to motion in the artificial muscles.

"When we had fully integrated enzymes on both sides of the actuator and it actually moved - well, it was just amazing", says Jose Martinez, a member of the research group.

The next step for the researchers will be to control the biochemical reactions in the enzymes, such that the motion can be reversible for many cycles. They have already demonstrated that the motion is reversible, but they had to use a small trick to do so. Now they want to create a system that is even closer to a biological muscle. The researchers also want to test the concept using other actuators as the "textile muscle", and apply it in microrobotics.

"Glucose is available in all organs of the body, and it's a useful substance to start with. But it is possible to switch to other enzymes, which would enable the actuator to be used in, for example, autonomous microrobots for environmental monitoring in lakes. The advances we present here make it possible to power actuators with energy from substances in their natural surroundings", says Edwin Jager.

The research has been funded with support of, among other bodies, Linköping University, the Carl Trygger Foundation, the Swedish Research Council, and EU Marie Curie Actions Initial Training Network "MICACT".

The article: "Artificial muscles powered by glucose", Fariba Mashayekhi Mazar, Jose G. Martinez, Manav Tyagi, Mahdi Alijanianzadeh, Anthony P.F. Turner, Edwin W. H. Jager, (2019), Advanced Materials, *published online 19 June 2019: https://onlinelibrary.wiley.com/doi/abs/10.1002/adma.201901677*

http://bit.ly/2WWAEJP

First-ever successful mind-controlled robotic arm without brain implants

Able to continuously track and follow a computer cursor

A team of researchers from Carnegie Mellon University, in collaboration with the University of Minnesota, has made a breakthrough in the field of noninvasive robotic device control. Using a noninvasive brain-computer interface (BCI), researchers have developed the first-ever successful mind-controlled robotic arm exhibiting the ability to continuously track and follow a computer cursor.

Being able to noninvasively control robotic devices using only thoughts will have broad applications, in particular benefiting the lives of paralyzed patients and those with movement disorders.

BCIs have been shown to achieve good performance for controlling robotic devices using only the signals sensed from brain implants. When robotic devices can be controlled with high precision, they can be used to complete a variety of daily tasks. Until now, however, BCIs successful in controlling robotic arms have used invasive brain implants. These implants require a substantial amount of medical and surgical expertise to correctly install and operate, not to mention cost and potential risks to subjects, and as such, their use has been limited to just a few clinical cases.

A grand challenge in BCI research is to develop less invasive or even totally noninvasive technology that would allow paralyzed patients to control their environment or robotic limbs using their own "thoughts." Such noninvasive BCI technology, if successful, would bring such much needed technology to numerous patients and even potentially to the general population.

However, BCIs that use noninvasive external sensing, rather than brain implants, receive "dirtier" signals, leading to current lower resolution and less precise control. Thus, when using only the brain to control a robotic arm, a noninvasive BCI doesn't stand up to using implanted devices. Despite this, BCI researchers have forged ahead, their eye on the prize of a less- or non-invasive technology that could help patients everywhere on a daily basis.

Bin He, Trustee Professor and Department Head of Biomedical Engineering at Carnegie Mellon University, is achieving that goal, one key discovery at a time.

"There have been major advances in mind controlled robotic devices using brain implants. It's excellent science," says He. "But noninvasive is the ultimate goal. Advances in neural decoding and the practical utility of noninvasive robotic arm control will have major implications on the eventual development of noninvasive neurorobotics."

Using novel sensing and machine learning techniques, He and his lab have been able to access signals deep within the brain, achieving a high resolution of control over a robotic arm. With noninvasive neuroimaging and a novel continuous pursuit paradigm, He is overcoming the noisy EEG signals leading to significantly improve EEG-based neural decoding, and facilitating real-time continuous 2D robotic device control.

Using a noninvasive BCI to control a robotic arm that's tracking a cursor on a computer screen, for the first time ever, He has shown in human subjects that a robotic arm can now follow the cursor continuously. Whereas robotic arms controlled by humans noninvasively had previously followed a moving cursor in jerky, discrete motions--as though the robotic arm was trying to "catch up" to the brain's commands--now, the arm follows the cursor in a smooth, continuous path.

In a paper published in Science Robotics, the team established a new framework that addresses and improves upon the "brain" and "computer" components of BCI by increasing user engagement and training, as well as spatial resolution of noninvasive neural data through EEG source imaging.

The paper, "Noninvasive neuroimaging enhances continuous neural tracking for robotic device control," shows that the team's unique approach to solving this problem not enhanced BCI learning by nearly 60% for traditional center-out tasks, it also enhanced continuous tracking of a computer cursor by over 500%.

The technology also has applications that could help a variety of people, by offering safe, noninvasive "mind control" of devices that can allow people to interact with and control their environments. The technology has, to date, been tested in 68 able-bodied human subjects (up to 10 sessions for each subject), including virtual

device control and controlling of a robotic arm for continuous pursuit. The technology is directly applicable to patients, and the team plans to conduct clinical trials in the near future.

"Despite technical challenges using noninvasive signals, we are fully committed to bringing this safe and economic technology to people who can benefit from it," says He. "This work represents an important step in noninvasive brain-computer interfaces, a technology which someday may become a pervasive assistive technology aiding everyone, like smartphones."

This work was supported in part by the National Center for Complementary and Integrative Health, National Institute of Neurological Disorders and Stroke, National Institute of Biomedical Imaging and Bioengineering, and National Institute of Mental Health.

http://bit.ly/2WYon2v

How information is like snacks, money, and drugs -- to your brain

Researchers demonstrate common neural code for information and money; both act on the brain's dopamine-producing reward system

Can't stop checking your phone, even when you're not expecting any important messages? Blame your brain.

A new study by researchers at UC Berkeley's Haas School of Business has found that information acts on the brain's dopamine-producing reward system in the same way as money or food.

"To the brain, information is its own reward, above and beyond whether it's useful," said Assoc. Prof. Ming Hsu, a neuroeconomist whose research employs functional magnetic imaging (fMRI), psychological theory, economic modeling, and machine learning. "And just as our brains like empty calories from junk food, they can overvalue information that makes us feel good but may not be useful--what some may call idle curiosity."

The paper, "Common neural code for reward and information value," was published this month by the Proceedings of the National Academy of Sciences. Authored by Hsu and graduate student Kenji Kobayashi, now a post-doctoral researcher at the University of Pennsylvania, it demonstrates that the brain converts information into same common scale as it does for money. It also lays the groundwork for unraveling the neuroscience behind how we consume information--and perhaps even digital addiction.

