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# Cold medicine could stop cancer spread

***Researchers have discovered that a nonsteroid anti-inflammatory drug used for treating colds suppresses the spread of bladder cancers and reduces their chemoresistance in mice, raising hopes of a future cure for advanced bladder cancers***

Bladder cancer is the seventh most common cancer in males worldwide. Every year, about 20,000 people in Japan are diagnosed with bladder cancer, of whom around 8,000--mostly men--succumb to the disease.

Bladder cancers can be grouped into two types: non-muscle-invasive cancers, which have a five-year survival rate of 90 percent, and muscle-invasive cancers, which have poor prognoses. The latter are normally treated with such anticancer drugs as cisplatin, but tend to become chemoresistant and, thus, spread to organs such as the lungs and liver, as well as bone.

In the latest research, human bladder cancer cells labeled with luciferase were inoculated into mice, creating a xenograft bladder cancer model. The primary bladder xenograft gradually grew and, after 45 days, metastatic tumors were detected in the lungs, liver and bone.

By using a microarray analysis including more than 20,000 genes for the metastatic tumors, the team discovered a three- to 25-fold increase of the metabolic enzyme aldo-keto reductase 1C1 (AKR1C1). They also found high levels of AKR1C1 in metastatic tumors removed from 25 cancer patients, proving that the phenomena discovered in the mice also occur in the human body. Along with anticancer drugs, an inflammatory substance produced around the tumor, such as interleukin-1β, increased the enzyme levels.

The researchers also identified for the first time that AKR1C1 enhances tumor-promoting activities and proved that the enzyme blocks the effectiveness of cisplatin and other anticancer drugs.

The researchers finally discovered that inoculating flufenamic acid, an inhibitory factor for AKR1C1, into cancerous bladder cells suppressed the cells' invasive activities and restored the effectiveness of anticancer drugs. Flufenamic acid is also known as a nonsteroid anti-inflammatory drug used for treating common colds.

The team's discovery is expected to spur clinical tests aimed at improving prognoses for bladder cancer patients. In the latest cancer treatments, expensive molecular-targeted drugs are used, putting a large strain on both the medical economy and the state coffers.

"This latest research could pave the way for medical institutions to use flufenamic acid--a much cheaper cold drug--which has unexpectedly been proven to be effective at fighting cancers," says Dr. Shinya Tanaka of the research group.

The research was conducted in collaboration with Dr. Nobuo Shinohara of the Department of Renal and Genitourinary Surgery at Hokkaido University; the article's lead author was postgraduate student Ryuji Matsumoto.

http://bit.ly/2eqDKvI

# Ancient hominid 'hanky panky' also influenced spread of STIs

***New pattern has emerged after reconstructing ancestry and timing of the family tree of HPV16***

With recent studies proving that almost everyone has a little bit of Neanderthal DNA in them----up to 5 percent of the human genome---it's become clear our ancestors not only had some serious hominid 'hanky panky' going on, but with it, a potential downside: the spread of sexually transmitted infections, or STIs.

For wherever life goes, germs are soon to follow.

In the case of the most common STI, human papillomaviruses (HPVs), almost everyone hosts a number of infections, with strain HPV16 responsible for most cervical and oral cancers.

By reconstructing the ancestry and timing of the family tree of HPV16 in greater detail than ever before, and by comparing the evolutionary

histories of viruses and humans, a new pattern has emerged. Now, researchers have generated compelling evidence that HPV16 co-diverged with archaic and modern humans---only to be repopulated at a much later date through their contact by Neanderthals, challenging the assumption that HPV16 co-evolved with modern humans. The study, by Ville Pimenoff at the Catalan Institute of Oncology and Ignacio Bravo at the French National Center for Scientific Research was published in the advanced online edition of Molecular Biology and Evolution (DOI: 10.1093/molbev/msw214).

During the evolution of HPV16, variants A and B/C/D co-diverged with archaic and modern humans, respectively. When populations of modern humans left Africa and had sexual intercourse with Neanderthals and Denisovans, they were infected by the viral variant that had evolved with archaic humans, and this virus thrived and expanded among modern humans

This scenario finally explains unsolved questions: why human diversity is largest in Africa, while HPV16 diversity is largest in East-Asia, and why the HPV16A variant is virtually absent in Sub-Saharan Africa while it is by far the most common one in the rest world.

"Oncogenic viruses are very ancient," said Ignacio Bravo. "The history of humans is also the history of the viruses we carry and we inherit. Our work suggests that some aggressive oncogenic viruses were transmitted by sexual contact from archaic to modern humans."

They propose that interactions between the host and viral genomes may explain why most humans are exposed to HPVs and cure the infection, while in a few unfortunate cases the infection persists and can lead to cancer.

The different degree of archaic ancestry in our genomes could be partly responsible for differential susceptibility to cancer. Since HPVs do not infect bones, current Neanderthal and Denisovan genomes do not contain HPVs. As a next step, the authors hope to trace HPVs sequences in ancient human skin remains as a more direct test of their hypothesis.

http://bit.ly/2eeQH0i

## How your BMI might affect your brain function

***There are plenty of reasons it's important to maintain a healthy weight, and now you can add one more to the list: It may be good for your brain.***

Researchers from the University of Arizona have found that having a higher body mass index, or BMI, can negatively impact cognitive functioning in older adults. How? They say inflammation is to blame.

"The higher your BMI, the more your inflammation goes up," said Kyle Bourassa, lead author of the study, which is published in the journal Brain, Behavior and Immunity. "Prior research has found that inflammation -- particularly in the brain -- can negatively impact brain function and cognition."

Previous studies also have linked higher BMI -- an index of body fat based on height and weight -- to lower cognitive functioning. But how and why the two are connected was far less clear.

"We saw this effect, but it's a black box. What goes in between?" said Bourassa, a UA psychology doctoral student. "Establishing what biologically plausible mechanisms explain this association is important to be able to intervene later."

Bourassa and his co-author, UA psychology professor David Sbarra, analyzed data from the English Longitudinal Study of Aging, which includes over 12 years' worth of information on the health, well-being and social and economic circumstances of the English population age 50 and older.

Using two separate samples from the study -- one of about 9,000 people and one of about 12,500 -- researchers looked at aging adults over a six-year period. They had information on study participants' BMI, inflammation and cognition, and they found the same outcome in both samples.

"The higher participants' body mass at the first time point in the study," Bourassa said, "the greater the change in their CRP levels over the next four years. CRP stands for C-reactive protein, which is a

marker in the blood of systemic inflammation in your body. Change in CRP over four years then predicted change in cognition six years after the start of the study. The body mass of these people predicted their cognitive decline through their levels of systemic inflammation."

The findings support existing literature linking inflammation to cognitive decline and take it a step further by illuminating the important role of body mass in the equation.

Sbarra added a word of caution in trying to understand the findings.

"The findings provide a clear and integrative account of how BMI is associated with cognitive decline through systemic inflammation, but we need to remember that these are only correlational findings," he said. "Of course, correlation does not equal causation. The findings suggest a mechanistic pathway, but we cannot confirm causality until we reduce body mass experimentally, then examine the downstream effects on inflammation and cognition." "Experimental studies finding whether reducing inflammation also improves cognition would be the gold standard to establish that this is a causal effect," Bourassa added.

Cognitive decline is a normal part of aging, even in healthy adults, and can have a significant impact on quality of life. The current research may provide valuable insights for possible interventions and new research directions in that area.

"If you have high inflammation, in the future we may suggest using anti-inflammatories not just to bring down your inflammation but to hopefully also help with your cognition," Bourassa said.

Of course, maintaining a healthy weight is also good for overall health, he added. "Having a lower body mass is just good for you, period. It's good for your health and good for your brain," Bourassa said.

***http://bit.ly/2esGVDW***

## Short walks after meals may prove important tool in managing diabetes

***New research from New Zealand's University of Otago suggests that people managing type 2 diabetes should walk after meals to gain the greatest blood sugar-lowering benefits.***

Current advice in New Zealand is for people with type 2 diabetes to walk at least 30 minutes a day. No particular time of the day is advised. The Otago research indicates that walking after meals is better at reducing blood sugar levels than taking a single 30 minute walk at any time of the day.

The researchers prescribed walking to 41 patients with type 2 diabetes in two-week blocks, separated by a month. The patients - who were fitted with accelerometers to measure their physical activity and devices that measured their blood sugar every five minutes - were to walk either for thirty minutes a day as advised by guidelines, or to walk for 10 minutes after each main meal.

Study first author Dr Andrew Reynolds says the study found that post-meal blood sugar levels dropped 12 per cent on average when the participants followed the walking after meals advice compared to walking at any time of the day.

"Most of this effect came from the highly significant 22 per cent reduction in blood sugar when walking after evening meals, which were the most carbohydrate heavy, and were followed by the most sedentary time," Dr Reynolds says.

Corresponding author Professor Jim Mann says that post-meal glucose is regarded as an important target in managing type 2 diabetes, given its independent contribution to overall blood sugar control and cardiovascular risk.

Professor Mann and his colleagues (Dr Reynolds, Dr Bernard Venn and Associate Professor Sheila Williams) write that "postprandial physical activity may avoid the need for an increased total insulin dose or additional mealtime insulin injections that might otherwise have been prescribed to lower glucose levels after eating. An increase in insulin dose might, in turn, be associated with weight gain in patients with type 2 diabetes, many of whom are already overweight or obese."

They conclude that: "The benefits relating to physical activity following meals suggest that current guidelines should be amended to

specify post-meal activity, particularly when meals contain a substantial amount of carbohydrate."

Their findings are published this week in the prestigious international journal Diabetologia. A second UK-based study in the same edition of the journal shows that increasing your amount of activity also confers greater benefit in blood sugar control.

***http://bit.ly/2eqWDym***

## Here's why putting tomatoes in the fridge makes them tasteless

***Some foods just aren't meant to go in the fridge – like tomatoes.***

**By Bob Holmes**

As some consumers have long known, refrigerating them permanently impairs their flavour, but the reasons were elusive. New insights into why this happens may some day help us develop varieties that retain their flavour during cold storage.

A team led by Harry Klee of the University of Florida in Gainesville got their teeth into the problem by studying the expression of more than 25,000 genes in two tomato varieties. They looked at these genes before and during chilling, and after returning the tomatoes to room temperature.

Chilling, a major stress for a tropical plant such as the tomato, reduced the activity of hundreds of genes. Some of these produce enzymes responsible for synthesising the volatile chemicals that make tomatoes taste sweeter and give them a more complex, appealing aroma.

Many of the enzymes never recovered, even after the tomatoes were back at room temperature. Taste tests confirmed that chilling did, indeed, give rise to less flavourful tomatoes.

Further analysis showed that chilling led to changes in DNA methylation, affecting many genes. Since methylation is a common mechanism for turning genes on and off for long periods, this may account for the long-lasting effect of chilling on flavour, says Klee.

With this knowledge, breeders may be able to modify the temperature-sensitive enzymes to be more robust, or else select tomato varieties with gene variants that are naturally less inhibited by cold, he says.

Elizabeth Baldwin, a plant physiologist with the US Department of Agriculture's research lab in Fort Pierce, Florida, agrees. "With this knowledge, we could definitely do breeding or genetic manipulation," she says.

The other message of Klee's work, of course, is a simple one: "Don't put your tomatoes in the fridge," says Baldwin. "They lose their aroma."

*Journal reference: PNAS, DOI: 10.1073/pnas.1613910113*

***http://nyti.ms/2enOVs0***

## Venus: Inhospitable, and Perhaps Instructional

***Why does the air on slow-spinning Venus speed around so much faster than the planet itself?***

**By KENNETH CHANG OCT. 17, 2016**

Venus is not a placid paradise — that much we know. In addition to searing surface temperatures, wind in the upper atmosphere howls at up to 250 miles per hour, carrying clouds around the planet once every four days.

Yet Venus itself spins very slowly: one rotation every 243 Earth days — in the wrong direction, no less, opposite to almost every other body in the solar system.

On the whole, the atmosphere on Earth rotates about the same speed as the planet. So why does the air on slow-spinning Venus speed around so much faster than the planet itself?

The Japanese space probe Akatsuki, now in orbit around Venus, seeks to solve the mystery of so-called super-rotation. Scientists working on the mission are presenting some of their early findings at a meeting this week of the American Astronomical Society's Division for Planetary Sciences in Pasadena, Calif.

That is not just an idle trivia question for planetary scientists. Computer models of our own weather fail when applied to Venus, and

knowledge of the planet's workings could better our understanding of Earth's.

"We don't know what is the missing point in meteorology," said Masato Nakamura, Akatsuki's project manager. "If we know what makes such a super-rotation, we will have a much deeper understanding of the atmospheric dynamics, not just on Venus but also on Earth. We will learn much more about the Earth climate."

In recent years, Venus has been a backwater of planetary exploration, even though it is much closer in size to Earth than is Mars. For a long time, scientists imagined there could be a habitable tropical paradise beneath Venus's thick clouds.

In the late 1950s, intense thermal emissions, measured by a radio telescope on Earth, told a different story. Venus broils.

The average surface temperature is more than 850 degrees Fahrenheit — an extreme demonstration of the heat-trapping prowess of carbon dioxide, the primary constituent of the Venusian atmosphere. Clouds of sulfuric acid make it an even less appealing place to visit.

In the 1990s, NASA's Magellan spacecraft precisely mapped the topography of Venus through radar. Except for a few flybys by spacecraft on the way to somewhere else, NASA has not returned to Venus, although the agency is considering two modest proposals.

A European mission, Venus Express, studied the planet from 2006 to 2014, discovering among other things a frigid layer of atmosphere, minus 280 degrees Fahrenheit at an altitude of 75 miles, sandwiched between two warmer layers.

But now Akatsuki, which entered orbit last December, has begun its work. Takehiko Satoh, one of the mission scientists, said that one of "the most exciting, most surprising results" so far came almost immediately after the spacecraft arrived.

The camera that captures long-wavelength infrared light from the cloud tops discovered an arc-shaped white streak that stretched some 6,000 miles from nearly the south pole to nearly the north pole.

