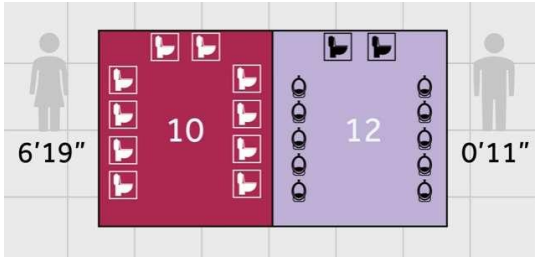
http://bit.ly/2uPYVD1

Researchers study lengths of restroom queues

Two queueing theorists of Ghent University investigated why queues at restrooms are invariably longer for ladies than for men.



Time and time again. What are the main causes for this disparity? And how can it be overcome? Moving to unisex toilets, it appears from this study, may reduce waiting times for women from over 6 minutes to less than a minute and a half. Already a symbol for transgender equality, unisex toilets can hence boast excellent figures when it comes to reducing waiting times. Or, how transgender-friendliness may help in battling female-unfriendly toilet culture.

It turns out there are three main causes for the difference in waiting time between men and women. A first factor explaining why women wait longer is that the net number of toilets for women is smaller than that for men. This is because the total surface area is often divided equally while a toilet cabin inevitably takes up more space than a urinal. Overall, an average toilet area can accommodate 20 to 30 percent more toilets for men (urinals + cabins) than for women.

A second reason is that according to scientific studies women spend one and a half up to two times as long on the toilet. The reasons are mostly practical. In contrast to a urinal, a door must be opened and closed twice, a toilet seat needs cleaning, and more and more difficult clothes have to be taken off and on. This results in an average time spent at the toilet of 1 minute for men and 1 minute and 30 seconds for women.

A third factor is the overall activity at the restroom. As long as it's not too busy, the overall effect of ladies having a smaller number of toilets and spending more time on those toilets does not lead to long queues. However when for example everybody heads home, more women arrive at the toilets than the system can handle. This condition amplifies the above effects and results in outrageous waiting times for women.

Based on these three major causes, 6 different but comparable layouts were simulated using a scenario of alternating busy and calm periods. A layout with comparable waiting times for men and women is possible, yet requires that for each male toilet at least one and a half and up to two female toilets are present. The holy grail, however, is to use unisex toilets. In these mixed toilets layouts, the toilet cabins are available for both sexes and optionally complemented with extra urinals for the men. As sharing the toilet capacity across sexes is more efficient, the average waiting time decreases. The available toilet surface can be used most efficiently when an ideally balanced layout with about two cabins per urinal is chosen. In this layout, men are still privileged, but to a much lesser extent than in the basic situation. The overall waiting time is reduced with 63 percent, which cannot be achieved by any other mixed layout, and definitely not by a separated layout.

http://bit.ly/2qQifJM

The earliest stages of life might be simpler than we thought

University of Copenhagen research from suggests development process may be simpler than thought

In the very earliest stages of life, mammalian cells multiply and form the embryo. New research from the University of Copenhagen suggests that this process might be much simpler than we thought. The development of the embryo can be cut down to the cell's ability to count their neighbouring cells.

One of the things that make human beings and other mammals unique in the animal kingdom is our cells' ability to remember how to make an embryo. Development is the process by which a single cell, a fertilised egg, makes a complex body with head, tail, arms and legs. Mammalian cells can begin this process without any apparent external

or additional information to tell them which side is up and down. More remarkable, even after they have made choices and developed into specialized cell types, individual mammalian cells can go back and do it again or twin, effectively starting from scratch. The big question is: How does the cell know how to do this? Researchers from the Faculty of Health and Medical Sciences and the Niels Bohr Institute at the University of Copenhagen have published a study that suggests that life at embryo stage is simpler than we thought.

"Cells are much smarter than we give them credit for. We have shown that they can build an embryo just by making four simple decisions. The most prominent of these is counting their neighbours. It almost sounds too simple to be true, but by counting their neighbours, the cells can determine whether they are placed on the outside or on the inside of the cell group. When they have made their decision, they adjust their properties, start to specialize and begin to form an embryo," says Professor Josh Brickman from The Danish Stem Cell Center (DanStem).