"We were able to demonstrate for the first time the existence of a common neural code for information and money, which opens the door to a number of exciting questions about how people consume, and sometimes over-consume, information," Hsu said.

The paper is rooted in the study of curiosity and what it looks like inside the brain. While economists have tended to view curiosity as a means to an end, valuable when it can help us get information to gain an edge in making decisions, psychologists have long seen curiosity as an innate motivation that can spur actions by itself. For example, sports fans might check the odds on a game even if they have no intention of ever betting.

Sometimes, we want to know something, just to know.

"Our study tried to answer two questions. First, can we reconcile the economic and psychological views of curiosity, or why do people seek information? Second, what does curiosity look like inside the brain?" Hsu said.

To understand more about the neuroscience of curiosity, the researchers scanned the brains of people while they played a gambling game. Each participant was presented with a series of lotteries and needed to decide how much they were willing to pay to find out more about the odds of winning. In some lotteries, the information was valuable--for example, when what seemed like a longshot was revealed to be a sure thing. In other cases, the information wasn't worth much, such as when little was at stake.

For the most part, the study subjects made rational choices based on the economic value of the information (i.e., how much money it

could help them win). But that didn't explain all their choices: People tended to over-value information in general, and particularly in higher-valued lotteries. It appeared that the higher stakes increased people's curiosity in the information, even when the information had no effect on their decisions.

The researchers determined that this behavior could only be explained by a model that captured both economic and psychological motives for seeking information. People acquired information based not only on its actual benefit, but also on the anticipation of its benefit, whether or not it had use.

Hsu said that's akin to wanting to know whether we received a great job offer, even if we have no intention of taking it. "Anticipation serves to amplify how good or bad something seems, and the anticipation of a more pleasurable reward makes the information appear even more valuable," he said.

How does the brain respond to information? Analyzing the fMRI scans, the researchers found that the information about the games' odds activated the regions of the brain specifically known to be involved in valuation (the striatum and ventromedial prefrontal cortex or VMPFC), which are the same dopamine-producing reward areas of the brain activated by food, money, and many drugs. This was the case whether the information was useful, and changed the person's original decision, or not.

Next, the researchers were able to determine that the brain uses the same neural code for information about the lottery odds as it does for valuation or money by using a machine learning technique (called support vector regression). That allowed them to look at the neural code for how the brain responds to varying amounts of money, and then ask if the same code can be used to predict how much a person will pay for information. It can.

In other words, just as we can convert such disparate things as a painting, a steak dinner, and a vacation into a dollar value, the brain converts curiosity about information into the same common code it uses for money and other concrete rewards, Hsu said.

"We can look into the brain and tell how much someone wants a piece of information, and then translate that brain activity into monetary amounts," he said.

While the research does not directly address overconsumption of digital information, the fact that information engages the brain's reward system is a necessary condition for the addiction cycle, he said. And it explains why we find those alerts saying we've been tagged in a photo so irresistible.

"The way our brains respond to the anticipation of a pleasurable reward is an important reason why people are susceptible to clickbait," he said. "Just like junk food, this might be a situation where previously adaptive mechanisms get exploited now that we have unprecedented access to novel curiosities."

https://go.nature.com/2X19tsd

A plant's sneeze spreads disease

Some plants send dewdrops hurtling off their leaves — and pathogens tag along.

Just as the common cold can spread through a cough, plant diseases can spread through pathogen-packed droplets that jump off leaves — a plant's version of a sneeze.

Scientists already knew that wind and splashes of rainwater can move bacteria and other pathogens from leaf to leaf. In a search for other transmission routes, Jonathan Boreyko at Virginia Tech in Blacksburg and his colleagues filmed tiny dewdrops merging on wheat (Triticum aestivum) leaves, which are extremely water repellent. When the drops coalesced, their surface tension was released and converted into kinetic energy, which catapulted the merged droplet as far as 5 millimetres from the leaf.

The researchers found that jumping droplets could disperse spores of Puccinia triticina, a fungus that causes the devastating plant

disease leaf rust. As many as 100 fungal spores could be launched from a single leaf every hour. Once hurled into the air by dewdrops, the spores could be transferred to neighbouring plants by just a gentle breeze, the scientists say.

J. R. Soc. Interface (2019)

https://bbc.in/2Y7JQr5

Early brain 'signs of Parkinson's' found

Scientists say they have identified the earliest signs of Parkinson's disease in the brain, 15 to 20 years before symptoms appear.

Scans of a small number of high-risk patients found malfunctions in the brain's serotonin system, which controls mood, sleep and movement. The King's College London researchers say the discovery could lead to new screening tools and treatments. Experts said larger studies and more affordable scans were needed first.

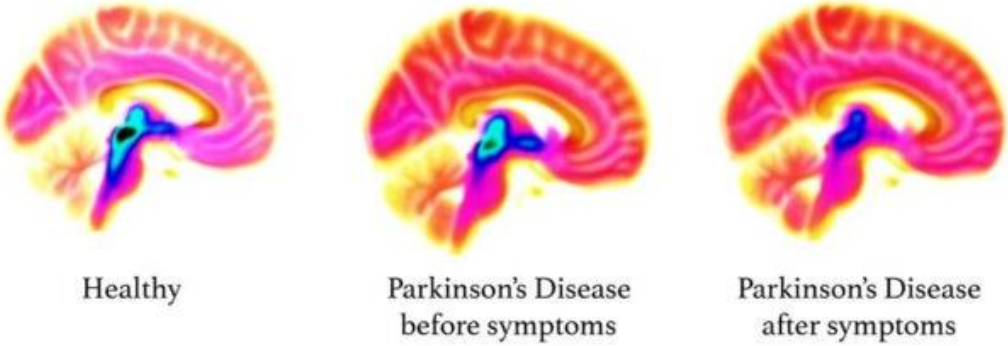
Parkinson's is a progressive neurological condition affecting about 145,000 people in the UK. The main symptoms are shaking, tremors and stiffness but depression, memory and sleep problems are also common. Traditionally, the disease is thought to be linked to a chemical called dopamine, which is lacking in the brains of people with the condition.

Although there is no cure, treatments do exist to control symptoms - and they focus on restoring dopamine levels. But the KCL research team, writing in Lancet Neurology, suggest that changes in the brain's serotonin levels come first - and could act as an early warning sign.