Curiously, this giant atmospheric feature does not move with the atmosphere. "It seems to be fixed to the ground," Dr. Satoh said.

The arc sits above Aphrodite Terra, a highland region about the size of Africa that rises up to three miles from the surface. Scientists working on data from the Venus Express reported a similar finding in July.

One possibility is that as the wind blows over Aphrodite Terra, clouds are pushed higher and the temperature of the cloud tops falls. "Our interpretation is there is some disturbance from the high mountain," Dr. Nakamura said.

Dr. Satoh said there were primarily two competing ideas for where the energy for the Venus wind comes from. One is that energy coming from the sun accelerates the wind. The second is that atmosphere is so thick that it gradually slows down the spinning of the planet, and that angular momentum is transferred to the air.

According to this theory, even though breezes on the surface are slight — a couple of miles per hour — the speeds increase at higher altitudes as the air thins.

The small spacecraft — the main body is a box a bit bigger than a refrigerator — carries five cameras, collecting light at different wavelengths to monitor the Venusian atmosphere at different altitudes.

In another experiment, scientists will observe how the radio signal from the spacecraft to Earth is distorted when it passes through the atmosphere. That will reveal temperature, abundance of sulfuric acid vapor and other properties. By observing the atmosphere at different altitudes, they can detect wavelike features that rise and fall, like blobs in a lava lamp.

"If the solar heating or thermal tide hypothesis is correct," Dr. Satoh said, "we may see different propagation of the wave, from cloud top to the lower level." If the viscosity theory is correct, the waves should propagate in the opposite direction, from the ground to the clouds.

Perhaps the answers will become clear in a year — or maybe four. "We need to analyze a lot of big data," Dr. Nakamura said.

That Akatsuki, which means “dawn” in Japanese, is there at all is the result of ingenuity and perseverance.

It launched in May 2010 and arrived at Venus seven months later. But when its main engine failed to fire properly, it sailed right past the planet.

“It was a very sad moment,” Dr. Satoh said.

Within a day, Dr. Satoh said, calculations indicated that in six years, Akatsuki, in orbit around the sun instead of Venus, could meet up with Venus again. But it was not clear the spacecraft still would be able to slow down and enter orbit.

An investigation found that a valve in the engine had leaked, leading to the formation of salts that fused it shut. The engine, as it fired, had overheated beyond repair.

Akatsuki still had the maneuvering thrusters that were to be used after it entered orbit. They were not as powerful as the broken engine, but they could apply enough force to slow it down enough so that Venus’ gravity could capture it.

Because of worries that the longer stay in space, with the bombardment of solar radiation and cosmic rays, would degrade the instruments, the craft was maneuvered so the second rendezvous would occur a year earlier, in November 2015.

Then calculations suggested that orbit might not be stable, and the spacecraft might crash into Venus shortly afterward. Another adjustment pushed the arrival back a couple of weeks to Dec. 7, exactly five years after the original arrival date.

This time, everything worked.

The Akatsuki’s orbit is different from the one originally envisioned. Instead of being synchronized to the spinning atmosphere, which would have allowed scientists to better track small changes, the spacecraft now loops around Venus in a large elliptical orbit.

That provides different benefits. Instead of intently staring at one spot, seeing the smallest changes, scientists are now able to see what happens on a global scale, although they will miss some of the details.

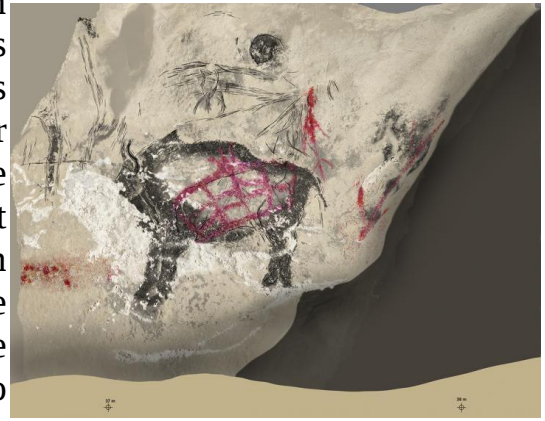
Akatsuki is to continue operating until at least April 2018, depending on how much fuel it has left. “We know at least we have one kilogram of fuel,” said Dr. Nakamura, likening the uncertainty to an imprecise fuel gauge in a car.

If it turns out that Akatsuki has more, the spacecraft could continue operating for perhaps up to six years, he said.

***http://bit.ly/2eBSo2x***

## The Higgs Bison -- mystery species hidden in cave art

***Ancient DNA research has revealed that Ice Age cave artists recorded a previously unknown hybrid species of bison and cattle in great detail on cave walls more than 15,000 years ago.***



The mystery species, known affectionately by the researchers as the Higgs Bison* because of its elusive nature, originated over 120,000 years ago through the hybridisation of the extinct Aurochs (the ancestor of modern cattle) and the Ice Age Steppe Bison, which ranged across the cold grasslands from Europe to Mexico.

***This is a reproduction of a putative wisent painted in the Marsoulas cave (Haute-Garonne, France) during the the Magdalenian period.*** **Picture from Carole Fritz**

Research led by the Australian Centre for Ancient DNA (ACAD) at the University of Adelaide, published today in Nature Communications, has revealed that the mystery hybrid species eventually became the ancestor of the modern European bison, or wisent, which survives in protected reserves such as the Białowieża forest between Poland and Belarus.

"Finding that a hybridisation event led to a completely new species was a real surprise - as this isn't really meant to happen in mammals,"

says study leader Professor Alan Cooper, ACAD Director. "The genetic signals from the ancient bison bones were very odd, but we weren't quite sure a species really existed - so we referred to it as the Higgs Bison."

The international team of researchers also included the University of California, Santa Cruz (UCSC), Polish bison conservation researchers, and palaeontologists across Europe and Russia. They studied ancient DNA extracted from radiocarbon-dated bones and teeth found in caves across Europe, the Urals, and the Caucasus to trace the genetic history of the populations.

They found a distinctive genetic signal from many fossil bison bones, which was quite different from the European bison or any other known species.

Radiocarbon dating showed that the mystery species dominated the European record for thousands of years at several points, but alternated over time with the Steppe bison, which had previously been considered the only bison species present in Late Ice Age Europe.

"The dated bones revealed that our new species and the Steppe Bison swapped dominance in Europe several times, in concert with major environmental changes caused by climate change," says lead author Dr Julien Soubrier, from the University of Adelaide. "When we asked, French cave researchers told us that there were indeed two distinct forms of bison art in Ice Age caves, and it turns out their ages match those of the different species. We'd never have guessed the cave artists had helpfully painted pictures of both species for us."

The cave paintings depict bison with either long horns and large forequarters (more like the American bison, which is descended from the Steppe bison) or with shorter horns and small humps, more similar to modern European bison.

"Once formed, the new hybrid species seems to have successfully carved out a niche on the landscape, and kept to itself genetically," says Professor Cooper. "It dominated during colder tundra-like periods, without warm summers, and was the largest European species to survive the megafaunal extinctions. However, the modern European bison looks genetically quite different as it went through a genetic bottleneck of only 12 individuals in the 1920s, when it almost became extinct. That's why the ancient form looked so much like a new species."

Professor Beth Shapiro, UCSC, first detected the mystery bison as part of her PhD research with Professor Cooper at the University of Oxford in 2001. "Fifteen years later it's great to finally get to the full story out. It's certainly been a long road, with a surprising number of twists," Professor Shapiro says.

**The Higgs Boson is a subatomic particle suspected to exist since the 1960s and only confirmed in 2012.*

**http://bit.ly/2eeMbMQ**

## Migraine sufferers have higher levels of nitrate-reducing microbes in their mouths

### *Association between migraines and microbes that reduce nitrates*

Washington, DC - Researchers at the University of California San Diego School of Medicine (UC San Diego) have found an association between migraines and microbes that reduce nitrates. Analyzing data from the American Gut Project, they found that migraine sufferers harbored significantly more microbes in their mouths and guts with the ability to modify nitrates compared to people who do not get migraine headaches. Their report, which is published this week in mSystems®, an open-access journal of the American Society for Microbiology, will spur more research to find out which oral microorganisms are related to migraines and how they affect health.

"There is this idea out there that certain foods trigger migraines--chocolate, wine, and especially foods containing nitrates," says Antonio Gonzalez, a programmer analyst in the laboratory of Rob Knight at UC San Diego, and lead author on the study. "We thought that perhaps there was a connection between someone's microbiome and what they were eating."

Many of the 38 million Americans who suffer from migraines have noticed an association between consuming nitrates and their severe headaches. Nitrates, found in foods like processed meats, green leafy vegetables, and in certain medicines, can be reduced to nitrites by bacteria found in the oral cavity. These nitrites when circulating in the blood can then be converted to nitric oxide (NO) under certain conditions, which is a powerful vasodilator that can aid cardiovascular health by improving blood flow and reducing blood pressure.

Using publicly available data from the American Gut Project run out of the Knight lab, Gonzalez and his colleague Embriette Hyde sequenced bacteria found in 172 oral samples and 1,996 fecal samples from healthy participants. The participants had previously filled out surveys indicating whether they suffered from migraines.

The sequencing first told them which bacterial species were found in different abundances between migraineurs and non-migraineurs. In terms of bacterial community composition, the team did not find huge differences in either fecal or oral samples from migraineurs compared to non-migraineurs.

Next, they used a bioinformatic tool called PICRUSt to analyze which genes were likely to be present in the two different sets of samples, given the bacterial species present. In fecal samples, they found a slight, but statistically significant increase in the abundance of genes that encoding nitrate, nitrite and nitric oxide reductases in migraineurs. In oral samples, these genes were significantly more abundant in migraineurs.

"We know for a fact the nitrate-reducing bacteria are found in the oral cavity," says Hyde, who is the project manager for the American Gut Project in the Knight laboratory. "We definitely think this pathway is advantageous to cardiovascular health, but now we have a potential connection to migraines as well."

About 80% of cardiac patients who take nitrate-containing drugs for chest pain or congestive heart failure report severe headaches as a side effect. The researchers speculate that we may have a symbiotic relationship with our oral microbes, which aids our cardiovascular health. But for certain people, this research suggests, too many nitrate-reducing bacteria in the mouth may also lead to migraines.

Gonzalez and Hyde say that the next steps will be to look at more defined groups of patients, separated into the handful of different types of migraines. Then, researchers can determine if their oral microbes really do express those nitrate-reducing genes, measure their levels of circulating NO and see how they correlate with migraine status.

Perhaps far into the future, Gonzalez says, "We will have a magical probiotic mouthwash for everyone that helps your cardiovascular health without giving you migraines." But for now, he says, "If you suspect that nitrates are causing you migraines, you should try to avoid them in your diet."

***http://bit.ly/2eQ3oOT***

## Age of 1st chief's ancient tomb reveals Pacific islanders invented new kind of society

***New uranium series analysis of chief's tomb suggests island's monumental structures are earliest evidence of a chiefdom in the Pacific -- yielding new keys to how societies emerge and evolve***

New dating on the stone buildings of Nan Madol suggests the ancient coral reef capital in the Pacific Ocean was the earliest among the islands to be ruled by a single chief.

The discovery makes Nan Madol a key locale for studying how ancient human societies evolved from simple societies to more complex societies, said archaeologist Mark D. McCoy, Southern Methodist University, Dallas. McCoy led the discovery team.

The finding was uncovered as part of a National Geographic expedition to study the monumental tomb said to belong to the first chief of the island of Pohnpei.

McCoy deployed uranium series dating to determine that when the tomb was built it was one-of-a-kind, making it the first monumental scaled burial site on the remote islands of the Pacific.

The discovery enables archaeologists to study more precisely how societies transform to more and more complex and hierarchical systems, said McCoy, an expert in landscape archaeology and monumental architecture and ideology in the Pacific Islands.

"The kind of society that we live in today, it wasn't born last year, or even 100 years ago," McCoy said. "It has its roots in a pre-modern era like Nan Madol where you have a king or chief. These islanders invented a new kind of society -- that is a socially creative achievement. The idea of chiefs, someone in charge, is not a new thing, but it's an extremely important precursor. We know tribes and bands predate chiefdoms and states. But it's not a straight line. By looking at these intermediate stages we get insight into that social phenomenon."

The analysis is the first time uranium-thorium series dating, which is significantly more precise than previously used radiocarbon dating, was deployed to calculate the age of the stone buildings that make up the famous site of Nan Madol (pronounced Nehn Muh-DOLL) - the former capital of the island of Pohnpei.

"The thing that makes this case special is Nan Madol happened in isolation, it happened very recently, and we have multiple lines of evidence, including oral histories to support the analysis," McCoy said. "And because it's an island we can be much more specific about the natural resources, the population, all the things that are more difficult when people are on a continent and all connected. So we can understand it with a lot more precision."

Nan Madol, which UNESCO this year named a World Heritage Site, was previously dated as being established in A.D. 1300. McCoy's team narrowed that to just a 20-year window more than 100 years earlier, from 1180 to 1200.

The finding pushes back even earlier the establishment of the powerful dynasty of Saudeleur chiefs who asserted authority over the island society for more than 1,000 years.

**First chief was buried in Pohnpei tomb by A.D. 1200**

An ancient city built atop a coral reef, Nan Madol has been uninhabited for centuries now. Located in the northwestern Pacific on the remote island of Pohnpei, it's accessible via a 10-hour flight from Hawaii interspersed with short hops from atoll to atoll, including a stop at a U.S. military installation. Nan Madol is the largest archaeological site in Micronesia, a group of islands in the Caroline Archipelago of Oceania.

Uranium dating indicates that by 1180, massive stones were being transported from a volcanic plug on the opposite side of the island for construction of the tomb. And by 1200, the burial vault had its first internment, the island's chief. Manipulate two 3D models of the burial monument, one with foliage and one without, at https://skfb.ly/StXA and https://skfb.ly/S9LF.