The researchers used a computer simulation to make a cell-behaviour model. The idea was to find the minimal requirements for the cells to develop into an embryo, and the researchers cut it down to four rules or decisions for the cells to make based on their neighbours: adopt polarity, make lineage choices, alter its adhesion or die. They then tested the model in mice cells. The results showed that the model predicted the behaviour of the cells perfectly.

Development and evolution

The question of how the cells are able to form a pattern and develop into an embryo has been a source of debate for years. One theory was that there had to be some unfound information from the mother placed on one side of the egg, which provided the cells with an essential map. Another theory was that master control genes vary at random until they find the right combination. What the researchers have essentially done is say that these explanations are unnecessary and that the very earliest stages of mammalian life are much simpler than we thought.

The results also offer a further understanding of how evolution is even possible. In order for evolution to work, the genes that direct development have to change at a quite significant range. However, it is hard to conceive how the master control genes can change that drastically without messing the whole thing up.

"We have shown that by following the four simple rules, the cells will develop themselves. They only need a little bit of information from the genome, which allows evolution to play with the genes as much as it likes. Basically, it provides the robustness to ensure that development will always work, but then it gives evolution the room to play with the genome. This gives rise to the diversity of the mammalian species," says PhD student from the Niels Bohr Institute Silas Boye Nissen.

The article 'Four simple rules that are sufficient to generate the mammalian blastocyst' is a product of StemPhys, a new multi-disciplinary initiative between SUND and the Niels Bohr Institute funded by the Danish National Research Foundation. The work is published in the journal PLoS Biology.

http://bbc.in/2uGPbdx

Surgeons remove 27 contact lenses from woman's eye

Surgeons have removed 27 contact lenses from the eye of a 67-year-old woman who had come to Solihull Hospital for routine cataract surgery.

"A bluish foreign body" turned out to be a "hard mass" of 17 lenses stuck together with mucus, and 10 more were then found under further examination. A report in the BMJ said she had worn disposable lenses for 35 years, and had not complained of any irritation. But after they were removed, she said her eyes felt a lot more comfortable.

'Shocked'

Specialist trainee in ophthalmology Rupal Morjaria told Optometry Today: "None of us have ever seen this before. "It was such a large mass. All the 17 contact lenses were stuck together. "We were really surprised that the patient didn't notice it because it would cause quite a lot of irritation while it was sitting there. "She was quite shocked. She thought her previous discomfort was just part of old age and dry eye."

'Hiding'

The case report said the patient had poorer vision in her right eye and deep-set eyes, which may have been a factor in the lenses becoming lost.

Association of Optometrists spokeswoman Ceri Smith-Jaynes said losing contact lenses in the eye was a common problem but they usually worked their way out. "They are normally hiding, folded up under the top lid of the eye," she said. "They can't go any further up than that because there is a pocket. "It's the same under the bottom lid - the lens can only be in one of those places."

She said it was important to see an optometrist or optician regularly to avoid any issues when using contact lenses.

Top tips for contact lens wearers:

Don't wear your lenses for longer than you have been told to, and not for more than 16 hours in a day - you should never sleep in them, unless specifically designed for wearing overnight

Wash and dry your hands thoroughly before putting anything in your eye

Never apply eye make-up before putting in contact lenses

Don't go swimming when wearing contact lenses

Replace your contact lens case regularly to reduce the risk of infection

If you spot any signs of redness, pain or loss of vision, consult your optometrist or optician immediately

Make sure you go for regular check-ups

If in doubt, take them out

http://bbc.in/2uJpIQH

North Carolina man cheats death after 40 minutes with no pulse

A North Carolina man whose heart stopped for about 40 minutes has paid tribute to the emergency workers who brought him back from the dead.

John Ogburn, 36, suffered a cardiac arrest while working on his laptop near his Charlotte home on 26 June. Two police officers who happened to be nearby began CPR on the father-of-three within a minute of the 911 call. They took turns resuscitating Mr Ogburn for around 42 minutes until his pulse returned.

Charlotte-Mecklenburg police officers Lawrence Guiler and Nikolina Bajic's lifesaving efforts are all the more praiseworthy given that emergency workers are not required to perform CPR after 20 minutes without any vital signs.

'I'm doing really well'

After Mr Ogburn was brought to hospital, doctors placed him in a medically induced coma to help him recover for the rest of the week.

He has been advised not to drive for six months and is easing back into work. But for the most part, he says he feels completely fine, apart from a sore chest.