The researchers looked at the brains of 14 people from remote villages in southern Greece and Italy who all have rare mutations in the SNCA gene, making them almost certain to develop the disease. Half of this group had already been diagnosed with Parkinson's and half had not yet shown any symptoms, making them ideal for studying how the disease develops.

By comparing their brains with another 65 patients with Parkinson's and 25 healthy volunteers, the researchers were able to pinpoint early brain changes in patients in their 20s and 30s.

These were found in the serotonin system, a chemical which has many functions in the brain, including mood, appetite, cognition, wellbeing and movement.



Brain scans show a reduction in serotonin (blue/black area) as Parkinson's progresses **King's College London**

'Could open doors'

Lead study author Prof Marios Politis, from the Institute of Psychiatry, Psychology and Neuroscience at King's, said the abnormalities had been found long before movement problems had begun and before dopamine levels had changed.

"Our results suggest that early detection of changes in the serotonin system could open doors to the development of new therapies to slow, and ultimately prevent, progression of Parkinson's disease," he said.

Prof Derek Hill, professor of medical imaging at University College London, said the research provided some valuable insights but also had some limitations. "Their results may not scale up to larger studies," he said. "Secondly, the imaging method they used is highly specialised and limited to a very small number of research centres, so isn't yet usable either to help diagnose patients or even to evaluate novel treatments in large clinical studies.

"The research does, however, provide encouragement for the approach of trying to treat Parkinson's disease at the earliest possible stage, which is likely to be the best chance of preventing the rising number of people whose lives are destroyed by this hideous disease."

Dr Beckie Port, research manager at charity Parkinson's UK, said: "Further research is needed to fully understand the importance of this discovery - but if it is able to unlock a tool to measure and monitor how Parkinson's develops, it could change countless lives."

http://bit.ly/2L7UmLv

Archaeological mystery solved with modern genetics

Y chromosomes reveal population boom and bust in ancient Japan

Researchers at the University of Tokyo conducted a census of the Japanese population around 2,500 years ago using the Y chromosomes of men living on the main islands of modern-day Japan. This is the first time analysis of modern genomes has estimated the size of an ancient human population before they were met by a separate ancient population.

"Evidence at archaeological dig sites has been used to estimate the size of ancient human populations, but the difficulty and unpredictability of finding those sites is a big limitation. Now we have a method that uses a large amount of modern data," said Associate Professor Jun Ohashi, an expert in human evolutionary genetics and leader of the research team that performed the analysis.

Archaeological mystery

The current theory on human migrations into Japan is that the original inhabitants, the Jomon people, were met about 2,500 years ago by a separate group coming mainly from the Korean Peninsula, the Yayoi people.

Archaeologists have identified fewer Jomon sites from the Late Jomon Period, the era immediately before the Yayoi arrival. Global temperatures and sea levels dropped during that period, which could have made life more difficult for the hunter-gatherer Jomon people.

When the Yayoi people arrived, they brought wet rice farming to Japan, which would have led to a more stable food supply for the remaining Jomon people living with the new Yayoi migrants.

The lesser amount of archaeological remains from the Late Jomon Period could be evidence of an actual population decline, or just that the archaeological dig sites have not yet been found.

Genetic evidence

Ohashi's research team decided to start digging through the human genome to address this archaeological mystery. They began by comparing the Y-chromosome sequences of modern Japanese men to those of Korean and other East Asian men. Y chromosomes are passed on from father to son with very little change over generations, so modern Y-chromosome sequences can reliably estimate the Y chromosomes of men thousands of years ago.

Researchers used DNA samples collected before 1990 from 345 men whose families were from the three main islands of Honshu, Shikoku, and Kyushu in Japan.

The research team identified one group of DNA sequences that only Japanese men had. That unique sequence group likely came from the Jomon people. The researchers identified six sequence groups common to both Japanese men and men with other East Asian heritage (Korean, Vietnamese, Chinese), which likely came from the Yayoi people or other ancestors common to Japanese and East Asian people.

DNA confirms archaeology

Researchers built evolutionary family trees using the Y-chromosome sequences and saw a pattern indicative of a population decrease and sudden increase: a remarkable decrease in the number of ancestral Y-chromosome sequences around 2,500 years ago.

Interestingly, modern Japanese men seem to have a greater percentage of Jomon ancestral DNA in their Y chromosomes than the rest of their genomes.

Previous genetic analyses concluded that modern ethnically Japanese people get about 12 percent of their entire genomes from Jomon ancestors and the rest from Yayoi ancestors. Ohashi's research team calculated that the one group of Jomon sequences they identified accounted for 35.4 percent of the entire Y chromosome, indicating that the specific sequence would have been extremely common in Jomon men.

Since it is easier for a sequence to become common in a small population, this is another indication that the size of the Jomon population decreased during the Late Jomon Period before the arrival of the Yayoi people.

"We hope this method might be useful to confirm other ancient human dynamics not fully explained by archaeology," said Ohashi.

Research Article

Yusuke Watanabe, Izumi Naka, Seik-Soon Khor, Hiromi Sawai, Yuki Hitomi, Katsushi Tokunaga, Jun Ohashi. 2019. Analysis of whole Y-chromosome sequences reveals the Japanese population history in the Jomon period. Scientific Reports *(in press). DOI: 10.1038/s41598-019-44473-z* https://www.nature.com/articles/s41598-019-44473-z