Construction of monumental buildings followed over the next several centuries on other islands not in the Saudeleur Dynasty across Oceania.

McCoy, an associate professor in the SMU Department of Anthropology, and his team reported their discovery in the journal Quaternary Research in "Earliest direct evidence of monument building at the archaeological site of Nan Madol identified using 230Th/U coral dating and geochemical sourcing of megalithic architectural stone."

Co-authors include Helen A. Alderson, University of Cambridge, U.K., Richard Hemi, University of Otago, New Zealand, Hai Cheng, Xi'an Jiaotong University, China, and R. Lawrence Edwards, University of Minnesota.

An inactive volcano that hasn't erupted in at least one million years, Pohnpei Island is much larger than its neighboring atolls at 128 square miles (334 square kilometers), making it about the physical size of Columbia, S.C.

Now part of the 607-island nation of the Federated States of Micronesia, Pohnpei Island and its nearby atolls have a population of 34,000.

**Pohnpei monument indicates invention of a new kind of society**

How Nan Madol was built remains an engineering mystery, much like Egypt's Pyramids.

"It's a fair comparison to the Pyramids, because the construction, like the Pyramids, didn't help anyone -- it didn't help society be fairer, or to grow crops or to provide any social good. It's just a really big place to put a dead person," McCoy said.

It's important to document such things, he said, because this architectural wonder indicates that independently of Egypt, another group of people put effort into building a monument.

"And we think that's associated with the invention of a new kind of society, a new kind of chiefdom that ruled the entire island," McCoy said.

Unlike Egypt and the Pyramids however, Nan Madol was invented much more recently in the big story of human prehistory, he said.

"At A.D. 1200 there are universities in Europe. The Romans had come and gone. The Egyptians had come and gone," he said. "But when you're looking at Pohnpei, it's very recent, so we still have the oral histories of the descendants of the people who built Nan Madol. There's evidence that you just don't have elsewhere."

**Monumental city built of coral and stone**

Pohnpei was originally settled in A.D. 1 by islanders from the Solomon or Vanuatu island groups. According to local oral history, the Saudeleur Dynasty is estimated to have begun its rule around 1160 by counting back generations from the modern day.

To build the tomb and other structures, naturally formed boulders of basalt, each weighing tons, were somehow transported far from existing quarries on the other side of the island to a lagoon overgrown with mangrove and stretching across 205 acres (83 hectares).

The basalt blocks formed when hot lava cooled and adopted the shape of long, column-shaped boulders and cobbles. Formed from 1 million to 8 million years ago, they came from a number of possible quarry locations on the island.

The city's stone structures were built atop 98 shallow artificial coral reef islets, each one built by the Saudeleur people. The structures were constructed about three feet above waterline by laying down framing stones, filling the void between them with crushed coral, then laying up double parallel walls and again filling the gap between with crushed coral. The islets are separated by tidal canals and protected from the ocean by 12 sea walls, making Nan Madol what many consider the Venice of the Pacific.

"The structures are very cleverly built," said McCoy. "We think of coral as precious, but for the architects of Nan Madol it was a building material. They were on a little island surrounded by huge amounts of coral reef that grows really quickly in this environment, so they could paddle out at low tide and mine the coral by smashing some off and breaking it up into rubble."

The largest and most elaborate architecture in the city is the tomb of the first Saudeleur, measuring 262 feet by 196 feet (80 meters by 60 meters), basically the size of a football field. It is more than 26 feet (8 meters) tall, with exterior walls about six feet to 10 feet (1.8 to 3 meters) thick. A maze of walls and interior walkways, it includes an underground crypt capped with basalt.

"The architecture is meant to be extremely impressive, and it is," McCoy said. "The structures were built to last -- this is one of the rainiest places on earth, so it can be muddy and slippery and wet, but these islets on the coral reef are very stable."

**Portable X-ray technology provides clue to source of megalithic stones**

McCoy and his team used portable X-ray fluorescence (XRF) to geochemically match the columnar-shaped basalt stones to natural sources on the island. The uranium-thorium technique calculates a date based on characteristics of the radioactive isotope thorium-230 and its radioactive parent uranium-234.

That enabled them to determine the construction chronology of a tomb that oral histories identify as the resting place of the first chief to rule the entire island.

"We used an X-ray gun, which looks like a 1950s-styled ray gun," McCoy said. "It allows you -- at a distance and without destroying the thing you're interested in -- to bounce X-rays off it and work out what the chemistry is. The mobile technology has gotten much more affordable, making this kind of study feasible."

Using uranium series dating on coral emerged in the last decade. Accuracy -- superior to radiocarbon -- is plus or minus a few years of when the coral died. A very good radiocarbon date only will get within 100 years.

"That's a monumental shift in terms of the precision with which we talk about things," McCoy said. "If Nan Madol had not been made of the kind of stone we could source, if the architects hadn't chosen to use coral, we wouldn't have been able to get this date. So it's a happy coincidence that the evidence at the site came together."

McCoy suggests that future research look at finding the cause for this major turning point on Pohnpei, and what sparked this new hierarchy of rule and monumental building in this society.

***http://bit.ly/2ejzO4w***

## Common infection-fighting white blood cells can be hijacked to support cancer spread

***Neutrophils eject DNA nets to trap invaders but can be commandeered by cancer cells to help cancers spread; the process is experimentally overcome in mice***

Cold Spring Harbor, NY - We think of the human immune system - for good reason - as our indispensable ally, our first line of defense against all kinds of invaders, including ones that can kill us if left unchecked. Yet in certain circumstances, cancer cells can turn the tables and make an enemy of our ally.

A discovery published today in Science Translational Medicine by a research team at Cold Spring Harbor Laboratory (CSHL) underlines the point. It reveals how neutrophils, the most common type of white blood cell and enemy of bacteria and other invaders, can be "hijacked" by cancer cells and used as an aid in metastasis - the process in which cancer cells take up residence in organs beyond the original tumor site. The study also shows a possible way of preventing this.

Associate Professor Mikala Egeblad and her team vividly demonstrate, using live-imaging technology, that a remarkable weapon sometimes deployed by neutrophils against invaders like bacteria and yeast can aid metastasis in a mouse model of triple-negative breast cancer, one of the most aggressive subtypes and known to be prone to spread and relapse in people.

This astonishing weapon appropriated by cancer cells is a lattice of DNA, ejected from an activated neutrophil when the neutrophil detects a threat. Such nets -- appropriately dubbed neutrophil extracellular traps or NETs -- form dense spider web-like structures outside the neutrophil. The DNA that forms the backbone of the web is studded with tiny toxic enzymes that can degrade and digest invaders.

"The remarkable thing we witnessed in live imaging was the ability of cancer cells to induce nearby neutrophils to eject their NETs even when no infection or invader was present," says Egeblad. "Our experiments showed that the NETs, in such situations, can promote metastasis."

Although the precise mechanism is still being explored, Egeblad thinks NETs help cancer cells by literally eating through the proteins that form a tissue's scaffolding - thus opening up small holes and crevices that cancer cells can occupy. This can be a first step in forming a cancer colony at a site distant from the primary tumor.

Is it possible to prevent neutrophils from deploying their NETs? Doing so throughout the body would be an awful idea, since we depend on their killing action every day. But, says Egeblad, "you don't have to prevent it. You can degrade and digest the NETs as they are being formed."

The team was inspired by a treatment used in cystic fibrosis, a disease in which the lungs cannot clear infections. Patients with cystic fibrosis are burdened, among other things, by innumerable deployed NETs, ejected from neutrophils trying to fight the persistent infections often occupying the patients' lungs. Patients can inhale a drug employing the enzyme DNAse, which cuts right through the NETs. As its name implies, DNAse will cut into anything made of DNA, as are the NETs sent out by neutrophils.

"We are incredibly lucky to have the help of Dr. Michael Goldberg and his team at the Dana- Farber Cancer Center," says Egeblad. "We were explaining our discovery at a conference and mentioned that we were lacking a way to get DNAse to work inside tissues and Dr. Goldberg said he might be able to help." His team had developed a way to stabilize enzymes such as DNAse by "gluing" them to extremely tiny drug-delivery devices called nanoparticles that can be injected into humans.

In this case, nanoparticles were not used as containers for a drug, but instead, as minuscule spherical objects coated with the drug, DNAse, so that it cutting effect would begin on contact with the NETs.

Egeblad's team successfully tested the method in mice modeling triple-negative breast cancer, markedly reducing, and for some mice even preventing, metastases to the lung, the most common site of metastasis in this animal model.

Since these experiments used the same formulation of DNAse that is used in an FDA-approved cystic fibrosis treatment, the way is clear to optimization of the system devised by Egeblad and Goldberg's teams. It will be very important, says Egeblad, to determine which breast cancer patients are most likely to benefit from such a treatment - presumably including those who have recently had an infection or who have undergone surgery and thus are at heightened infection risk. The optimal timing of drug delivery is also under study.

Egeblad stresses that the work is also pertinent to current cancer treatments, since a neutrophil-boosting growth factor, called G-CSF, is given to many cancer patients during chemotherapy. That is because chemo is quick to kill white blood cells, a loss which can expose a patient to potentially lethal infections.

Based on what they now know about the impact of neutrophils on metastasis, "it will be important to evaluate if this practice may actually be dangerous in some cases," Egeblad observes. Her team is studying this problem while it works on optimizing DNAse treatment to counter neutrophils when metastatic risk is high.

*The research described in this release was supported by: CSHL Cancer Center Support Grant 5P30CA045508; funds from the Department of Defense (W81XWH-14-1-0078); the Long Island 2-Day Walk to Fight Breast Cancer; the Joni Gladowsky Breast Cancer Foundation. Support was also provided by NIH (5U01CA180944-02); the Hope Foundation, the Cancer Research Institute CLIP grant; an NIHGM MSTP Training Award (T32-GM008444); Aid for Cancer Research; the Boehringer Ingelheim Fonds; Formación de Profesorado Universitario (FPU) fellowship (AP2010-2197); National Cancer Institute (K99 CA181490); and a DFG research fellowship (KU 3264/1-1).*

*"Cancer cells induce metastasis-supporting neutrophil extracellular DNA traps" appears online October 19, 2016 in Science Translational Medicine. The authors are: Juwon Park, Robert W. Wysocki, Zohreh Amoozgar, Laura Maiorino, Miriam R. Fein, Julie Jorns, Anne F. Schott, Yumi Kinugasa-Katayama, Youngseok Lee, Nam H. Won, Elizabeth S. Nakasone, Stephen A. Hearn, Victoria Küttner, Jing Qiu, Ana S. Almeida, Naiara Perurena, Kai Kessenbrock, Michael S. Goldberg and Mikala Egeblad.*

***http://bit.ly/2eym3ej***

## Removal of lobe instead of total thyroid may benefit papillary thyroid cancer patients

### *Lobectomy is less expensive but more clinically effective than total thyroidectomy*

Most Americans with thyroid cancer have an operation to remove the thyroid gland, but those with a smaller, less-threatening form of thyroid cancer may be missing out on a less extensive, less costly, and safer operation that's actually more effective in treating their cancer, according to study results presented at the 2016 Clinical Congress of the American College of Surgeons.

Investigators from Tulane University School of Medicine, New Orleans, and Johns Hopkins School of Medicine, Baltimore, determined that for patients who have had a biopsy suspicious for

papillary thyroid cancer, a total thyroidectomy to remove the thyroid gland, located at the base of the neck, is more expensive and results in a lower quality of life after the operation than a less extensive lobectomy that removes only the cancerous thyroid lobe.

"Our findings are showing that from the economic standpoint, performing lobectomy instead of total thyroidectomy in patients who have had a biopsy suspicious for papillary thyroid carcinoma is associated with a lower cost and better effectiveness," said lead investigator Zaid Al-Qurayshi, MD, MPH, Department of Otolaryngology-Head & Neck Surgery, University of Iowa Hospitals and Clinics in Iowa City, and formerly of Tulane University.

"It is important to note, this finding does not mean that lobectomy is only a cost-effective alternative; we call a strategy 'cost-effective' compared with the alternative if it costs more, or the same, but is associated with better effectiveness." In this study, lobectomy costs less but was also associated with better outcomes, he reported.

"Lobectomy is a shorter operation typically performed on an outpatient basis and with less risk factors than total thyroidectomy," said study coauthor Ralph P. Tufano, MD, MBA, FACS, who is the Charles W. Cummings MD Professor and professor of otolaryngology-head and neck surgery at Johns Hopkins. "American Thyroid Association (ATA) Clinical Guidelines now support lobectomy alone for differentiated thyroid cancers, like papillary thyroid carcinoma, of 4 cm or less in carefully selected situations." In these cases, a lobectomy can both help diagnose cancer type and treat the cancer itself, Dr. Tufano explained.

About 62,000 new cases of thyroid cancer are diagnosed in the United States each year, resulting in about 2,000 deaths, and papillary thyroid cancer accounts for about four of five cases, according to the American Cancer Society.* Papillary thyroid cancers are typically small, tend to grow slowly and carry little risk of spreading beyond the thyroid gland, and have much higher cure and survival rates than medullary thyroid cancer. Although ATA guidelines recommend lobectomy for Stage I and II papillary thyroid cancer, complete thyroidectomy remains the most common procedure for all types of thyroid cancers.

The researchers used a Markov model to determine the effectiveness of a treatment in terms of a measure called Quality-Adjusted Life Year (QALY). The model helps to calculate the cost and clinical effectiveness of lobectomy versus total thyroidectomy when the biopsy is suspicious for papillary thyroid cancer. "QALY is a standardized value from 0 to 1 that represents the burden of certain disease," Dr. Al-Quarayshi said. "It is based on two elements: quality of life and time. A value of 0 represents death, and a value of 1 represents a year of perfect health without any diseases." The study found lobectomy had a QALY 0.25 greater than total thyroidectomy in a model that assumed 20 years of patient follow-up.