"My energy level hasn't been what it was before, but that might be because my routine changed a bit," he told the BBC. "The combination of [the chest compressions and an internal defibrillator] is a little sore, but if that's all I got to complain about, then I'm doing really well."

Mr Ogburn said he is still figuring out how to make the most of his second chance at life. Above all he feels indebted to the first responders who went above and beyond the call of duty to make each new day possible for him. "In certain time frames they're supposed to call it, and they didn't, they continued to try to save me," he said. "And I am just so grateful for that and for them."

Golden minutes

Dr Michael Kurz, associate professor at the University of Alabama at Birmingham School of Medicine, and American Heart Association volunteer, says: "The evidence does tell us that for every minute the heart is stopped and that high-quality cardiopulmonary resuscitation (CPR) is not conducted, there is a 10% reduction in survival.

This case in North Carolina highlights the value of CPR in extending that window of survivability. Immediate CPR can double or treble chances of survival from cardiac arrest. Most US employees are not prepared to handle cardiac emergencies, and that needs to change."

More than 350,000 out-of-hospital cardiac arrests occur in the US each year, with 90% of those victims dying as a result. Just 46% of people who experience cardiac arrests outside of hospital receive any form of help before professional paramedics arrive.

http://bit.ly/2uKZAEy

Study: Omega-3 fatty acids fight inflammation via cannabinoids

Cascade of chemical reactions converts omega-3 fatty acids into cannabinoids that have anti-inflammatory benefits

CHAMPAIGN, Ill. -- Chemical compounds called cannabinoids are found in marijuana and also are produced naturally in the body from omega-3 fatty acids. A well-known cannabinoid in marijuana, tetrahydrocannabinol, is responsible for some of its euphoric effects, but it also has anti-inflammatory benefits. A new study in animal tissue reveals the cascade of chemical reactions that convert omega-3 fatty acids into cannabinoids that have anti-inflammatory benefits -- but without the psychotropic high. The findings are published in the Proceedings of the National Academy of Sciences.

Foods such as meat, eggs, fish and nuts contain omega-3 and omega-6 fatty acids, which the body converts into endocannabinoids -- cannabinoids that the body produces naturally, said Aditi Das, a University of Illinois professor of comparative biosciences and biochemistry, who led the study. Cannabinoids in marijuana and endocannabinoids produced in the body can support the body's immune system and therefore are attractive targets for the development of anti-inflammatory therapeutics, she said.

In 1964, the Israeli chemist Raphael Mechoulam was the first to discover and isolate THC from marijuana. To test whether he had found the compound that produces euphoria, he dosed cake slices with 10 milligrams of pure THC and gave them to willing friends at a party. Their reactions, from nonstop laughter, to lethargy, to talkativeness, confirmed that THC was a psychotropic cannabinoid.

It wasn't until 1992 that researchers discovered endocannabinoids produced naturally in the body. Since then, several other endocannabinoids have been identified, but not all have known functions.

Cannabinoids bind to two types of cannabinoid receptors in the body - one that is found predominantly in the nervous system and one in the immune system, Das said. "Some cannabinoids, such as THC in marijuana or endocannabinoids can bind to these receptors and elicit anti-inflammatory and anti-pain action," she said.

"Our team discovered an enzymatic pathway that converts omega-3-derived endocannabinoids into more potent anti-inflammatory molecules that predominantly bind to the receptors found in the immune system," Das said. "This finding demonstrates how omega-3 fatty acids can produce some of the same medicinal qualities as marijuana, but without a psychotropic effect."

The study was an interdisciplinary effort led by recent comparative biosciences alumnus Daniel McDougle and supported by current biochemistry graduate student Josephine Watson. The team included U. of I. animal sciences professor Rodney Johnson; U. of I. bioengineering professor Kristopher Kilian; Michael Holinstat, of the University of Michigan; and Lucas Li, the director of the Metabolomics Center at the Roy J. Carver Biotechnology Center at Illinois. The National Institutes of Health and the American Heart Association supported this research.

http://bit.ly/2vuy7VH

Study throws dog domestication theories to the wolves

The tiny chihuahua traces its roots to a single group of wolves that crossed the path of humans as long as 40,000 years ago, researchers say

July 18, 2017 by Laurence Coustal

From the tiny chihuahua to the massive Saint Bernard, domestic dogs today trace their roots to a single group of wolves that crossed the path of humans as long as 40,000 years ago, researchers said Tuesday.