http://bit.ly/2WWNIK7

Retracing ancient routes to Australia

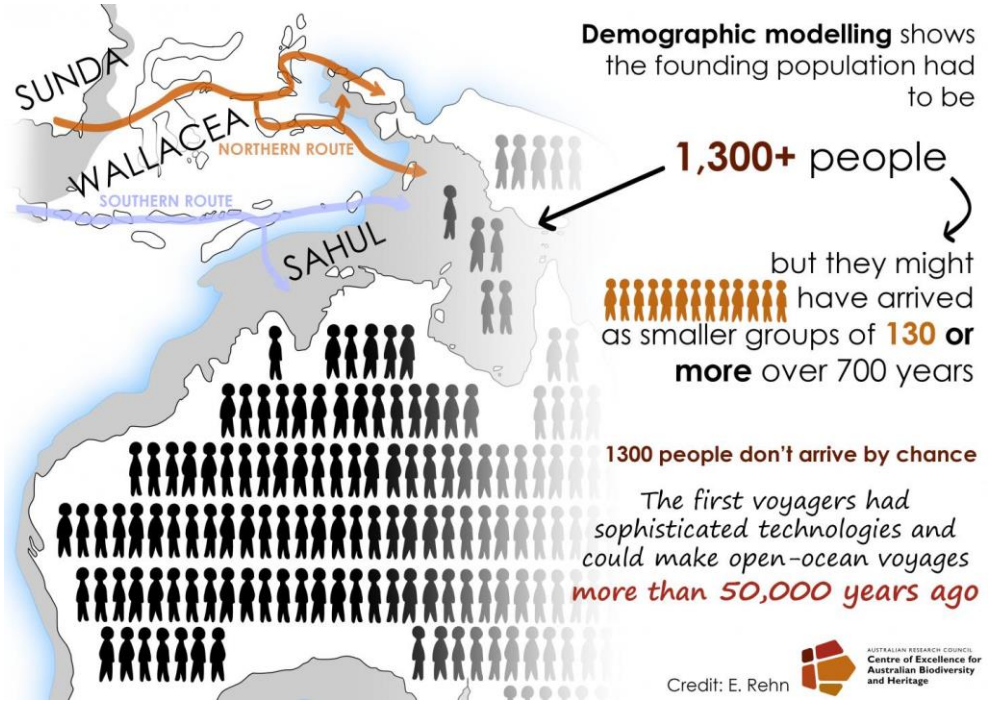
Modelling reveals First Australians arrived in large groups using complex technologies

New insights into how people first arrived in Australia have been revealed by a group of experts brought together to investigate the continent's deep history.

They used sophisticated modelling to determine not only the likely routes travelled by Aboriginal people tens of thousands of years ago, but also the sizes of groups required for the population to survive in harsh conditions.

The research, published today in two companion papers (one in Scientific Reports and the other in *Nature Ecology and Evolution*), confirms the theory that people arrived in several large and deliberate migrations by island-hopping to reach New Guinea more than 50,000 years ago.

While many Aboriginal cultures believe people have always been here, others have strong oral histories of ancestral beings arriving from the north.



Arrival of First Australians infographic **Australian Research Council Centre of Excellence for Australian Biodiversity and Heritage (CABAH)**

"We know that Aboriginal people have lived here for more than 50,000 years. This research offers a greater understanding of how migration events took place and further evidence of the marine and navigation capabilities used to make these deliberate journeys," said Professor Michael Bird, from the Australian Research Council

Centre of Excellence for Australian Biodiversity and Heritage (CABAH) and James Cook University.

The team of multidisciplinary researchers from CABAH and the CSRIO set out to establish the most likely route travelled to reach the ancient mega-continent, known as Sahul (New Guinea, Australia and Tasmania joined at times of low sea level).

"We developed demographic models to determine which island-hopping route ancient people most likely took," said CABAH's Professor Corey Bradshaw, from Flinders University.

"A northern route connecting the islands of Mangoli, Buru, and Seram into West Papua New Guinea would probably have been easiest to navigate and survive. This route was easiest when compared to the southern route from Timor that leads to the now-drowned Sahul Shelf in the modern-day Kimberley region."

The researchers also used complex mathematical modelling -- considering factors including fertility, longevity, past climate conditions, and other ecological principles -- to calculate the numbers of people required for the population as a whole to survive. The simulations indicate that at least 1300 people arrived in either a single migration event or smaller, successive waves averaging at least 130 people every 70 years or so, over the course of about 700 years. "This suggests planned and well-organised maritime migration, rather than accidental arrival" Professor Bradshaw added.

The studies confirm the ancestors of Aboriginal and Torres Strait Islander people possessed sophisticated technology and knowledge to build watercraft. This research also showcases the remarkable ability at that time to plan, navigate, and make multiple complicated, open-ocean voyages to directly transport large numbers of people.

"Both studies are unique because they relied on past environmental information and did not use any genetic data. We are very excited to see how further archaeological and genetics studies in CABAH can contribute to this story," says Dr Laura Weyrich, a CABAH investigator at the University of Adelaide.

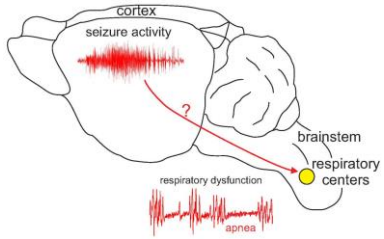
The papers *Early human settlement of Sahul was not an accident* and *Minimum founding populations for the first peopling of Sahul*, were co-authored by scientists from around Australia, including Flinders University, James Cook University, University of Wollongong, University of New South Wales, University of Adelaide, Australian National University, and the CSIRO.

CABAH brings together expertise from diverse academic disciplines to answer fundamental questions about the natural and human history of our region, including how and when people first came to Australia.

http://bit.ly/2KwlnbV

Epilepsy and sudden death linked to bad gene

The same gene mutation causes both severe epilepsy and breathing irregularities



In sudden death in epilepsy, people stop breathing for no apparent reason and die. Now, a group of UConn neuroscientists have a lead as to why, they report in the journal eLife.

Keep on Breathing: People with epilepsy can stop breathing and die suddenly, with or without a seizure. A group of UConn neuroscientists traced the problem to a gene that causes both seizures in the cortex and respiratory irregularities in the brainstem. **Dan Mulkey and Virge Kask, University of Connecticut.**

"People with epilepsy have a high mortality rate, but it's mysterious," says Dan Mulkey, a neuroscientist in UConn's physiology and neurobiology department.

More than one of every 1,000 people with epilepsy die each year from what's called sudden unexpected death in epilepsy (SUDEP). No one knows why.

The explanation usually given is that the patient had a seizure that killed them. But seizures happen in the cortex, the top of the brain, and life-sustaining processes like breathing are controlled somewhere else entirely: the brainstem, the very bottom part of the brain that connects to the spinal cord. The two parts of the brain are quite distant from each other.

"It's like, if the seizure is in New York, the brainstem is in San Francisco," Mulkey says.

Many neurologists argue that a particularly bad seizure can travel down through the brain from the cortex to the brainstem to cause breathing or heartbeat malfunction, and that's what kills in SUDEP. But Mulkey doesn't buy it. People die of SUDEP without having an obvious seizure, and epilepsy patients can have breathing problems in the absence of seizures.

Instead, Mulkey and his colleagues, graduate students Fu-Shan Kuo and Colin Clearly, wondered if there was a genetic basis for SUDEP. Perhaps the same genetic mutation that causes the seizures also disrupts the cells in the brainstem that control breathing.