The cost analysis found that total thyroidectomy was $2,678 more than lobectomy, even when taking into account that a person with a biopsy suspicious for papillary thyroid cancer has a 12 percent chance of having more advanced Stage III or IV cancer after lobectomy and would need a total thyroidectomy later. "Cost-analysis studies are designed to answer questions at the administrative and policy-making levels," Dr. Al-Qurayshi said. "However, they do not assess which strategy is clinically better for patients at the individual level."

These findings may be more meaningful for patients who have benign or papillary thyroid carcinoma Stages I or II confirmed by pathology studies after surgery, Dr. Al-Qurayshi explained. "This population represents the overwhelming majority of patients with suspicious-for papillary thyroid carcinoma on biopsy," he said. "Avoiding total thyroidectomy in those patients not only will have better clinical outcomes as shown previously, but will also have economic advantage at the population level as shown in the current analysis."

The next step for the investigators is to re-evaluate their findings. "If these outcomes are consistently proven to hold true, it would be worthwhile to assess potential cost savings that are attainable given

the number of patients who have suspicious papillary thyroid carcinoma annually in the United States," Dr. Al-Qurayshi said. "On the other hand, if the American Thyroid Association Clinical Guidelines become widely adopted, further study is warranted to re-evaluate the clinical outcomes on long-term follow-up in patients who underwent lobectomy instead of total thyroidectomy."

*Study co-authors are Salem I. Noureldine, MD, of Johns Hopkins, and Emad Kandil, MD, FACS, of Tulane.*

*"FACS" designates that a surgeon is a Fellow of the American College of Surgeons.*

** Thyroid Cancer Overview. American Cancer Society. Revised February 12, 2016. Available at: http://www.cancer.org/acs/groups/cid/documents/webcontent/acspc-030369-pdf.pdf. Accessed September 21, 2016.*

***http://bit.ly/2dxG9rA***

## Monkeys are seen making stone flakes so humans are 'not unique' after all

***Researchers have observed wild-bearded capuchin monkeys in Brazil deliberately break stones, unintentionally creating flakes that share many of the characteristics of those produced by early Stone Age hominins***

Researchers have observed wild-bearded capuchin monkeys in Brazil deliberately break stones, unintentionally creating flakes that share many of the characteristics of those produced by early Stone Age hominins. The difference is that the capuchins' flakes are not intentional tools for cutting and scraping, but seem to be the by-product of hammering or 'percussive behaviour' that the monkeys engage in to extract minerals or lichen from the stones.

In a paper, published in Nature, the research team says this finding is significant because archaeologists had always understood that the production of multiple stone flakes with characteristics such as conchoidal fractures and sharp cutting edges was a behaviour unique to hominins. The paper suggests that scholars may have to refine their criteria for identifying intentionally produced early stone flakes made by hominins, given capuchins have been observed unintentionally making similar tools.

The research is authored by researchers from the University of Oxford, University College London and University of São Paulo in Brazil. The team observed individual monkeys in Serra da Capivara National Park unintentionally creating fractured flakes and cores. While hominins made stone flake tools for cutting and butchery tasks, the researchers admit that it is unclear why monkeys perform this behaviour. They suggest that the capuchins may be trying to extract powdered silicon (known to be an essential trace nutrient) or to remove lichen for some as yet unknown medicinal purpose. At no point did the monkeys try to cut or scrape using the flakes, says the study.

***This image made available by the journal Nature shows examples of flaked stones made by wild capuchin monkeys in Brazil. The scale bar at the center is 5 cm (2 inches). In a report released on Oct. 18, 2016, researchers say wild capuchin monkeys in Brazil deliberately break stones, unintentionally producing flakes similar to the ancient sharp-edged tools made by human ancestors.* (Tomos Proffitt, Angeliki Theodoropoulou via AP)**

Lead author Dr Tomos Proffitt, from the School of Archaeology at the University of Oxford, comments: 'Within the last decade, studies have shown that the use and intentional production of sharp-edged flakes are not necessarily linked to early humans (the genus Homo) who are our direct relatives, but instead were used and produced by a wider range of hominins. However, this study goes one step further in showing that modern primates can produce archaeologically identifiable flakes and cores with features that we thought were unique to hominins.

'This does not mean that the earliest archaeological material in East Africa was not made by hominins. It does, however, raise interesting questions about the possible ways this stone tool technology developed before the earliest examples in the archaeological record

appeared. It also tells us what this stone tool technology might look like. There are important questions too about the uniqueness of early hominin behaviour. These findings challenge previous ideas about the minimum level of cognitive and morphological complexity required to produce numerous conchoidal flakes.'

The monkeys were observed engaging in 'stone on stone percussion', whereby they individually selected rounded quartzite cobbles and then using one or two hands struck the 'hammer-stone' forcefully and repeatedly on quartzite cobbles embedded in a cliff face. This action crushed the surface and dislodged cobbled stones, and the hand-held 'hammer stones' became unintentionally fractured, leaving an identifiable primate archaeological record. As well as using the active hammer-stone to crush 'passive hammers' (stones embedded in the outcrop), the capuchins were also observed re-using broken hammer-stones as 'fresh' hammers.

The research team examined 111 fragmented stones collected from the ground immediately after the capuchins had dropped them, as well as from the surface and excavated areas in the site. They gathered complete and broken hammer-stones, complete and fragmented flakes and passive hammers. Around half of the fractured flakes exhibited conchoidal fracture, which is typically associated with the hominin production of flakes.

Bearded capuchins and some Japanese macaques are known to pound stones directly against each other, but the paper remarks that the capuchins in Serra da Capivara National Park are the only wild primates to be observed doing this for the purpose of damaging the stones.

Co-author and leader of the Primate Archaeology (Primarch) project Michael Haslam, from the University of Oxford, says: 'Our understanding of the new technologies adopted by our early ancestors helps shape our view of human evolution. The emergence of sharp-edged stone tools that were fashioned and hammered to create a cutting tool was a big part of that story. The fact that we have discovered monkeys can produce the same result does throw a bit of a spanner in the works in our thinking on evolutionary behaviour and how we attribute such artefacts. While humans are not unique in making this technology, the manner in which they used them is still very different to what the monkeys seem capable of.'

*The paper, 'Wild monkeys flake stone tools', by Tomos Proffitt, Lydia V Luncz, Tiago Falótico, Eduardo B Ottoni, Ignacio de la Torre and Michael Haslam will be published in Nature. It is embargoed until 1800 London time / 1300 US Eastern Time on 19 October 2016. Once live, the paper will appear at: http://dx.doi.org/10.1038/nature20112*

***http://bit.ly/2eFYIaq***

## Scientists find new genetic roots of schizophrenia

### *UCLA study used 3-D chromosome-mapping technology to advance understanding of disorder's cause*

UCLA scientists have made a major advance in understanding the biology of schizophrenia. Using a recently developed technology for analyzing DNA, the scientists found dozens of genes and two major biological pathways that are likely involved in the development of the disorder but had not been uncovered in previous genetic studies of schizophrenia. The work provides important new information about how schizophrenia originates and points the way to more detailed studies -- and possibly better treatments in the future.

Schizophrenia is a chronic, disabling mental illness whose symptoms can include hallucinations, delusions and cognitive problems. The illness afflicts about 1 percent of the human population -- more than 50 million people worldwide. Because the causes of schizophrenia are poorly understood, current medications can help diminish the symptoms but do not cure the disorder.

The study, which is published online in the journal Nature, is likely to have an impact beyond schizophrenia research because it demonstrates a general and potentially powerful new strategy for illuminating the mechanisms of human disease.

"This work provides a road map for understanding how common genetic variation associated with a complex disease affects specific genes and pathways," said principal investigator Dr. Daniel

Geschwind, the Gordon and Virginia MacDonald Distinguished Chair in Human Genetics and professor of neurology and psychiatry at UCLA's David Geffen School of Medicine at UCLA.

Schizophrenia has long been known to be highly genetic; it often runs in families. A large genome-wide association study of people with schizophrenia, published in 2014, linked the disorder to small DNA variations at more than 100 distinct locations on the human genome. However, most of those locations lie outside of actual genes, so their roles in schizophrenia have been unclear. Genome-wide study analyses of other major diseases have come up with similarly puzzling results.

In some cases, the non-gene locations identified in these studies have turned out to be what are known as "regulatory regions," which serve to enhance or repress the activity of genes lying near them on the genome. But many of these disease-linked locations have no obvious gene target nearby on the genome.

One possibility is that these mysterious disease-linked locations are also regulatory regions that target genes lying relatively far away on the genome. They could do this if they are brought physically close to those "distant" genes by the complex twisting and looping that DNA undergoes when packaged into a chromosome, just as two opposite ends of a rope can end up close together when the rope is coiled. To investigate that possibility, Geschwind and his team used a relatively new, high-resolution version of a technology called "chromosome conformation capture," which chemically marks and then maps the locations where loops of chromosomal DNA come into contact.

Because each cell type in the body can have subtly different 3-D chromosome structures, the researchers applied the technique to immature human brain cells from the cortex -- the large region across the top of the brain that handles higher cognitive tasks. Schizophrenia is believed to be a disorder of abnormal cortical development.

The mapping revealed that most of the more than 100 schizophrenia-linked sites from the 2014 study contact known genes during brain development. Many of these are genes that already have been linked to schizophrenia in previous studies. Others had been suspected of involvement, for example because their level of activity in schizophrenics is known to be abnormal in the cortex.

The genes newly linked to schizophrenia in the study include several for brain cell receptors that are activated by the neurotransmitter acetylcholine, implying that variations in the functions of these receptors can help bring about schizophrenia.

"There's a lot of clinical and pharmacologic data suggesting that changes in acetylcholine signaling in the brain can worsen schizophrenia symptoms, but until now there's been no genetic evidence that it can help cause the disorder," Geschwind said.

The analysis also pointed for the first time to several genes that are involved in the early-life burst of brain cell production that gives rise to the cerebral cortex of humans.

In all, the researchers identified several hundred genes that may be abnormally regulated in schizophrenia but had not been linked to the disorder before. In further experiments and analyses of two dozen of those genes, they found additional evidence of abnormal regulation in schizophrenia.

As further studies clarify the roles of these genes in schizophrenia, scientists will get a more complete picture of how the disorder develops and persists, and should then be able to develop more effective treatments.

"In the near term we're using the findings from this study to help us understand schizophrenia better, but we're also planning to apply this same strategy to identify key genes in the development of autism and other neurodevelopmental disorders," Geschwind said.

In principle, the 3-D chromosome mapping technology can be used to make sense of gene association data for any disease involving genetic risk. This same approach also can be used to discover relationships between genes and their regulatory regions in ordinary biological processes.

*The first author of the study was postdoctoral fellow Hyejung Won. Other co-authors were Luis de la Torre-Ubieta, Jason Stein, Neelroop Parikshak, Jerry Huang, Carli Opland, Michael Gandal, Farhad Hormozdiari, Daning Lu, Changhoon Lee, Eleazar Eskin and Jason Ernst, all of UCLA at the time of the study; and Irina Voineagu and Gavin Sutton, of the University of New South Wales.*

*The research was supported by the National Institutes of Health, the National Science Foundation, Glenn/AFAR Postdoctoral Fellowship Program and the National Research Foundation of Korea.*

***http://bit.ly/2etZNpM***

## Scientists link single gene to some cases of autism spectrum disorder

### *Findings could provide clues about other genes involved in autism*

Scientists have linked mutations in a single gene to autism in people who have a rare tumor syndrome typically diagnosed in childhood.

The findings, in patients with neurofibromatosis type 1 (NF1), may lead to a better understanding of the genetic roots of autism in the wider population. The findings are published Oct. 19 in the journal JAMA Psychiatry.

Studying 531 patients at six clinical centers in the United States, Belgium, the United Kingdom and Australia, the researchers found that mutations in the NF1 gene that cause the disease also contributed to autistic behaviors in almost half of the patients.

"NF1 is caused by mutations in a single gene -- NF1," said first author Stephanie M. Morris, MD, an instructor in neurology. "Our research indicates that this single gene also is associated with autism spectrum disorders in these same patients. That may make it possible to look downstream from the gene to find common pathways that contribute to autism in the wider population."

NF1, the disorder caused by NF1 mutations, usually appears during childhood. Symptoms can vary in severity, but they include café au lait spots, which are flat, brown spots on the skin. Other symptoms include tiny nodules on the iris of the eye, nerve tumors, bone deformities such as a curved spine or a bowed lower leg, and optic gliomas, tumors of the optic nerve. Kids with NF1 also can have learning disabilities.

"In the 25-plus years that I've taken care of kids with NF1, we've only recently started to recognize that these children also often have symptoms of autism," said senior investigator David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor of Neurology and director of the Washington University NF Center. "In the past, we didn't really understand the association between NF1 and autism, but now we have new insights into the problem, which will allow us to design better treatments for children with NF1 and autism."

The findings also could help scientists who study the genetics of autism understand how mutations in a single gene can contribute to symptoms of autism, such as problems with social and language skills and repetitive behaviors.

About 100,000 people in the United States have NF1. It is equally common in both sexes and in all ethnic groups. Autism, meanwhile, affects 1 percent to 2 percent of all children in the United States and is four to five times more common in boys than in girls.

"What's unique about our findings is that it's likely mutations in the NF1 gene are driving most of the symptoms of autism in children with NF1," said the study's other senior investigator, John N. Constantino, the Blanche F. Ittleson Professor of Psychiatry and Pediatrics and director of the William Greenleaf Eliot Division of Child & Adolescent Psychiatry. "Here, we have a single-gene disorder that affects a fairly large number of people and is causing autism in a significant number of those who are affected. This work could provide us with an opportunity to study a single gene and figure out what it is doing to cause autistic syndromes."

Constantino said most autism spectrum disorders are influenced by multiple genes but that isolating this one gene can aid efforts to learn how other, unrelated genes may interact along that same pathway to contribute to autism in people who don't have NF1. Learning how those various genes come together to cause symptoms eventually could lead to better treatments. But already the findings are benefiting children and families treated at the Washington University NF Center.