Their findings are bound to reignite the scientific disagreement over when, and where, "man's best friend" first split from its wolf ancestor.

One school of thought maintains this happened in Europe around 15,000 years ago, another said it happened in central Asia or China about 2,500 years later.

Last year, a study in the journal Science said domestication happened from two separate wolf populations, one in Europe and the other in Asia.

The authors of the latest report said their DNA analysis shows that ancient dogs first split from wolves around 40,000 years ago, likely triggered by the presence of humans. The team cannot say where in the world this happened.

The process of dog domestication was probably a "passive" process, they added. Rather than humans actively taming wild wolves, it would have started with the animals approaching hunter-gatherer camps in search of food. "Those wolves that were tamer and less aggressive would have been more successful at this" and more likely to befriend humans, explained the researchers.

These were not dogs as we know them today—they rather resembled "village dogs" which roamed freely, did not live in specific people's homes and scrounged for food.

Fossils shed light

By 20,000 years ago, said the team, the first dogs split geographically between Eastern and Western canines. The first gave rise to East Asian dogs, and the other to dogs in Europe, central and south Asia, and Africa. "By... 7,000 years ago, they (dogs) were pretty much everywhere, including North America," study co-author Krishna Veeramah of Stony Brook University in New York, told AFP.

The European dog of that period is the one that went on to father most modern dog breeds found today, the researchers concluded.

The team relied on the fossilised DNA of two dogs dug up in Germany—7,000 and 4,700 years old—which they compared to modern hounds. The fossils came from the Neolithic period, the closing chapter of the Stone Age, when prehistoric humans first tried their hand at farming and building permanent villages.

Last month, another DNA study said the first cats were also tamed during this time. The first wildcat to travel abroad, and the forefather of domestic cats today, was Felis silvestris lybica—a small, striped Middle Eastern sub-species that went on to colonise the entire world, that study found. The mother (or father) of all cats is thought to have travelled to Europe by ship from the region of Anatolia around modern-day Turkey 6,000 years ago.

http://bbc.in/2qRtB0n

Zion Harvey: Double hand transplant boy plays baseball

A US boy who made history as the world's first child to have a double hand transplant is now swinging a baseball bat well, his doctors say.

It is two years since Zion Harvey, who is now 10, was given new hands, and his doctors say they are amazed by and incredibly proud of his progress.

Zion can now write and feed and dress himself, as well as grip a bat. Although his hands came from a donor, his brain has accepted them as his own, medical tests show.

Dr Sandra Amaral, a member of the team treating Zion at the Children's Hospital of Philadelphia, told the BBC that Zion continues to make significant progress. "He is able to swing a bat with much more co-ordination, and he can write his name quite clearly.

"His sensation continues to improve. It's amazing. "Now he can pat his mother's cheek and feel it." Dr Amaral said there was evidence that his brain had rewired to take account of his new hands.

The team has published medical notes about his remarkable story in The Lancet Child and Adolescent Health journal.

Zion was born with two hands but when he was aged two, doctors had to amputate them. In his own words: "When I was two I had to get my hands cut off because I was sick."

Zion had sepsis, a life-threatening infection. Doctors removed both his hands at the wrist, and his legs below the knee because they were dying. His kidneys also failed.

At the age of four, after two years of dialysis, Zion had a kidney transplant using a kidney donated by his mother Pattie Ray. It was another four years before the boy from Baltimore got his new hands.

Risky procedure

Zion's hand operation in June 2015 was a big deal. Although not the first ever double-hand transplant - that was in 1998 - he was the youngest to ever have the procedure.

His doctors say Zion's medical story, along with his positive personality and determination, made him a great candidate.

Transplant patients need to take lifelong anti-rejection drugs and these can have bad side-effects, which means the benefits of the surgery must outweigh the risks.

Zion was already on this medication for his kidney and after 18 months of close assessment, the medical team was confident a double-hand transplant could benefit him.

Next came the wait for a donor of the right size, skin tone and blood group compatibility. Three months later they found a donor.

A team of 40 medical staff, including 10 surgeons, operated through the night and into the early hours of the morning to fit Zion's new hands.

One of the biggest challenges was connecting up all the tiny blood vessels that would keep the hands alive.