Kuo raised mice with the human mutation for a severe form of epilepsy called Dravet syndrome. Dravet syndrome is caused by mutations in a gene that shapes the channels through which sodium moves in and out of cells in the brain. If the sodium channels don't function properly, cells can get overexcited. One cell's overexcitement can travel through the brain like hysteria through a crowded stadium, stampeding into a seizure.

The gene mutated in Dravet syndrome is called sodium channel gene 1a, or Scn1a. It's considered a super-culprit for epilepsy, with more than 1,200 different Scn1a mutations identified. The severity of the epilepsy caused by Scn1a depends on whether the mutation causes partial or complete loss of the sodium channel's function. The Dravet mutation is on the severe end of the spectrum. People with Dravet syndrome tend to have dramatic seizures, exacerbated by hot weather, and the syndrome is very hard to control with anti-epileptic medications. SUDEP is sadly a frequent way for people with Dravet syndrome to die.

There's a somewhat paradoxical part of Dravet syndrome, too: this Scn1a mutation makes the sodium channels less active, not more. Instead of making cells overactive, it makes them underactive. But there's a catch. This mutation mostly affects inhibitory cells - that is, cells in charge of calming the brain down. They're the stadium bouncers, so to speak. And if the bouncers are asleep on the job, the overexcited neurons can stampede uninhibited.

To understand how this might lead to SUDEP, Kuo wanted to test two things: first, whether the mice with the Dravet syndrome mutation show breathing problems and die prematurely of SUDEP, and second, whether the cells in the part of the mice's brainstem that controls breathing were normal or were somehow perturbed by the mutation.

The first question was answered quickly: the mice with Dravet syndrome had bad seizures that became more severe when the mice got hot, exactly like humans with Dravet syndrome. They tended to die very young, in a manner similar to SUDEP; none lived much past three weeks.

The second question took longer to answer, but there were early clues that Kuo and Mulkey were on to something. The mice with Dravet Syndrome had disordered breathing. They tended to hypoventilate (breathe too little) for no apparent reason sometimes. Other times they would have long apneas, or pauses between breaths. And these mice didn't breathe more in response to high carbon dioxide levels in the air, the way humans and normal mice do.

"We felt really good that our model was reflecting the human condition," Mulkey says.

The next step was to actually look at the mice's brainstems and see if something was wrong.

When Kuo zoomed in on the part of the brainstem that controls breathing, she saw that the inhibitory cells - the stadium bouncers of the brainstem - were definitely less active than they should have been. This led the excitatory neurons to run wild, and constantly tell the part of the brain that generates the breathing rhythm to push faster. But shouldn't this lead to increased breathing, not stopping?

There is definitely something wrong with the breathing circuit in the brainstem in these mice, but Mulkey and Kuo cannot pinpoint the exact problem. So they're still on the case. The next steps will be to look at mice that only express the Scn1a mutation in the brainstem or only in the cortex, and see if they also have problems. If mice with a mutation in the cortex but not the brainstem don't have SUDEP, that would argue against the 'seizure descending from cortex to brainstem' hypothesis. The researchers also plan on looking at other parts of the breathing circuit to see whether other parts have gone haywire, too. Eventually, they hope to identify a key player that can be calmed - or prodded - to prevent the breathing system from breaking down, and ultimately save the lives of people with epilepsy.

http://bit.ly/2FsLfS5

Cancer genes help deer antlers grow

Suggests antlers may reveal new ways to fight cancer

By Elizabeth Pennisi

Antlers are some of the fastest-growing bone in the animal kingdom: Deer, moose, elk, and reindeer sprout up to half a meter of new bone growth in a month prior to the mating season. Now, researchers studying their genomes have discovered how. Genes that both promote and suppress cancer are partially responsible, suggesting the bony tissue may reveal new ways to fight cancer.

The study started when scientists in China and their colleagues abroad sequenced the genomes of 44 ruminants, including cows, deer, giraffes, pronghorn sheep, and other mammals that have complex stomachs for digesting plants. Many of these ruminants sprout bony protrusions, including the skin- and hair-covered bony ossicles of giraffes; the horns of cattle, which have an additional hard sheath; pronghorns in which this sheath is shed every year; and the annually shed antlers of deer, elk, and moose.

The scientists then looked for the genes underlying the evolution and development of this headgear. Qiang Qiu, a geneticist from Northwestern Polytechnical University in Xi'an, China, and colleagues mapped out which genes were active in 16 live tissues from sheep, goats, and deer, including horns and antlers. They also assessed which genes were active in the developing embryos of some animals.

Horns and antlers evolved once in an ancestor to all these animals, they found. What's more, these new structures emerged when genes that help build nerve, bone, and skin tissue altered and became active in forming these bony protrusions, Qiu and colleagues report today in *Science*. In particular, changes to genes involved in bone formation and the development of an embryonic tissue called the neural crest likely helped lead to headgear in the first place. As further evidence of a single origin for bony headgear, Chinese water deer and two species of musk deer, both of which lack antlers, have a mutation in one of the genes linked to bone formation.

In regular deer, the researchers found eight active genes that are normally involved in promoting tumor formation and growth. That suggests, Qiu says, that antler growth is more like that of bone cancer than that of typical bones. However, in contrast to bone cancer, where tumors grow unchecked, antler growth is tightly regulated by the activity of tumor-suppressing and tumor-growth-inhibiting genes, the team reports.

“Deer antlers [are] using essentially a controlled form of bone cancer growth,” says Edward Davis, an evolutionary paleobiologist at the University of Oregon in Eugene who was not involved with the work. The involvement of the tumor-promoting genes isn’t surprising, he says; what’s surprising is the involvement of the cancer-controlling genes.

But that surprise may have done more than just turbocharge deer antler growth. The cancer-suppressing genes that keep growth in check also protect against cancer in general, Qiu says. Zoos, for example, have documented cancer rates in deer that are five times lower than rates in other mammals—perhaps, Davis says, a “happy accident” of antler evolution.

http://bit.ly/31Ph3tJ

Dirty Surgical Instruments Tied to Hundreds of Infections at Colorado Hospital, Lawsuit Alleges

Dozens of people are suing a hospital in Colorado, alleging that improper cleaning and sterilization of surgical instruments at the facility led to hundreds of infections, according to news reports.

By Rachael Rettner, Senior Writer

The lawsuit was filed this week by 67 patients who underwent surgery at Porter Adventist Hospital in Denver between 2015 and 2018, according to The Denver Post. The patients allegedly developed serious infections at the surgical site or in the bloodstream — hepatitis B, meningitis, and urinary tract, *E. coli* and staph infections — following their surgeries, the Post reported. One patient died after developing sepsis and pneumonia following surgery for a fractured femur, the lawsuit says.