"We've been able to screen children at our center, identify autism spectrum disorder, attention-deficit disorder and problems with executive cognitive function," Morris said. "And when we identify these deficits in kids, we can tell their parents, inform their schools and enable these children to get the resources and support they need -- specifically academic and social support - to improve their quality of life."

*Morris, SM, Acosta MR, Garg S, Green J, Huson S, Legius E, North KN, Payne JM, Plasschaert E, Frazier TW, Weiss LA, Zhang Y, Gutmann DH, Constantino JN, and the International NF1-ASD Consortium Team (INTACT). NF1 gene mutations engender the full spectrum of autism. JAMA Psychiatry. Oct. 19, 2016.*

*This work was supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health (NIH), grant number U54 HD087011. Additional funds came from Schnuck Markets, Inc., the Neurological Sciences Academic Development Award at Washington University School of Medicine, the NIH New Innovator Award 1DP2OD007449, and the Opening the Future grant of KU Leuven.*

***http://bit.ly/2eVHWIf***

## Science shows cheese can make wine taste better

***A new scientific study shows that eating cheese may actually increase how much someone likes the wine they are drinking.***

CHICAGO - The study, published in the October issue of the Journal of Food Science, used a new sensory evaluation method and found consuming cheese while drinking wine impacted the description and preference of different wines.

The study was conducted at the Center for Taste and Feeding Behavior in France with frequent wine and cheese consumers from the city of Dijon. The subjects evaluated four wines (Pacherenc, Sancerre, Bourgogne and Madiran) using a new sensory evaluation method developed by the researchers to show how perception and liking of wine change after cheese intake over several sips, which is closer to what happens in typical consumption. The subjects were given a list of sensations which they used to indicate what caught their attention (called the dominant sensation) as they consumed the wine over three consecutive sips and after they swallowed.

Once the wines were initially evaluated, the task was repeated, but with a piece of cheese eaten in-between sips. Four different cheeses (Epoisses, Comté, Roquefort, Crottin de Chavignol) were sampled over different sessions with each wine.

Results showed that cheese consumption had an impact on the description for all wines, and impacted preference for most. None of the four cheeses included in the study had a negative impact on wine preference. Liking of each wine was increased or remained the same after cheese intake. In both red wines (Bourgogne and Madiran), the four cheeses decreased the duration of dominance of astringency and increased that of red fruits aroma. In the sweet white (Pacherenc), the duration of dominance of sweetness was not changed by cheese intake, but in the white dry wine, cheeses had an impact on the main aroma.

"Thanks to our research we learned that the duration of the perception of astringency of a certain wine could be reduced after having cheese and that the four evaluated cheeses had the same effect. In short, when having a plate of assorted cheeses, the wine will probably taste better no matter which one they choose," lead author Mara V. Galmarini explained.

According to the authors, the sensory method developed in their work can help build better understanding of how the perception of one product is changed when consumed in combination with another. This information can help food brands communicate their products' characteristics, thus improving consumers' experiences.

*Read the Journal of Food Science abstract here.*

***http://bit.ly/2etH1wV***

## Curious tilt of the sun traced to undiscovered planet

***Planet Nine--the undiscovered planet at the edge of the Solar System that was predicted by the work of Caltech's Konstantin Batygin and Mike Brown in January 2016--appears to be responsible for the unusual tilt of the sun, according to a new study.***

The large and distant planet may be adding a wobble to the solar system, giving the appearance that the sun is tilted slightly.

"Because Planet Nine is so massive and has an orbit tilted compared to the other planets, the solar system has no choice but to slowly twist out of alignment," says Elizabeth Bailey, a graduate student at Caltech and lead author of a study announcing the discovery.

All of the planets orbit in a flat plane with respect to the sun, roughly within a couple degrees of each other. That plane, however, rotates at a six-degree tilt with respect to the sun--giving the appearance that the sun itself is cocked off at an angle. Until now, no one had found a compelling explanation to produce such an effect. "It's such a deep-rooted mystery and so difficult to explain that people just don't talk about it," says Brown, the Richard and Barbara Rosenberg Professor of Planetary Astronomy.

Brown and Batygin's discovery of evidence that the sun is orbited by an as-yet-unseen planet--that is about 10 times the size of Earth with an orbit that is about 20 times farther from the sun on average than Neptune's--changes the physics. Planet Nine, based on their calculations, appears to orbit at about 30 degrees off from the other planets' orbital plane--in the process, influencing the orbit of a large population of objects in the Kuiper Belt, which is how Brown and Batygin came to suspect a planet existed there in the first place.

"It continues to amaze us; every time we look carefully we continue to find that Planet Nine explains something about the solar system that had long been a mystery," says Batygin, an assistant professor of planetary science. Their findings have been accepted for publication in an upcoming issue of the Astrophysical Journal, and will be presented on October 18 at the American Astronomical Society's Division for Planetary Sciences annual meeting, held in Pasadena.

The tilt of the solar system's orbital plane has long befuddled astronomers because of the way the planets formed: as a spinning cloud slowly collapsing first into a disk and then into objects orbiting a central star.

Planet Nine's angular momentum is having an outsized impact on the solar system based on its location and size. A planet's angular momentum equals the mass of an object multiplied by its distance from the sun, and corresponds with the force that the planet exerts on the overall system's spin. Because the other planets in the solar system all exist along a flat plane, their angular momentum works to keep the whole disk spinning smoothly.

Planet Nine's unusual orbit, however, adds a multi-billion-year wobble to that system. Mathematically, given the hypothesized size and distance of Planet Nine, a six-degree tilt fits perfectly, Brown says.

The next question, then, is how did Planet Nine achieve its unusual orbit? Though that remains to be determined, Batygin suggests that the planet may have been ejected from the neighborhood of the gas giants by Jupiter, or perhaps may have been influenced by the gravitational pull of other stellar bodies in the solar system's extreme past. For now, Brown and Batygin continue to work with colleagues throughout the world to search the night sky for signs of Planet Nine along the path they predicted in January. That search, Brown says, may take three years or more.

***http://bit.ly/2etQIeX***

## Rich People Really Do Ignore You When They Walk By

***Wealthy people appear to spend less time looking at other human beings, compared with how much time people in lower social classes look at others, according to a new study that used Google Glass headsets to track people's gazes.***

**By Rachael Rettner, Senior Writer**

The findings suggest that your social class influences how much other people grab your attention, the researchers said.

More research is needed to know why the wealthy may look less often at other people, the researchers noted. But one possible explanation may be that, for people in higher social classes, other human beings hold less "motivational relevance" — a psychology term that means how worthy of one's attention something or someone is, based on how much reward or threat might be linked with that object or person, the researchers said.

Because the time people spend looking at something may be related to how much motivational relevance the object or person holds, the "findings make a compelling case that social classes differ in their judgments of other people's significance," the researchers wrote in their paper, published Oct. 3 in the journal Psychological Science.

In the study, the researchers asked 61 people to wear a Google Glass headset while walking around in New York City. Google Glass has a video camera near the right eye, and the device records video from the users' perspective. Participants were told to focus on whatever captured their attention.

In addition, the researchers asked the participants several questions, to gauge their social class — for example, whether they viewed themselves as belonging to the poor, the working class, the middle class, the upper-middle class or the upper class.

The researchers found that a person's social class wasn't related to the number of times he or she looked at other people, but it was related to how much total time the person spent looking at people. People who viewed themselves as belonging to a higher social class spent less time looking at others, compared with those who viewed themselves as belonging to a lower social class.

Although Google Glass can show which way a person's head is turned, it doesn't show exactly where the person's eyes may be looking. So the researchers conducted a follow-up study in a laboratory using eye-tracking technology. The study recorded the eye movements of 76 participants as they looked at images of New York City street scenes.

Again, the researchers found that people in higher social classes spent less time looking at people in the images, compared with people in lower social classes.

Finally, the researchers wanted to determine whether the people were conscious of this behavior. So they had nearly 400 people look at images on a computer screen, with each image containing a single face along with five objects. The participants were asked to determine whether two consecutive images were identical, or whether there was a difference between them.

The results showed that people in higher social classes took longer to notice when a face changed, compared with people in lower social classes. This finding suggests that this effect is spontaneous, and that the people were not aware that they were choosing this behavior, the researchers said.

"This finding suggests that social class, like other forms of culture … can shape human cognitive functioning at a deep level," they said.

The reasons for the link are not clear, but one possibility is that people from privileged backgrounds are less dependent on others socially, so they are less likely to view other people as motivationally relevant, compared with people from less-privileged backgrounds, the researchers said.

"The more we know about the effect of social class differences, the better we can address widespread societal issues — this research is just one piece of the puzzle," study co-author Pia Dietze, a psychological scientist at New York University, said in a statement. The researchers plan to conduct more studies in other countries and using virtual-reality technology to better understand the link between social class and visual attention, they said.

***http://nyti.ms/2dyGqDj***

## Reported Cases of Sexually Transmitted Diseases Are on Rise

***There were more cases of sexually transmitted diseases reported in the United States last year than ever before, according to new federal data.***

**By Abby Goodnough Oct. 19, 2016**

WASHINGTON - Rates of chlamydia, gonorrhea and syphilis — three of the most common S.T.D.s — grew for the second consecutive year, with sharper increases in the West than other regions. And while all three diseases are treatable with antibiotics, most cases continue to go undiagnosed, potentially causing infertility and other problems.

The syphilis rate rose most sharply, by 19 percent. Public health officials are particularly worried about an increase in the number of babies whose mothers are passing it to them in utero, which can cause stillbirths and infant deaths. Progress in the fight against S.T.D.s has "unraveled," according to a report from the Centers for Disease Control and Prevention.

**Who is most affected by the rise in S.T.D.s?**

Young people, members of racial minorities and men who have sex with other men are at most risk of getting an S.T.D.

Chlamydia rates are highest among 15-to 24-year-olds, who accounted for nearly two-thirds of diagnoses last year, and among blacks. While chlamydia disproportionately affects women, the rate of reported cases among men grew more sharply last year. Over all, the rate of reported cases grew by 5.9 percent.

Chlamydia is the most common of the S.T.D.s that have to be reported to the C.D.C., with more than 1.5 million cases last year.

Most of the new gonorrhea and syphilis cases were among gay men, although rates are climbing for women, too. Public health officials are worried that gonorrhea is becoming resistant to the some of the last antibiotics capable of treating it. Although gonorrhea rates are highest among blacks, they have jumped over the last few years among whites and other ethnic groups.

Syphilis rates increased among men and women in every region of the country. Most cases were among men who have sex with men. But the rate of syphilis diagnosis among women grew by 27 percent, and the rate of congenital syphilis, passed from pregnant women to their babies, by 6 percent.

**Why is the number of cases growing?**

Public health officials point to a number of possible reasons, from budget cuts to what might be called the Tinder effect. Since the beginning of the economic downturn, more than half of state and local programs that provide testing and treatment for S.T.D.s have had budget cuts, according to the C.D.C. "Those are among the primary places where we actually diagnose and treat S.T.D.s as well as H.I.V.," said Dr. Jonathan Mermin, the director of the agency's National Center for H.I.V./AIDS, Viral Hepatitis, S.T.D. and TB Prevention.

Dr. Mermin also said that the rise of dating apps like Tinder could possibly be contributing to rising S.T.D. rates, and that some local health departments believed there was a connection. "But it's not completely clear, the cause and effect, at this point," he added.

**Where is the problem worst?**

Over the past few years, the West has had bigger increases in S.T.D. rates than any other region of the country. The number of gonorrhea cases reported in Montana almost doubled last year, for example, to 844 from 434. In California, the number of reported syphilis cases grew by 28 percent, to 4,908 from 3,835.

But the South still has the highest overall rates of chlamydia and gonorrhea. Louisiana has the highest rates of gonorrhea (221 cases per 100,000 residents, compared with 124 nationally) and syphilis (15 cases per 100,000 residents, twice the national average). California and Louisiana had the most babies born with syphilis last year, about 40 percent of the total.

***http://nyti.ms/2dLTUBG***

## Children 14 or Under Need Fewer HPV Vaccine Doses

***11 to 14 year-olds need only two doses of HPV vaccine to protect against cervical cancer and other cancers caused by the human papillomavirus***

**By Denise Grady Oct. 19, 2016**

Children 11 to 14 years old need only two doses of the HPV vaccine, not the previously recommended three doses, to protect against cervical cancer and other cancers caused by the human papillomavirus, the Centers for Disease Control and Prevention said on Wednesday.

But teenagers and young adults who start the vaccinations later, at ages 15 through 26, should stick with the three-dose regimen, the disease centers said.

The new advice is based on a review of studies showing that two doses in the younger group "produced an immune response similar or higher than the response in young adults (aged 16 to 26 years) who received three doses," the C.D.C. said in a statement. The two doses should be given at least six months apart, the agency said.

The statement also noted that the two-dose schedule will make the process simpler and easier for families to complete and could increase the number of young teenagers who receive the vaccine. Despite the vaccine's proven effectiveness, immunization rates have remained low.

HPV is a group of more than 150 related viruses, according to the disease centers. They are spread by intimate, skin-to-skin contact, and by vaginal, oral and anal intercourse. HPV is so common that nearly all sexually active people become infected at some point. In most people, the immune system destroys the virus. But in some, the infection lingers. Some viral strains cause genital warts, and others can cause cancers of the cervix, vagina, vulva, penis and back of the throat.

Every year, about 17,600 women and 9,300 men in the United States are affected by cancers caused by HPV, and about 180,000 women and 160,000 men develop genital warts caused by the viruses.

Vaccination is recommended for preteenagers and early teenagers, ideally before they become sexually active, because the vaccine works best if given before a person is exposed to HPV But the C.D.C. still recommends vaccination for young people who have already had sex, saying that it should provide "at least some protection."

***http://bit.ly/2eGBK1A***

## Our ancestors chose reeds over grain when quitting nomadic life

### *The grass is always greener… than the grain?*

**By Bob Holmes**

When ancient hunter-gatherers first began to give up their nomadic life, they weren't just chasing the grain. Rather than looking for big payoffs from harvesting cereal grains, it seems at least some groups may have been playing it safe. If so, the transition to sedentary life — the first big step toward agriculture — may have been more complex, and more varied, than archaeologists thought.