Dr Benjamin Chang, co-director of the hand transplant programme at the hospital, recalls: "We wanted to really make sure that this was going to work for our patient and work for a lifetime."

Two years on, Zion is doing well.

There were a few times in the first year after the transplant that Zion's doctors feared his body was starting to reject the new hands. Thankfully, tweaking his medication helped.

His doctors say one of the most promising things they have seen during the recovery period is how well Zion's brain has responded "despite the absence of hands during a developmental period of rich fine motor development between the ages of two and eight years".

Speaking about Zion last year, lead surgeon Dr Scott Levin said: "His brain is communicating with his hands. His brain says for his hands to move and they move. And that in and of itself is remarkable."

http://bbc.in/2uJYWaS

Plan not to give HPV vaccine to boys causes concern

A decision not to vaccinate boys against a cancer-causing sexually transmitted infection has attracted fierce criticism.

Reported cases of human papilloma virus (HPV) - thought to cause about 80% of cervical cancers - have fallen sharply since girls were given the vaccine. But the Joint Committee on Vaccination and Immunisation (JCVI) found little evidence to justify treating boys too.

Critics said vaccinating boys could help reduce the risk still further.

Across the UK, all girls aged 12-13 are offered HPV vaccination as part of the NHS childhood vaccination programme.

Mary Ramsay, head of immunisation at Public Health England, said: "Evidence from around the world suggests that the risk of HPV infection in males is dramatically reduced by achieving high uptake of the HPV vaccine among girls.

"While there are some additional benefits to vaccinating both males and females, the current models indicate that extending the programme to boys in the UK, where the uptake in adolescent girls is consistently high (over 85%), would not represent a good use of NHS resources."

This initial recommendation by JCVI will now be subject to a public consultation and a final decision will be made in October. The British Dental Association said it would urge the committee to reconsider the evidence.

The chair of the BDA, Mick Armstrong, said: "HPV has emerged as the leading cause of oropharyngeal cancers, so JCVI's unwillingness to expand the vaccination programme to boys is frankly indefensible."

Shirley Cramer of the Royal Society for Public Health said: "We are deeply disappointed by the JCVI's decision today, which suggests that fundamental priorities are focused more on saving money than on saving lives.

"Such a simple vaccination programme has the potential to make such a big impact on the public's health on a national scale. "We hope that

the government's advisory committee reconsider this decision as soon as possible and put the public's health and wellbeing before cost-saving."

The argument for vaccinating boys HPV

- ***About 15% of UK girls eligible for vaccination are currently not receiving both doses, a figure which is much higher in some areas***
- ***Men may have sex with women too old to have had the HPV vaccination***
- ***Men may have sex with women from other countries with no vaccination programme***
- ***Men who have sex with men are not protected by the girls' programme***
- ***The cost of treating HPV-related diseases is high - treating anogenital warts alone in the UK is estimated to cost £58m a year, while the additional cost of vaccinating boys has been estimated at about £20m a year***

Source: HPV Action

http://bit.ly/2ul10nf

Kakadu find confirms earliest Australian occupation

Aboriginal people have been in Australia for at least 65,000 years - much longer than the 47,000 years believed by some archaeologists.

The discovery, by a team of archaeologists and dating specialists led by Associate Professor Chris Clarkson from The University of Queensland School of Social Science, has been detailed in the Nature journal this week. The researchers found new evidence at the Madjedbebe site on Mirarr land within the Jabiluka mineral lease, surrounded by the World Heritage-listed Kakadu National Park.

Madjedbebe rock shelter has been excavated four times since the 1970s, most recently by an international team led by Dr Clarkson in partnership with the Mirarr Traditional Owners.

Dr Clarkson said more than 10,000 artefacts were revealed in the lowest layer at the site. "The site contains the oldest ground-edge stone axe technology in the world, the oldest known seed-grinding tools in Australia and evidence of finely made stone points which may have served as spear tips," he said. "Most striking of all, in a region known for its spectacular rock art, are the huge quantities of ground ochre and evidence of ochre processing found at the site, from the older layer continuing through to the present."

The dig discovered a maxillary (upper jaw) fragment of a Tasmanian Tiger coated in red pigment, giving insight to the central role ochre played in local customs at the time.