In 2018, Porter Adventist Hospital acknowledged that problems with its sterilization procedures for surgical instruments may have put some patients at risk for contracting infections, including HIV, hepatitis B and hepatitis C, although the risk was said to be "very low."

An investigation by state officials also identified 76 instances in which contaminated surgical instruments were brought into operating rooms, including tools tainted with "blood, chunks of bone, cement, hair and even a dead insect," the Post reported.

The lawsuit also alleges that the sterilization problems weren't limited to instruments used for orthopedic and spine surgeries, as the hospital had previously stated. For example, one of the plaintiffs developed an infection after a mastectomy and another after an eye procedure.

In a statement, Joel Malecka, a spokesperson for Porter Adventist Hospital, said, "We acknowledge the concern of these patients and are aware of existing lawsuits," according to U.S. News & World Report. Malecka added that hospital officials have provided reports to the state showing that the facility continues to meet guidelines for sterilization procedures. "We will be addressing this matter through the legal process which is underway," Malecka said.

http://bit.ly/31ZLrlo

Synthetic biology roadmap could set research agenda for next 10 years

A new roadmap for synthetic biology could help to set research goals for improving food production, public health and the environment.

by Ryan O'hare, Imperial College London

Synthetic biology is an umbrella term for the growing field of changing the fundamental design of living organisms to engineer solutions to complex problems—editing their genetic components to change their function.

To date, achievements in the field include creating engineered trees for fire resistant timber, yeast which can produce biofuel, and synthetic gut microbes that could be used to detect the early signs of disease.

In medicine, one of the greatest hopes for synthetic biology lies in genetically engineered bacteria which are able to specifically target tumors in the body. The latest roadmap, published by the US Engineering Biology Research Consortium (EBRC), is a consensus of more than 80 scientists and engineers from a range of disciplines, representing more than 30 universities around the world—including Imperial College London—and a dozen commercial companies.

The report provides a strong case that for governments to invest in this area of research, not only to improve public health, agriculture and the environment, but also to fuel economies around the world.

Professor Paul Freemont, Head of the Section of Structural Biology in the Department of Medicine at Imperial, member of EBRC and co-author of the roadmap, said: "We believe this roadmap will firmly set the research strategy for the whole synthetic biology field for at least the next 10 years. It is a major achievement."

Meeting global challenges

Freemont is one of only a few international members of the US-based EBRC, along with Professor Richard Kitney from the Department of Bioengineering, and has been part of the technical road mapping group. The group has worked for nearly two years on a deep technical roadmap for synthetic biology.

"Over the past two decades synthetic biology has grown rapidly, using microbes like yeast and E.coli as the blueprint for engineering new and innovative solutions to complex problems—like meeting global growing demand for medicines, clean energy and sustainable food sources," he explained.

"This latest report lays out the current opportunities and technical challenges for the field, including whether or not countries make it a research priority in order to realize its full potential."

Imperial College London is a leader in the field of synthetic biology, with a wide portfolio of research spanning fuel production, pharmaceuticals, as well as flavorings and fragrances.

Earlier this year, the College led a new alliance of biofoundries—institutes which design, build and distribute the components for synthetic biology, as well as driving innovation in the field.

http://bit.ly/2RuHuQG

A new drug target for chemically induced Parkinson's disease

Researchers believe an enzyme targeted to the neuronal mitochondria may be responsible for converting compounds from alcohol, tobacco, and certain foods into chemicals that trigger or advance the disease.

More than three decades ago, scientists discovered that a chemical found in a synthetic opioid, MPTP, induced the onset of a form of Parkinson's disease. In a new study led by scientists from the School of Veterinary Medicine, researchers found that an enzyme in the body can metabolize compounds formed in the brain from alkaloids present in certain foods and tobacco into MPTP-like chemicals, triggering a neurodegenerative condition in mice.

The researchers, led by Narayan Avadhani and Mrittika Chattopadhyay, suggest that the enzyme, mitochondrial CYP2D6, presents a potentially powerful new target for Parkinson's treatment.

"Over the past two or three decades, researchers have tried inhibiting the process by which they believed MPTP was metabolized, with mixed success," says Avadhani. "We believe that mitochondrial CYP2D6 is the more direct drug target, which might prove better in treating idiopathic Parkinson's disease."

The study, which appears in the Journal of Biological Chemistry, investigates the mechanism of Parkinson's disease when a specific cause cannot be pinpointed, which is a majority of examples of the chemically induced disease.

Previous studies have shown that MPTP and similar toxic compounds induce Parkinson's disease in rodents and primates. The mechanism of action, as scientists understood it, involved the

compounds being oxidized to form MPP+, a toxic metabolite. The enzyme that was believed to be responsible is called monoamine oxidase B (MAO-B), present in the nervous system's glial cells. In that conception of the mechanism, MPP+ was thought to then be transferred to dopamine neurons by dopamine transporter proteins, and, indeed, Parkinson's is characterized by unusually low dopamine levels in the brain.

Researchers have tried to stem the effects of Parkinson's by targeting two players in this presumed pathway, both MAO-B and the dopamine transporter protein, with only mixed success.

Yet the Penn-led study implicates an entirely separate mechanism. In earlier work, Avadhani and colleagues had shown that the enzyme CYP2D6, localized to the body's energy factories, the mitochondria, could play a role in metabolizing MPTP to MPP+. In the new investigation, they took a closer look at beta-carbolines and isoquinolines, toxins that resemble MPTP which the body produces from substances found in tobacco smoke, alcohol, and some foods.

They found that, instead of MAO-B, it was mitochondrial CYP2D6 that activate the beta-carbolines and isoquinolines inside the dopamine-producing neurons, rather than the glial cells. This route of activation, in a mouse model, results in neuronal damage and oxidative stress, symptoms akin to Parkinson's.

"CYP2D6 is known to play a role in influencing the activity of a number of drugs," says Avadhani.

In an attempt to target this pathway, the researchers showed that mice lacking CYP2D6 did not exhibit the severe symptoms that mice with the protein did. In addition, an inhibitor of CYP2D6 prevented neuronal damage in the nice.

"The CYP2D6 inhibitor ajmalicine is a member of the reserpine family of alkaloids, found in the plant Rauwolfia serpentine and was long used in India for treating mental illness, such as paranoia and schizophrenia," Avadhani says. "Mitochondrial targeting of such compounds is likely to be effective in treating Parkinson's patients, and pursuing that is our future strategy."