The standard view has been that around 20,000 years ago, our ancestors began to stay in one place for long periods so that they could exploit the wild grains growing there, which provided a dense source of energy. After many generations of selection, these grains became the modern domesticated cereals on which most of our civilisations depend.

Archaeologists have had few opportunities to test this view because plant remains from the early stages of this transition are scarce. Recently, however, researchers have begun to use phytoliths — microscopic silica crystals that form in plant tissues and persist for millennia — to investigate which plants would have been around at early archaeological sites.

**Cereal monogamy**

Monica Ramsey, an environmental archaeologist at the University of Toronto, Canada, and her colleagues studied phytoliths at the 22,000-year-old Kharaneh IV site in Jordan, one of the first places to show evidence of long-term residence.

To their surprise, they found few phytoliths from cereal grains. Instead, the vast majority of phytoliths came from wetland plants such as rushes and sedges. These plants yield many fewer calories than grains do, but they are available year-round, and in dry years as well as wet ones.

Most likely, Ramsey suggests, the inhabitants of Kharaneh began spending longer periods near the wetlands to take advantage of this dependable resource. That dependability, in turn, may have let them experiment with harvesting grains in the surrounding steppes during good years.

In other words, the inhabitants of Kharaneh were taking advantage of what the local environment gave them. "At Kharaneh, they're sitting on the edge of this nice big marsh wetland," says Ramsey. "In other

areas, they might not have had those resources available, so their lifestyle might have been very different."

The result would have been a complex pattern of reasons for settling into sedentary life, in contrast to the simple, grain-centred explanation usually given.

Other archaeologists say Ramsey's ideas make sense. "It is clear that these are not wild cereal-focused foragers, which some have assumed must have characterised the pre-agricultural stages," says Dorian Fuller, an archaeologist at University College London.

However, he notes that cereal-focused groups may have also existed in nearby environments.

*Journal reference: PLoS One, DOI: 10.1371/ journal.pone.0164081*

***http://bit.ly/2dyMxPv***

## New study questions the safety of caspase inhibitors for the treatment of liver disease

***Although effective in preventing apoptosis, caspase inhibitors may lead to necrotic cell death, according to a report in The American Journal of Pathology***

Philadelphia, PA - Many acute and chronic liver diseases, including alcoholic hepatitis, result from apoptotic (programmed) cell death mediated by the enzyme caspase. Caspase inhibitors have therapeutic potential to treat and prevent apoptosis-mediated liver injury, and some are currently in clinical trials. However, a new study published in The American Journal of Pathology raises serious safety concerns regarding the clinical use of caspase inhibitors by demonstrating the occurrence of delayed-onset necrotic, non-caspase-dependent liver cell injury.

"Our data suggest that one should be cautious in treating apoptotic cell death just with caspase inhibitors as, despite their efficacy in preventing apoptosis, these inhibitors may trigger necrotic cell death," noted Wen-Xing Ding, PhD, Associate Professor, Department of Pharmacology, Toxicology and Therapeutics of The University of Kansas Medical Center (Kansas City). "The failure to protect against endotoxin-induced liver injury raises concerns on the clinical use of caspase inhibitors."

Liver health and injury depend upon a complex interaction between physiological processes affecting cell survival and death. "A liver cell can die in many different ways, but caspase-dependent apoptosis and caspase-independent necrosis are the predominant cell death pathways that contribute to liver injury," explained Dr. Ding.

Researchers investigated endotoxin and tumor necrosis factor (TNF)-α-induced cell death in cultured hepatocytes and in mouse livers, similar to certain acute human hepatitis and liver failure. Apoptotic cell death is associated with many human liver diseases such as alcoholic hepatitis and nonalcoholic steatohepatitis (NASH). In this study, the researchers found that blocking apoptosis can trigger alternative necrotic cell death.

Apoptotic cell death was caused by TNF-α/actinomycin D (ActD) after 24 hours in primary cultured mouse hepatocytes. Adding the caspase inhibitor ZVAD blocked early apoptotic cell death but revealed the presence of necrotic cell death at 48 hours. Researchers also found that the TNF-ZVAD-induced necrosis was not due to autophagy. More importantly, researchers also confirmed these cell culture findings in an endotoxin-induced liver injury mouse model. Although blocking caspase protected against endotoxin-induced liver injury at an early time point (six hours), this protection was lost after 24 hours due to the switch of liver cell apoptosis to necrosis.

According to Dr. Ding, "We still don't know the mechanism underlying caspase inhibitor-induced necrosis of the liver. Nevertheless, our findings raised concerns about the safety of the current ongoing clinical trials using the caspase inhibitors."

This study provides important insights on the inter-relationship of different types of cell death: apoptosis, necrosis, and autophagy. Apoptosis refers to the death of apoptotic cells that still maintain relative cell membrane integrity without inflammation under physiological and pathological conditions. Apoptosis often occurs

during an organism's growth or development. Necrosis refers to the cell death of necrotic cells characterized by rupture of plasma membranes and release of intracellular contents, which are associated with inflammation. Necrosis often occurs under harsh conditions, severe tissues injury, or organ blood supply failure. Autophagy is a conserved lysosomal degradation pathway that regulates homeostasis of proteins and organelles in hepatocytes and plays a critical role in normal liver physiology and liver diseases. However, under certain conditions, excessive activated autophagy may also cause cell death.

***http://bit.ly/2ezLi00***

## Study finds earliest evidence in fossil record for right-handedness

***Teeth striations of Homo habilis fossil date back 1.8 million years***

LAWRENCE -- Perhaps the bias against left-handers dates back much further than we thought.

By examining striations on teeth of a Homo habilis fossil, a new discovery led by a University of Kansas researcher has found the earliest evidence for right-handedness in the fossil record dating back 1.8 million years.

"We think that tells us something further about lateralization of the brain," said David Frayer, a KU professor emeritus of anthropology and the lead author of the study. "We already know that Homo habilis had brain lateralization and was more like us than like apes. This extends it to handedness, which is key."

The findings were published online this week in the prestigious Journal of Human Evolution. The researchers made the discovery after analyzing small cut marks, or labial striations, which are the lip side of the anterior teeth in an intact upper jaw fossil, known as OH-65, found in a stream channel of the Olduvai Gorge in Tanzania.

Frayer said among the network of deep striations found only on the lip face of the upper front teeth most cut marks veered from left down to the right. Analysis of the marks makes it likely they came from when OH-65 used a tool with its right hand to cut food it was holding in its mouth while pulling with the left hand. The scratches can be seen with the naked eye, but a microscope was used to determine their alignment and to quantify their angulation.

"Experimental work has shown these scratches were most likely produced when a stone tool was used to process material gripped between the anterior teeth and the tool occasionally struck the labial face leaving a permanent mark on the tooth's surface," Frayer said.

Based on the direction of the marks, it's evident the Homo habilis was right-handed. It's a sample of one, but because this is the first potential evidence of a dominant handed pre-Neanderthal, Frayer said, the study could lead to a search for the marks in other early Homo fossils.

"Handedness and language are controlled by different genetic systems, but there is a weak relationship between the two because both functions originate on the left side of the brain," he said. "One specimen does not make an incontrovertible case, but as more research is done and more discoveries are made, we predict that right-handedness, cortical reorganization and language capacity will be shown to be important components in the origin of our genus."

Multiple lines of research point to the likelihood that brain reorganization, the use of tools and use of a dominant hand occurred early in the human lineage. Today, researchers estimate that 90 percent of humans are right-handed, and this differs from apes which are closer to a 50-50 ratio. Until now, no one looked for directionality of striations in the earliest specimens representing our evolutionary lineage.

"We think we have the evidence for brain lateralization, handedness and possibly language, so maybe it all fits together in one picture," Frayer said.

*Co-authors of the study are Ronald J. Clarke, Evolutionary Studies Institute at the University of Witwatersrand, Johannesburg, South Africa; Ivana Fiore and Luca Bondioli, Polo Museale del Lazio, Museo Nazionale Preistorico Etnografico "L. Pigorini, Rome, Italy; Robert J. Blumenschine, Paleontological Scientific Trust, Johannesburg, South Africa, Alejandro Pérez-Pérez, Laura M. Martinez and Ferran Estebaranz, Department on Animal Biology, University of Barcelona, Barcelona, Spain and Ralph Holloway, Department of Anthropology, Columbia University, New York.*

http://bit.ly/2exwos6

# 'Planet Nine' Can't Hide Much Longer, Scientists Say

***Planet Nine's days of lurking unseen in the dark depths of the outer solar system may be numbered.***

**By Mike Wall, Space.com Senior Writer | October 20, 2016 02:33pm**

The hypothetical giant planet, which is thought to be about 10 times more massive than Earth, will be discovered within 16 months or so, astronomer Mike Brown predicted.

"I'm pretty sure, I think, that by the end of next winter — not this winter, next winter — I think that there'll be enough people looking for it that … somebody's actually going to track this down," Brown said during a news conference Wednesday (Oct. 19) at a joint meeting of the American Astronomical Society's Division for Planetary Sciences (DPS) and the European Planetary Science Congress (EPSC) in Pasadena, California. Brown said that eight to 10 groups are currently looking for the planet.

At the "next one of these [DPS-EPSC meetings], we'll be talking about finding Planet Nine instead of just looking for it," added Brown, who's based at the California Institute of Technology (Caltech) in Pasadena.

That would be a pretty quick path from hypothetical planet to confirmed world. The existence of Planet Nine was seriously proposed for the first time just in 2014, by astronomers Scott Sheppard and Chadwick Trujillo, of the Carnegie Institution for Science in Washington, D.C., and the Gemini Observatory in Hawaii, respectively.

Sheppard and Trujillo noted that the dwarf planet Sedna, the newfound object 2012 VP113 and several other bodies far beyond Pluto share certain odd orbital characteristics, a coincidence that would make sense if their paths through space had been shaped by an unseen, giant "perturber" in the region.

The researchers suggested that this putative planet is perhaps two to 15 times more massive than Earth and lies hundreds of astronomical units (AU) from the sun. (One AU is the Earth-sun distance, about 93 million miles, or 150 million kilometers.)

This interpretation was bolstered in January of this year by Brown and fellow Caltech astronomer Konstantin Batygin, who found evidence of a perturber's influence in the orbits of a handful of additional distant objects. This "Planet Nine," as Batygin and Brown dubbed the putative world, likely contains about 10 Earth masses and orbits on a highly elliptical path whose aphelion (farthest distance from the sun) is about 1,000 AU, the researchers said. (For perspective, Pluto gets just 49.3 AU from the sun at aphelion.)

The evidence for Planet Nine's existence has continued to grow over the past nine months, as several different research teams have determined that the orbits of other small, distant objects appear to have been sculpted as well.

One team, led by Renu Malhotra of the University of Arizona, discussed four such objects at the DPS/EPSC meeting Wednesday. And Brown's team, led by Elizabeth Bailey of Caltech, announced at the meeting on Tuesday (Oct. 18) that Planet Nine appears to have tilted the orbits of all eight "official" planets by 6 degrees relative to the sun.

The ongoing Planet Nine research also includes efforts to pin down where the world might be in the sky these days. This is a key part of the discovery effort, since a blind search for an object so far away, and with such a huge and elliptical orbit, has little chance of success in the near term, Brown has said.

It's likely that Planet Nine is currently at or near aphelion, located perhaps 1,000 AU from the sun, in a patch of sky measuring about 400 square degrees, Brown said. (For comparison, the full moon viewed from Earth covers about 0.5 degrees of sky.)

Astronomers have said Planet Nine is perhaps four times wider than Earth, and such an object would be easily visible with professional-grade equipment if it were relatively close to Earth, Brown explained. In addition, planets on highly elliptical orbits spend most of their time

near aphelion, since they're traveling most slowly on this part of their path, he said.

An object four times bigger than Earth that's located at 1,000 AU would have a magnitude of about +25 on astronomers' brightness scale, Brown added.

"This is well within reach of the giant telescopes," he said. "The Subaru telescope, I think, on Mauna Kea, [in Hawaii] — the Japanese national telescope — is the prime instrument for doing the search. But there are a lot of other people who have clever ideas on how to find it, too, that are trying with their own telescopes."

So which research team will ultimately find Planet Nine? Brown said he isn't sure, and he stressed that getting credit for the historic discovery should be a secondary concern for astronomers.

"There are a lot of people looking, and we are trying as hard as we can to tell people where to look," he said. "We want it to be found."

***http://bit.ly/2e0xXMT***

## How a Volcano in Japan Halted an Earthquake

***Mount Aso, one of the most active volcanoes in Japan, recently helped to stop a powerful earthquake before it subsided on its own, researchers discovered.***

**By Mindy Weisberger, Senior Writer | October 20, 2016 05:38pm ET**

When a 7.1-magnitude quake struck Kumamoto, Japan, on April 16, 2016, it opened surface ruptures in a zone extending 25 miles (40 kilometers) in length. But scientists found evidence suggesting that the powerful earthquake was halted by a magma chamber under the Aso volcanic cluster, located 19 miles (30 km) from where the quake originated.

This finding provided scientists with a rare glimpse of how two geological phenomena — volcanoes and earthquakes — may interact. This topic is of particular interest in Japan, which is particularly vulnerable to both volcanoes and earthquakes.

An earthquake is a sudden release of pent-up energy in Earth's crust that has accumulated over time, generated by shifting tectonic plates. When two sides of a fault, or crack along a plate boundary, move apart or slide suddenly past each other, energy gets released. The waves of energy radiate outward from that jolt, often producing shaking on Earth's surface, according to the U.S. Geological Survey (USGS).

Japan is especially prone to earthquakes, as it lies in the Pacific Ring of Fire, a U-shaped area in the Pacific Ocean where several tectonic plates meet, and where many earthquakes are generated.

A number of volcanoes are also found in this Ring of Fire. And it was the particular interaction of the April 2016 earthquake with the Mount Aso volcano that triggered the researchers' interest in how seismic activity could be affected by the structure of volcanic clusters.