Dating carried out by Professor Zenobia Jacobs at the University of Wollongong has revealed that Aboriginal people lived at Madjedbebe at the same time as extinct species of giant animals were roaming around Australia, and the tiny species of primitive human, Homo floresiensis, was living on the island of Flores in eastern Indonesia.

In addition to showing the deep antiquity of Aboriginal occupation, the dig revealed new evidence of activities and lifestyle.

Gundjeihmi Aboriginal Corporation Chief Executive Officer Justin O'Brien said a landmark agreement had made it possible for Dr Clarkson and colleagues to dig the site. "This study shatters previous understandings of the sophistication of the Aboriginal toolkit and underscores the universal importance of the Jabiluka area," Mr O'Brien said.

The study, funded through an Australian Research Council Discovery Project grant, promotes discussion about the timing and ways that modern humans first left Africa.

Other UQ researchers involved in the study included Dr Tiina Manne, Dr Andrew Fairburn, Professor James Schulmeister and Kate Connell.

Numerous completed and continuing PhD and honours students Dr Kelsey Low, Dr Xavier Carah, Anna Florin, Delyth Cox, Jessica McNeil and Kasih Norman collaborated on the study.

http://bit.ly/2uJe48s

Rare Human Syndrome May Explain Why Dogs are So Friendly

Scientists have found that extreme friendliness in dogs and humans may share common genetic roots

By Nala Rogers, ISNS Staff Writer | July 19, 2017 04:01pm ET

(Inside Science) -- When it comes to sheer friendliness, few humans can match the average dog. But people with Williams syndrome may come close, their unusual genetics granting them a puppyish zeal for

social interaction. Now, scientists have found that extreme friendliness in both species may share common genetic roots.

A friendly condition

Williams syndrome, also known as Williams-Beuren syndrome, occurs when people are missing of a chunk of DNA containing about 27 genes. The syndrome affects about one in 10,000 people, and it is associated with a suite of mental and physical traits, including bubbly, extroverted personalities, a broad forehead, full cheeks, heart defects, intellectual disability and an affinity for music.

The first hint of a link between dogs and Williams syndrome came in 2010, when evolutionary biologist Bridgett vonHoldt and her colleagues examined DNA from 225 wolves and 912 dogs from 85 breeds. They were looking for parts of the genome that have been shaped by selection since dogs diverged from wolves.

One gene that popped out was WBSCR17, suggesting that it or other genes near it were important in dog evolution. This region of the genome is similar in dogs and humans, and the human version of WBSCR17 is located near the sequence that is deleted in people with Williams syndrome.

Doggie DNA

In the new study, vonHoldt, now an evolutionary biologist at Princeton University in New Jersey, and her colleagues took a closer look at the region surrounding WBSCR17. First, they tested the friendliness of 18 dogs and 10 wolves, all raised with regular attention from human caretakers. They measured how much time each dog or wolf spent within a 1-meter radius of a human, as well as how hard the animal worked to solve a puzzle box.

As expected, wolves spent less time near humans, and most worked equally hard to solve their puzzle box regardless of whether a human was present. In contrast, dogs tended to look at the human instead of the puzzle box, focusing on the puzzle only when left alone.

While dogs were more sociable than wolves on average, individuals varied, with some wolves acting more friendly and some dogs acting more aloof. When the researchers analyzed DNA from 16 of the dogs and eight of the wolves, the behavioral differences turned out to be correlated with variations in three genes -- the WBSCR17 gene highlighted in the 2010 study, and two additional genes from within the canine equivalent of the Williams syndrome region.

For each of these three genes, the researchers found multiple variants that differed in structural ways, such as whether or not they contained an extra sequence of DNA. Some gene variants were found mostly in the friendly dogs and wolves, while others were found more often in unfriendly animals.

While personality traits like friendliness are probably shaped by hundreds or thousands of genes, these three genes appeared to play a surprisingly large role in controlling social behavior, said vonHoldt.

"Some of these structural variants could explain a huge shift in a behavioral profile -- that you go from being a wolf-like, aloof creature, to something that's obsessed with a human," she said.

When the researchers examined those same three genes in 201 dogs from 13 breeds, they found similar patterns of genetic variation between breeds traditionally associated with friendly behavior, and breeds generally considered to be more standoffish.