Narayan Avadhani is the Harriet Ellison Woodward Professor of Biochemistry in the School of Veterinary Medicine's Department of Biomedical Sciences at the University of Pennsylvania.

Mrittika Chattopadhyay is a postdoctoral research in the Avadhani lab at the University of Pennsylvania School of Veterinary Medicine.

The study was supported by the National Institutes of Health (grants GM34883 and GM118122) and the Harriet Ellison Woodward Trust.

http://bit.ly/2Y6EGvv

Scientists Find Early Evidence of Humans Cooking Starches

More than 100 millennia ago, people were roasting tubers—a practice that fueled their bodies and may have aided migrations

By Sarah Wild, Sapiens

More than 100,000 years ago, humans lived in the caves that dot South Africa's coastline. With the sea on their doorstep and the Cape's rich diversity of plant life at their backs, these anatomically modern *Homo sapiens* flourished. Over several millennia, they collected shells that they used as beads, created toolkits to manufacture red pigment, and sculpted tools from bones.

Now some of these caves, along the country's southern coast, have shed light on humanity's earliest-known culinary experiments with carbohydrates, a staple in many modern diets. Small pieces of charred tubers found at the Klasies River site in South Africa date back 120,000 years, making them the earliest-known evidence of *H. sapiens* cooking carbs, according to recent research published in the *Journal of Human Evolution*.

The study joins a suite of new findings that illuminate the evolution of our ancestors' diet. For example, in recent years, scientists have determined that hominins have been eating meat for at least 2.6 million years—with some researchers contending that hominins were butchering bones for marrow as much as 3.4 million years ago.

And hominins were roasting nuts, tubers, and seeds about 780,000 years ago. Humans specifically, as another South African find revealed, ate shellfish some 164,000 years ago. And last year, ancient crumbs revealed that *H. sapiens* has been eating bread for 14,400 years.

Cynthia Larbey, an archaeologist at Cambridge University in the United Kingdom and lead author of the new study, suspects that roasting tubers provided critical nutrition to our species. "It was the way we were able to continue feeding ourselves as we moved and migrated," she says. Hunting was difficult and unreliable, so "it was a skill to be able to find food as they moved to different ecologies."

For the study, an international team of researchers excavated blocks of rock and compacted earth from the Klasies River cave floor and identified the remains of small fire pits within them. The team then used a technique called micromorphology, in which one excavates each block in tiny layers or sheets. They then removed the charred fragments and looked at them under an electron microscope.

"When you put something into a fire that's still fresh, it has water in it," explains Larbey. "When it cooks quickly, the escaping steam distorts the cells." Using an electron microscope, the researchers detected this distortion, which suggests the tubers were likely not used as kindling. In addition, the charred pieces of tubers appeared often enough in the ancient hearths that researchers ruled out the possibility they had fallen into the fire by accident.

"This is really a very nice find," says Simcha Lev-Yadun, a paleobotanist at the University of Haifa in Israel. Lev-Yadun was part of the team that discovered evidence of hominins roasting nuts and tubers 780,000 years ago.

Larbey and her colleagues believe that early modern humans' consumption of cooked starches could have aided our species significantly. The Klasies River inhabitants had to have possessed the knowledge to identify the correct plants from their leaves, remember their location, avoid toxic tubers, and recognize ripeness. These abilities enabled humans to reliably find food, even while on the move.

In addition, starches are a source of energy-rich sugars; when cooked, that energy is more readily accessible to the body and able to support the development of human brains and fetuses. Consumption of cooked starches, the researchers argue, was therefore evolutionarily advantageous.

Although previous studies have shown that a meat-based diet was critical for brain development, a growing body of scholarship argues that easily digestible carbohydrates were also necessary to meet the energy demands of growing brains. "This new paper provides compelling evidence to support this idea, at least for those humans living at the site [at the time]," says Peter Ungar, an anthropologist at the University of Arkansas, who was not involved in the study.

Early humans, this study and others suggest, were versatile and consumed a variety of items, including both starchy plant material and animal protein, Ungar says. Diets likely varied with food availability and personal preference, much as they do in the present-day.

https://nyti.ms/2IByYwA

NASA Rover on Mars Detects Puff of Gas That Hints at Possibility of Life

The Curiosity mission's scientists picked up the signal this week, and are seeking additional readings from the red planet.

By Kenneth Chang

Mars, it appears, is belching a large amount of a gas that could be a sign of microbes living on the planet today.

In a measurement taken on Wednesday, NASA's Curiosity rover discovered startlingly high amounts of methane in the Martian air, a gas that on Earth is usually produced by living things. The data

arrived back on Earth on Thursday, and by Friday, scientists working on the mission were excitedly discussing the news, which has not yet been announced by NASA.

"Given this surprising result, we've reorganized the weekend to run a follow-up experiment," Ashwin R. Vasavada, the project scientist for the mission, wrote to the science team in an email that was obtained by The Times.

The mission's controllers on Earth sent new instructions to the rover on Friday to follow up on the readings, bumping previously planned science work. The results of these observations are expected back on the ground on Monday.

People have long been fascinated by the possibility of aliens on Mars. But NASA's Viking landers in the 1970s photographed a desolate landscape. Two decades later, planetary scientists thought Mars might have been warmer, wetter and more habitable in its youth some 4 billion years ago. Now, they are entertaining the notion that if life ever did arise on Mars, its microbial descendants could have migrated underground and persisted.

Methane, if it is there in the thin Martian air, is significant, because sunlight and chemical reactions would break up the molecules within a few centuries. Thus any methane detected now must have been released recently.

On Earth, microbes known as methanogens thrive in places lacking oxygen, such as rocks deep underground and the digestive tracts of animals, and they release methane as a waste product. However, geothermal reactions devoid of biology can also generate methane.

It is also possible that the methane is ancient, trapped inside Mars for millions of years but escaping intermittently through cracks.

NASA acknowledged the methane detection in a statement Saturday afternoon, but called it an "early science result."

The agency's spokesperson added, "To maintain scientific integrity, the project science team will continue to analyze the data before confirming results."

Scientists first reported detections of methane on Mars a decade and a half ago using measurements from Mars Express, an orbiting spacecraft built by the European Space Agency and is still in operation, as well as from telescopes on Earth. However, those findings were at the edge of the detection power of these tools, and many researchers thought the methane might just be a mirage of mistaken data.