Shortly after the Kumamoto quake, the researchers visited the epicenter - the place on Earth's surface directly above where the earthquake originated - and spent 10 days investigating the ruptures left behind by the quake. They discovered fresh ruptures that extended into Aso's caldera - a large, bowl-shaped depression at the volcano's summit - from the southwest to the northeast edge. And they abruptly ended there, at depths of 3.7 miles (6 km) below the surface.

Investigations of seismic activity deep under the caldera where the ruptures stopped indicated that there was a chamber holding magma — the same hot, fluid material called lava when it reaches Earth's surface — at that very spot,

Energy waves from the quake traveled toward Mount Aso through cool, brittle rock, the study authors wrote. But the sudden encounter with the extreme heat generated by rising magma under the volcano dispersed the energy upward and outward, sapping the strength of the quake's flow and stopping the rupture, they explained.

"This is the first case concerning the interaction between the volcano and co-seismic rupturing as we know so far," study lead author Aiming Lin told Live Science in an email.

Lin, a professor in the Department of Earth and Planetary Sciences at the Faculty and Graduate School of Science at Kyoto University in

Japan, said that although this is the first reported evidence of a volcano putting a stop to an earthquake, there are other historical examples that could represent similar activity.

In 1707, ruptures generated by the Houei-Tokai-Nankai earthquake (magnitude 8.7) extended northward and eventually terminated at the western side of Mount Fuji, Lin wrote. And in 1930, the rupturing of the magnitude-7.3 North Izu earthquake was interrupted at the Hakone volcano in Izu Peninsula. "Along this line, we are studying the interaction between the active faults — including co-seismic rupturing — and large earthquakes in Japan," Lin said.

This discovery could help researchers more accurately anticipate earthquakes' duration relative to their interaction with volcanoes, according to seismologist Gregory Beroza, deputy director of the Southern California Earthquake Center and a professor of geophysics at Stanford University.

"What it might mean for earthquakes is that magmatic systems might segment faults and, by doing so, limit the size of earthquakes in a predictable way," Beroza, who was not involved in the study, told Live Science in an email. "This is just one earthquake, however," Beroza added. "No matter how interesting it is, or compelling it looks, it's potentially hazardous to generalize to future earthquakes." The findings were published online today (Oct. 20) in the journal Science.

***http://bit.ly/2ewBmmY***

## $100 million project to make intelligence-boosting brain implant

***If you could implant a device in your brain to enhance your intelligence, would you do it?***

**By Jessica Hamzelou**

A new company has just invested $100 million into developing such a device, and is being advised by some of the biggest names in science.

The company, Kernel, was launched earlier this year by entrepreneur Bryan Johnson. He says he has spent many years wondering how best to contribute to humanity. “I arrived at intelligence. I think it’s the most precious and powerful resource in existence,” says Johnson.

His goal is for human intelligence to expand and develop in the same way that artificial intelligence has in recent years.

The first experiments planned will be on memory. Johnson is working with Theodore Berger, at the University of Southern California in Los Angeles, who is looking at the hippocampus – a brain region key for memory.

Berger is currently studying people with epilepsy, who already have electrical implants in their brains to treat their seizures.

Rather than using these implants to stimulate the brain, Berger’s team have been using them to record brain activity instead, to tell us more about how our memory works.

**Memory prosthesis**

Once we learn how a healthy brain functions, we should eventually be able to mimic it, says Johnson.

By electrically stimulating the same pattern of activity, the team think they should be able to restore memory in people with memory disorders.

Berger has already had some success with animals, and has started experiments in people. Kernel will be starting new human studies in the coming months, says Johnson.

“The idea is that if you have loss of memory function, then you could build a prosthetic for the hippocampus that would help restore the circuitry, and restore memory,” says Johnson.

People with memory disorders, for example due to a traumatic experience or ageing, are intended to be the first people to test such a prosthesis.

“The first super-humans are those who have deficits to start with,” says Johnson.

But Johnson then plans to develop this prosthesis to enhance memory, and potentially other functions, in healthy people.

He envisions a future in which it is normal for people to walk around with chips in their brains, providing them with a cognitive boost as they go about their everyday business.

**What next?**

The $100 million – from Johnson's own pocket – will be spent on developing such a device. Ideally, it will be as tiny and easy to implant as possible, while being able to record or stimulate multiple neurons.

The team are also working on ways to develop personalised algorithms – a set of rules that dictate normal brain function for an individual.

Johnson hopes that memory enhancement will just be the start. "If we can mimic the natural function of the brain, and we can truly work with neural code, then I posit the question – what can't we do?" says Johnson. "Could we learn a thousand times faster? Could we choose which memories to keep and which to get rid of? Could we have a connection with our computers?"

Johnson has some big names advising him, including neuroengineer Ed Boyden at the Massachusetts Institute of Technology, who is known for his work in optogenetics, and Craig Venter, who is famous for creating synthetic life.

"They too believe we are at a special point in neuroscience," says Johnson. "I think that human intelligence will be one of the largest industries, if not the largest industry, to ever emerge."

But others aren't convinced. Neil Burgess, at University College London, points out that even if the team manage to record the activity of neurons in normal memory processing, it will still be difficult to find out which bits of the code to turn up and which to dampen down in order to enhance the process. "I can't see it working," he says.

An optogenetic approach might be more likely to work, says Burgess. Research in mice has shown that the technique can be used to tag and then activate the neurons associated with a specific memory, for example.

***http://bit.ly/2eHq140***

## Uninsured children more often transferred from ERs than those with private insurance

***Study calls into question the effectiveness of federal law requiring hospitals to make decisions about patients transfers and admissions independent of insurance status***

SAN FRANCISCO - New research shows children seen in emergency departments who don't have insurance, or who have public Medicaid coverage, are significantly more likely to be transferred to another facility than to be admitted for inpatient care within the same receiving hospital compared to children with private insurance.

The abstract, "Association between Insurance and Transfer of Children from Emergency Departments," will be presented at the American Academy of Pediatrics (AAP) 2016 National Conference & Exhibition in San Francisco on Oct. 24. The abstract authors, who published a related article in the August 2016 Annals of Emergency Medicine, said further analysis calls into question the effectiveness of the three-decade-old Emergency Medical Treatment and Active Labor Act (EMTALA). This law requires hospitals to make decisions on patient transfer and admission based on clinical factors or the need for specialty services, independent of insurance status.

The study included Healthcare Cost and Utilization Project 2012 Nationwide Emergency Department Sample data and analyzed two groups of children - those with injuries and those without injuries. Among non-injured children, 240,620 pediatric emergency department visits at 950 hospitals located in 30 U.S. states who were either admitted or transferred were analyzed.

The researchers determined that patients who were uninsured or identified as self-paying (also considered uninsured) had almost four times the odds of being transferred to another facility for admission compared to patients with private insurance. Among the injured children, which included data analyzed separately from 9,461 emergency department encounters at 386 non-trauma centers,

researchers found patients had 1.25 times the odds of being transferred to another facility for admission compared to patients with private insurance, even after adjusting for injury severity and other variables.

"Our findings suggest a systematic bias toward admitting children with private medical insurance and transferring those who either don't have insurance or who have Medicaid," said abstract author Yunru Huang, a Ph.D. candidate in epidemiology at University of California, Davis. This reinforces ongoing concerns about inequities in the delivery of care and call into question the effectiveness of the EMTALA, she said.

"Not having health insurance or having Medicaid coverage unfortunately is still an important factor in the type and quality of care delivered to children," Huang said. She called for efforts to reduce the number of children without medical insurance as well as equity in payments between Medicare and private insurance with Medicaid. In the meantime, she said, further studies of hospitals and physicians are needed to identify when children are treated differently because of their insurance status.

***http://bit.ly/2dMqU3r***

## Presence of certain oral bacterium in esophageal cancer samples associated with shorter survival

***Esophageal cancer patients whose cancer tested positive for Fusobacterium nucleatum had shorter survival compared with those without DNA from the bacterium***

Bottom Line: Among Japanese patients with esophageal cancer, those whose cancer tested positive for DNA from the bacterium Fusobacterium nucleatum had shorter cancer-specific survival compared with those whose cancer had no DNA from the bacterium.

Journal in Which the Study was Published: Clinical Cancer Research, a journal of the American Association for Cancer Research.

Author: Hideo Baba, MD, PhD, a professor in the Department of Gastroenterological Surgery in the Graduate School of Medical Sciences at Kumamoto University, Japan.

Background: More than 100 trillion bacteria naturally inhabit every person's body; they are collectively referred to as the microbiome, Baba explained.

"The gut microbiome has recently been shown to play an important role in health, as well as in diseases such as obesity, inflammatory bowel disease, diabetes, nonalcoholic fatty liver disease, and several types of cancers," said Baba. "We set out to investigate whether F. nucleatum, which is part of many people's oral microbiome, is associated with esophageal cancer development and/or progression."

How the Study Was Conducted and Results: Baba and colleagues collected esophageal cancer tissue samples from 325 consecutive patients who were having the cancer surgically removed at Kumamoto University Hospital from April 2005 to June 2013 and tested them for the presence of F. nucleatum DNA. Patients were followed until January 31, 2016, or death. During this time, there were 75 deaths attributable to esophageal cancer.

The researchers detected F. nucleatum DNA in 23 percent of the esophageal cancer tissue samples they tested. The presence of F. nucleatum DNA was associated with shorter survival. Specifically, after controlling for factors associated with survival, such as age, tobacco use, and tumor stage, patients with tumors positive for F. nucleatum DNA were significantly more likely to have died as a result of esophageal cancer.

Author Comment: "Our findings suggest that testing for the presence of F. nucleatum DNA in esophageal cancer tissue could provide a biomarker of prognosis," said Baba. "If they are replicated in a large, international, multi-institutional study, such testing could provide physicians with important information to consider while deciding how best to manage the care of a patient with esophageal cancer. In addition, the data suggest that therapeutic targeting of F. nucleatum could be a potential new approach to suppress the development and growth of esophageal cancer.

"It is important to note that our data provide no insight into whether F. nucleatum causes esophageal cancer," added Baba. "However, this is something we are hoping to study in the future."

Limitations: According to Baba, the main limitation of the study is that this is a single-institution study. Because the component bacteria of a person's microbiome differ according to numerous factors, including age, place of residence, food consumed, and race, these data cannot be generalized to all individuals unless they are confirmed in a large, international, multi-institutional study.

*Funding & Disclosures: The study was funded in part by SGH Foundation. Baba declares no conflicts of interest.*

***http://bit.ly/2ed26tM***

## Study links changes in collagen to worse pancreatic cancer prognosis

***A study in the current journal Oncotarget provides the first evidence linking a disturbance of the most common protein in the body with a poor outcome in pancreatic cancer.***

MADISON, Wis. -- The study reinforces growing evidence that collagen, which forms fibrous networks in skin, tendons and muscles, is intimately involved in several cancers, says the paper's corresponding author, Kevin Eliceiri, director of the Laboratory for Optical and Computational Instrumentation (LOCI) at the University of Wisconsin-Madison.

For the study, the Wisconsin researchers examined surgical tissues from 114 pancreatic cancer patients and identified a particular rearrangement of collagen fibers surrounding the tumor as a "biomarker" of early death.

A similar rearrangement of collagen has also been found in breast cancer, head, neck, esophageal and colorectal cancers.

"Collagen is the most abundant protein in the body," says Eliceiri. "It's a beautiful molecule -- wavy, with a fibrous nature. Without it we would be a sack of nothing. With this little molecule, the specific fiber organization really matters to metastasis."

The images were created using an automated laser scanning microscope developed at LOCI that shines a laser at tumor specimens mounted on microscope slides. The laser's bright, rapid pulses interact with the collagen fibers, which glow and reveal exquisite details of their structure and relationship to nearby fibers.

The new study tested how collagen formation might affect metastasis, Eliceiri says.

"We did not know anything about survival when we measured the alignment of the collagen in tumors from 114 pancreatic cancer patients. When we looked at the clinical records, we found that the tumors with highly aligned collagen fibers had the worst survival. To our knowledge, this is the first time this technique was used for prognostic purposes in pancreatic cancer."

First author Cole Drifka, a biomedical engineering postdoctoral researcher, conceived and performed the study under the supervision of Eliceiri and W. John Kao, a professor of pharmacy.

"The powerful tissue resource used in this study was made possible by generous financial donations from Teresa's Foundation for Pancreatic Cancer and the Tim and Mary Ann McKenzie Chair of Surgical Oncology Professorship," says Drifka.

"Above all, it was made possible by the selfless tissue donations by UW Health patients. The new tissue collection represents a blossoming institutional focus on pancreatic cancer and is now available to all campus researchers seeking to comprehend this challenging disease."

Finding and fighting metastases is a focus in cancer treatment, Eliceiri explains. "The original tumor seldom kills; poor prognosis is usually due to metastases as they spread to new tissues and organs."

The LOCI lab specializes in developing new imaging techniques for living things, with a special interest in studying cells in their microenvironment rather than in isolation. In the case of several major tumor types, the collagen matrix plays a critical role, Eliceiri says.

For reasons yet to be determined, he adds, "cancer progression seems to be associated with the reorientation of the direction of the collagen. The tumor starts with collagen wrapped around it, but when it's time to metastasize, the collagen fiber changes it alignment."

If alignment matters to metastasis, "We want to know what causes the alignment shift, because then maybe we could block that change," Eliceiri says. For example, if a signaling molecule initiates the realignment, it could be a target for drugs.

Collagen, a structural protein often involved in scarring and wound healing, is emerging as an important factor in a number of other diseases, Eliceiri says. "Collagen may be harmful or protective, but in every disease where collagen is present, it's part of the disease process."

More than a dozen labs at UW-Madison are working on various aspects of collagen. For example, Patricia Keely, professor and chair of cell and regenerative biology who studies the matrix surrounding cells, is exploring its link to breast cancer. Paul Campagnola, a professor of biomedical engineering, is exploring its link in ovarian and lung cancer. Sharon Weber, a co-author on the Oncotarget paper and a professor of surgery, concentrates on pancreatic cancer.