When Curiosity arrived on Mars in 2012, it looked for methane and found nothing, or at least less than 1 part per billion in the atmosphere. Then, in 2013 it detected a sudden spike, up to 7 parts per billion that lasted at least a couple of months.

The methane ebbed away.

The measurement this week found 21 parts per billion of methane, or three times the 2013 spike.

Even before this week's discovery, the mystery of methane has been deepening.

Curiosity scientists developed a technique that enabled the rover to detect even tinier amounts of methane with its existing tools. The gas seems to rise and fall with the red planet's seasons. A new analysis of old Mars Express readings confirmed Curiosity's 2013 findings. One day after Curiosity reported a spike of methane, the orbiter, passing over Curiosity's location, also measured a spike.

But the Trace Gas Orbiter, a newer European spacecraft launched in 2016 with more sensitive instruments, did not detect any methane at all in its first batch of scientific observations last year.

Marco Giuranna, a scientist at the National Institute for Astrophysics in Italy, who leads the Mars Express orbiter's methane measurements, said scientists on the Curiosity, Mars Express and Trace Gas Orbiter missions had been discussing the

latest findings. He confirmed he had been told of the reading of 21 parts per billion but added that the finding was preliminary.

He said Mars Express passed over Gale Crater, the 96-mile-wide depression that Curiosity has been studying, on the same day that Curiosity made its measurements. There are other observations on earlier and subsequent dates, Dr. Giuranna said, including joint observations with the Trace Gas Orbiter.

“A lot of data to be processed,” Dr. Giuranna said in an email. “I’ll have some preliminary results by next week.”

Rovers scheduled for launch next year — one by NASA, one by a Russian-European collaboration — will carry instruments designed to search for the building blocks of life, although neither is designed to answer the question of whether there is life on Mars today.

http://bit.ly/2N8MwUF

Cannabidiol is a powerful new antibiotic

Cannnabidiol is active against Gram-positive bacteria, with potency similar to that of established antibiotics

San Francisco, CA - New research has found that Cannnabidiol is active against Gram-positive bacteria, including those responsible for many serious infections (such as Staphyloccocus aureus and Streptococcus pneumoniae), with potency similar to that of established antibiotics such as vancomycin or daptomycin. The research is presented at ASM Microbe, the annual meeting of the American Society for Microbiology.

Cannabidiol, the main non-psychoactive chemical compound extracted from cannabis and hemp plants, has been approved by FDA for the treatment of a form of epilepsy, and is being investigated for a number of other medical conditions, including, anxiety, pain and inflammation. While there is limited data to suggest Cannabidiol can kill bacteria, the drug has not been thoroughly investigated for its potential as an antibiotic.

Work led by Dr Mark Blaskovich at The University of Queensland's Institute for Molecular Bioscience's Centre for Superbug Solutions, in collaboration with Botanix Pharmaceuticals Ltd, an early stage drug discovery company investigating topical uses of synthetic cannabidiol for a range of skin conditions, found that Cannabidiol was remarkably effective at killing a wide range of Gram-positive bacteria, including bacteria that have become resistant to other antibiotics, and did not lose effectiveness after extended treatment.

"Given cannabidiol's documented anti-inflammatory effects, existing safety data in humans, and potential for varied delivery routes, it is a promising new antibiotic worth further investigation," said Dr. Blaskovich. "The combination of inherent antimicrobial activity and potential to reduce damage caused by the inflammatory response to infections is particularly attractive."

Importantly, the drug retained its activity against bacteria that have become highly resistant to other common antibiotics. Under extended exposure conditions that lead to resistance against vancomycin or daptomycin, Cannabidiol did not lose effectiveness. Cannabidiol was also effective at disrupting biofilms, a physical form of bacteria growth that leads to difficult-to-treat infections.

The project was co-funded by Botanix and Innovation Connections, an Australian government grant scheme to commercialize new products, processes and services. The paper will be presented on Sunday June 23rd from 11am-1 pm at the annual conference of the American Society for Microbiology, ASM Microbe 2019, at the Moscone Convention Center in San Francisco.

http://bit.ly/2Rwik49

Could coffee be the secret to fighting obesity?

A cup of coffee can stimulate the body's own fat-fighting defenses, which could be the key to tackling obesity and diabetes

Scientists from the University of Nottingham have discovered that drinking a cup of coffee can stimulate 'brown fat', the body's own fat-fighting defenses, which could be the key to tackling obesity and diabetes.

The pioneering study, published today in the journal Scientific Reports, is one of the first to be carried out in humans to find components which could have a direct effect on 'brown fat' functions, an important part of the human body which plays a key role in how quickly we can burn calories as energy.

Brown adipose tissue (BAT), also known as brown fat, is one of two types of fat found in humans and other mammals. Initially only attributed to babies and hibernating mammals, it was discovered in recent years that adults can have brown fat too. Its main function is to generate body heat by burning calories (opposed to white fat, which is a result of storing excess calories).

People with a lower body mass index (BMI) therefore have a higher amount of brown fat.

Professor Michael Symonds, from the School of Medicine at the University of Nottingham who co-directed the study said: "Brown fat works in a different way to other fat in your body and produces heat by burning sugar and fat, often in response to cold. Increasing its activity improves blood sugar control as well as improving blood lipid levels and the extra calories burnt help with weight loss. However, until now, no one has found an acceptable way to stimulate its activity in humans.

"This is the first study in humans to show that something like a cup of coffee can have a direct effect on our brown fat functions. The potential implications of our results are pretty big, as obesity is a major health concern for society and we also have a growing diabetes epidemic and brown fat could potentially be part of the solution in tackling them."

The team started with a series of stem cell studies to see if caffeine would stimulate brown fat. Once they had found the right dose, they then moved on to humans to see if the results were similar.

The team used a thermal imaging technique, which they'd previously pioneered, to trace the body's brown fat reserves. The non-invasive technique helps the team to locate brown fat and assess its capacity to produce heat.

"From our previous work, we knew that brown fat is mainly located in the neck region, so we were able to image someone straight after they had a drink to see if the brown fat got hotter," said Professor Symonds.

"The results were positive and we now need to ascertain that caffeine as one of the ingredients in the coffee is acting as the stimulus or if there's another component helping with the activation of brown fat. We are currently looking at caffeine supplements to test whether the effect is similar.

Once we have confirmed which component is responsible for this, it could potentially be used as part of a weight management regime or as part of glucose regulation programme to help prevent diabetes."