Understanding collagen's role in cancer could have several uses, Weber says. "Prognosis, which is our focus in this paper, is one. Can we identify some signature in the pattern of collagen that will help us understand which patients are going to do well and which are not? Might collagen patterns also help us sort out which patients should undergo surgery? The patterns of collagen in cancer might also be used to ascertain the effectiveness of chemotherapy or radiation so that we can utilize those toxic treatments in those patients who will benefit most."

In cancer, Weber says, knowledge is power. "It would be amazing if we could use these differences in collagen patterns to help discover new therapeutic targets for this devastating disease."

***http://bit.ly/2dBXpXL***

# Neandertal DNA Affects Modern Ethnic Difference in Immune Response

***Two studies may explain why people of African descent respond more strongly to infection, and are more prone to autoimmune diseases***

- **By Sara Reardon, Nature magazine on October 21, 2016**

DNA acquired from breeding with Neanderthals may explain why people of European descent respond differently to infection than those of African descent, two studies suggest. The findings might also offer insight into why people of African descent are more prone to autoimmune diseases caused by an overactive immune system.

***Neandertal skull.*** **LEEMAGE Getty Images**

In a paper published on October 20 in *Cell*, geneticist Luis Barreiro of the University of Montreal in Canada and his colleagues collected blood samples from 80 African Americans and 95 people of European descent. From each sample, they isolated a type of immune cell called macrophages, which engulf and destroy bacteria, and grew these cells in a dish. Next, they infected each culture with two types of bacteria and measured how the cells responded. Macrophages from African Americans, they found, killed the bacteria three times faster than those of European Americans.

The researchers then measured how gene expression changed in response to the infection. About 30% of the approximately 12,000 genes that they tested were expressed differently between the two groups, even before infection. And many of the genes whose activity changed the most during the immune reaction had sequences that were very similar between Europeans and Neanderthals, but not Africans.

**Immune mixing**

Barreiro suspects that when modern humans first left Africa—some time between 100,000 and 60,000 years ago—they had to adapt to a different set of pathogens on the European continent. Breeding with Neanderthals, and obtaining their different immune response, probably helped them to better fight off the new kinds of infections that they encountered there.

In the second study, population geneticist Lluis Quintana-Murci and his colleagues at the Pasteur Institute in Paris collected samples from 200 people living in Belgium, half of whom were of African descent and the other half of European descent. The researchers grew a different type of immune cells called monocytes in a dish and infected them with bacteria and viruses. Once again, the two groups showed differences in the activity of numerous genes, and Neanderthal-like gene variants in the European group played a major role in altering their immune response. The differences were especially stark in the way that the two groups responded to viral infection.

Paul Norman, an immunogeneticist at Stanford University in California, says that the two studies are unusual in looking at how the level of gene expression differs in response to infection, rather than just comparing the genome sequences of individuals. Norman now wants to see the study repeated in more types of immune cell.

Immune systems tend to evolve rapidly because infections produce immediate evolutionary pressure, says computational biologist Janet Kelso of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. So it makes sense that European ancestors would have held onto any advantage they could get from the Neanderthals. “There’s an appreciation now that contributions are coming from many sources, and archaic humans are one,” she says.

**Trigger behind the change**

Kelso says that the studies cannot reveal exactly what drove the evolution—such as a particular viral outbreak in Europe, for instance. For some diseases, such as tuberculosis, a lower immune response tends to help with survival, and modern humans in Europe adopted the Neanderthal traits that helped with this. “Maybe the most important thing is to live in peace with the microbes,” Quintana-Murci says.

Overactive immune systems could help to explain why African American women, for instance, are up to three times more prone to the autoimmune disease lupus than white Americans, Barreiro says. The differences seem to persist irrespective of socioeconomic status and other environmental factors such as smoking and diet, although these probably have a role. Determining how much of the difference is due to genetics could help researchers to tease out the role of environmental factors, and therefore could guide public-health efforts.

Norman says that more research should include genomes and biological samples from different ethnic groups. About 80% of people included in genome-wide association studies are of European descent, and a Comment in *Nature* last week called for more racial diversity in genomic databases. Norman says that the latest studies show how useful this diversity can be in elucidating the roots of diseases. “We need to look at African populations as well, not just because some diseases affect Africans worse, but because we can get to the answers easier.”

***http://bit.ly/2eAfskJ***

## New strategy to prevent Alzheimer's disease

***Taking a pill that prevents the accumulation of toxic molecules in the brain might someday help prevent or delay Alzheimer's disease, according to scientists.***

Taking a pill that prevents the accumulation of toxic molecules in the brain might someday help prevent or delay Alzheimer's disease, according to scientists at Baylor College of Medicine, Texas Children's Hospital and Johns Hopkins University School of Medicine. The study, published in Cell Press journal Neuron, took a three-pronged approach to help subdue early events that occur in the brain long before symptoms of Alzheimer's disease are evident. The scientists were able to prevent those early events and the subsequent

development of brain pathology in experimental animal models in the lab.

"Common diseases like Parkinson's, Alzheimer's and dementia are caused in part by abnormal accumulation of certain proteins in the brain," said senior author Dr. Huda Zoghbi, professor of molecular and human genetics and of pediatrics -- neurology and developmental neuroscience at Baylor and director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital. "Some proteins become toxic when they accumulate; they make the brain vulnerable to degeneration. Tau is one of those proteins involved in Alzheimer's disease and dementia."

"Scientists in the field have been focusing mostly on the final stages of Alzheimer's disease," said first author Dr. Cristian Lasagna-Reeves, postdoctoral fellow in the Zoghbi lab. "Here we tried to find clues about what is happening at the very early stages of the illness, before clinical irreversible symptoms appear, with the intention of preventing or reducing those early events that lead to devastating changes in the brain decades later."

The scientists reasoned that if they could find ways to prevent or reduce tau accumulation in the brain, they would uncover new possibilities for developing drug treatments for these diseases.

Cells control the amount of their proteins with other proteins called enzymes. To find which enzymes affect tau accumulation, the scientists systematically inhibited enzymes called kinases. "We inhibited about 600 kinases one by one and found one, called Nuak1, whose inhibition resulted in reduced levels of tau," said Zoghbi, who is also an investigator at the Howard Hughes Medical Institute.

The scientists screened the enzymes in two different systems, cultured human cells and the laboratory fruit fly. Screening in the fruit fly allowed the scientists to assess the effects of inhibiting the enzymes in a functional nervous system in a living organism.

"Screening hundreds of kinases in the fruit fly animal model was critical because we could assess degeneration caused by tau in the fly's nervous system and measure neuronal dysfunction. Screening such a large number cannot be done with other animal models like the mouse, and cultured cells cannot model complex nervous system functions," said co-senior author Dr. Juan Botas, professor of molecular and human genetics and of molecular and cellular biology at Baylor.

"We found one enzyme, Nuak1, whose inhibition consistently resulted in lower levels of tau in both human cells and fruit flies," said Zoghbi. "Then we took this result to a mouse model of Alzheimer's disease and hoped that the results would hold, and they did. Inhibiting Nuak1 improved the behavior of the mice and prevented brain degeneration."

"Confirming in three independent systems -- human cells, the fruit fly and the mouse -- that Nuak1 inhibition results in reduced levels of tau and prevents brain abnormalities induced by tau accumulation, has convinced us that Nuak1 is a reliable potential target for drugs to prevent diseases such as Alzheimer's," said Zoghbi. "The next step is to develop drugs that will inhibit Nuak1 in hope that one day would be able to lower tau levels with low toxicity in individuals at risk for dementia due to tau accumulation."

Scientific studies like this one that uncover basic biological mechanisms of disease make it possible to develop new strategies to prevent or treat diseases such as Alzheimer's, Parkinson's or dementia.

In the future it might be possible to treat people at risk for Alzheimer's disease by keeping tau low. Think of how taking drugs that lower cholesterol has helped control the accumulation of cholesterol in blood vessels that leads to atherosclerosis and heart disease.

"When people started taking drugs that lower cholesterol, they lived longer and healthier lives rather than dying earlier of heart disease," said Zoghbi. "Nobody has thought about Alzheimer's disease in that light. Tau in Alzheimer's can be compared to cholesterol in heart disease. Tau is a protein that when it accumulates as the person ages, increases the vulnerability of the brain to developing Alzheimer's. So maybe if we can find drugs that can keep tau at levels that are not toxic for the brain, then we would be able to prevent or delay the

development of Alzheimer's and other diseases caused in part by toxic tau accumulation."

*Materials provided by Baylor College of Medicine. Note: Content may be edited for style and length.*

*Cristian A. Lasagna-Reeves, Maria de Haro, Shuang Hao, Jeehye Park, Maxime W.C. Rousseaux, Ismael Al-Ramahi, Paymaan Jafar-Nejad, Luis Vilanova-Velez, Lauren See, Antonia De Maio, Larissa Nitschke, Zhenyu Wu, Juan C. Troncoso, Thomas F. Westbrook, Jianrong Tang, Juan Botas, Huda Y. Zoghbi. Reduction of Nuak1 Decreases Tau and Reverses Phenotypes in a Tauopathy Mouse Model. Neuron, 2016; 92 (2): 407 DOI: 10.1016/j.neuron.2016.09.022*

***http://bit.ly/2e3xeKP***

## Genetics play a key role in how your body metabolizes caffeine

***Depending on a person's genetic make-up, he or she might be able to guzzle coffee right before bed or feel wired after just one cup.***

Genetic variants play a key role in how individuals metabolize coffee. Some can drink coffee before bed and go right to sleep, while others a wired after just a single cup.

Studying how genes impact coffee consumption habits is nothing new. A 2014 study identified genetic variants that are associated with coffee consumption behavior. Two variants were linked to genes involved in caffeine metabolism, POR and ABCG2 (two others, AHR and CYP1A2 had been identified previously). Two variants were also identified near genes BDNF and SLC6A4 that potentially influence the rewarding effects of caffeine. Two others - near GCKR and MLXIPL, genes involved in glucose and lipid metabolism - had not previously been linked to the metabolism or neurological effects of coffee.

Another study published earlier this year also found that the amount of coffee a person drinks was also due to a genetic variation (or lack thereof). This variation occurs in a gene called PDSS2, and people who possess this variation tend to drink fewer cups than those without it. The researchers suggest that the gene reduces the ability of cells to breakdown caffeine, causing it to stay in the body for longer. This means that a person would not need to consume as much coffee to get the same caffeine hit.

While these studies examined genetics variants related to coffee consumption behavior, similar methodologies have now been used to study metabolites in the blood - or chemicals found in one's blood after consuming caffeine.

The new study, Marilyn Cornelis, assistant professor in the department of Preventive Medicine at Northwestern University Feinberg School of Medicine, found the same variants identified in 2014, as well as an additional variant. Additionally, she discovered that a variant in the gene CYP2A6, which previously had been linked to smoking behavior and nicotine metabolism, is also linked to caffeine metabolism.

"Each of us could be potentially responding to caffeine differently, and it's possible that those differences can extend beyond that of caffeine," Cornelis said.

"How this gene relates to both caffeine metabolism and caffeine-seeking behavior is unclear but worthy of further study, given its link to several health outcomes," Cornelis said.

Cornelis' research also found genetic variants were linked to lower levels of caffeine metabolites, which imply faster caffeine metabolism, are the same variants previously linked to higher coffee consumption.

"This makes sense, conceptually, but the genetic research confirms it and further re-emphasizes the notion that not everyone responds to a single cup of coffee (or other caffeinated beverage) in the same way," Cornelis said. "It's important to know, given coffee has been implicated in so many diseases."

Additionally, many of the genes found to metabolize caffeine also coded for proteins that function in the metabolism of other clinically important drugs, such as those that treat insomnia, Parkinson's Disease, hypertension and more.

The findings, published in *Human Molecular Genetics*, support additional links between metabolism of caffeine, nicotine and possibly

other pharmaceutical drugs. At this point, Cornelis said this is largely unknown but could have great implications for the field of precision medicine.

***http://bit.ly/2enEGph***

## International study proves old blood is as good as new

***It's been long thought that when blood transfusions are needed, it may be best to use the freshest blood, but McMaster University researchers have led a large international study proving that it is not so.***

Hamilton, ON - The study of almost 31,500 patients at six hospitals in four countries showed that having a transfusion with the freshest blood did not reduce the proportion of patients who died in hospital. The McMaster study was published in the New England Journal of Medicine today.

"It's been a contentious issue, but our study finally puts an end to the question about whether stored blood could be harmful and fresher blood would be better," said Nancy Heddle, lead author and a professor emeritus of medicine for McMaster's Michael G. DeGroote School of Medicine. She is also the research director of the McMaster Centre for Transfusion Research.

"Our study provides strong evidence that transfusion of fresh blood does not improve patient outcomes, and this should reassure clinicians that fresher is not better."

She added that the results are also good news for blood suppliers worldwide as having a supply of stored blood helps to ensure that blood is available when a patient needs it.

The 31,497 adult patients studied were at hospitals in Australia, Canada, Israel and the U.S. The mortality rate was 9.1 per cent with people receiving the freshest blood, and 8.7 per cent among those receiving the oldest blood. There was no significant difference when looking at the patients' blood type, diagnosis, hospital or country.

John Eikelboom, a co-principal investigator of the study and professor of medicine of the Michael G. DeGroote School of Medicine, said more than 40 studies published earlier have failed to adequately answer the question about whether the freshest blood was best.

"Blood transfusions are a common medical intervention," he said. "Advances in blood storage now allow blood to be stored up to 42 days before transfusion and the usual practice is to use up the blood that has been in storage the longest. But, because there are biochemical, structural and functional changes in the blood during storage, there had been concerns about the use of 'older' blood.

"This study reassures us that aging is not bad - even for blood."

*The study was funded by the Canadian Institutes of Health Research, Canadian Blood Services and Health Canada.*