Same genes, different species

Two of the genes, GTF2I and GTF2IRD1, had previously been linked to social behavior in mice as well as in people with Williams syndrome. In 2009, Uta Francke and her colleagues at Stanford University in California found that mice wer unusually eager to socialize when they were missing those two genes. But until Francke saw the new study, she had no idea that the genes she had studied might help explain the behavior of her own dog, a Bernese mountain dog named Minna.

"She walks up to strangers and wants interaction with everybody, just like the Williams kids," said Francke, who has worked with people with Williams syndrome in her career as a medical geneticist. "To

think that this is because of the involvement of these genes in some way -- I find that extremely exciting."

The connection between dogs and Williams syndrome will likely ring true for people within the Williams syndrome community as well, said Jocelyn Krebs, a biomedical researcher at the University of Alaska Anchorage who has studied Williams syndrome and was not involved in the new study. Krebs has a son with Williams syndrome, and she sits on the Williams syndrome Association board of trustees, so she knows how friendly people with the condition can be.

"If they had tails, they would wag them," she said.

Roots of domestication

The findings are consistent with current theories of dog domestication. Once, researchers assumed that ancient humans domesticated dogs on purpose, adopting wolf pups and breeding them for useful traits. Biologists Ray and Lorna Coppinger have pioneered a different view, seeing early dogs as scavengers on human trash. According to this theory, shy wolves continued to hunt in the forest, while bolder wolves that could tolerate humans took up residence at village rubbish heaps.

Ray Coppinger himself avoids words like "friendly" when referring to these ancestral dogs. But according to Clive Wynne, a behavioral scientist at Arizona State University in Tempe, Arizona, and one of the new study's authors, sociability could have been a key trait that helped early dogs get access to human scraps. The new study suggests that dogs achieved that friendliness in part through changes to the genes that are equivalent to those affected in people with Williams syndrome.

"Outside of, like, Disney movies, animals all just making friends with each other and being lovey-dovey out in the forest is pretty much a catastrophe," said Wynne. But, he said, "If you have a mutation that makes you more willing to make friends, well then, you're going to get a lot more out of the trash dump."

Wynne can't say for sure whether the domestication process happened at multiple villages at different times, or if it happened just once, as indicated by another recent study that looked at DNA from ancient dog fossils.

It's too soon to know just how important the genes identified in the study were in dog domestication, cautioned Ray Coppinger, during an interview with Inside Science. But it's possible that they played a pivotal role, not just for dogs, but for other species as well, said Carlos Driscoll, a geneticist who studies cat domestication at the National Institutes of Health in Rockville, Maryland. The next step, said Driscoll, is to test other domestic species, and see whether the same three genes may contribute to tame temperaments in everything from cats to goats.

"The only thing that's common among all domesticates is that they're sociable -- that they get along with people," said Driscoll. "This very strongly suggests that this region and these genes are important in domestication."

http://bit.ly/2uJFUBp

Deadly Kiss: Can a Baby Contract a Lethal Virus from a Cold Sore?

A newborn baby in Iowa died this week from an infection with the virus that causes cold sores, which she likely contracted from a kiss, her doctors say. But how does this happen?

By Rachael Rettner, Senior Writer | July 19, 2017 06:31pm ET

The baby, Mariana Reese Sifrit, was healthy when she was born July 1, according to ABC News. Six days later, Mariana's parents got married, and just hours after the wedding, Mariana looked sick — she became lethargic and stopped feeding, and her parents took her to the hospital, according to ABC.

Doctors diagnosed Mariana with meningitis, which is a swelling of the membranes that cover the brain and spinal cord. They said her meningitis was due to an infection with herpes simplex virus 1 (HSV-1), the virus that causes cold sores. Both parents tested negative for

the virus, and her doctors said Mariana likely caught the virus from a kiss from someone who came to see the newborn, according to ABC. Mariana died Tuesday (July 18).

"Just keep your babies isolated," Mariana's mother, Nicole Sifrit, advised parents when she spoke with the ABC affiliate WQAD-TV. "Don't let people kiss your baby. Make sure they ask before they pick up your baby," Sifrit said.

In newborns, catching HSV-1 infection from a kiss is "unusual but not unheard of," said Dr. Otto Ramos, medical director of the Division of Pediatric Infectious Diseases at Nicklaus Children's Hospital in Miami. That's because people with HSV-1 infection — either with or without cold sores — can shed the virus and transmit it to others, said Ramos, who was not involved in Mariana's case and so cannot comment on the case directly.

However, in most cases of HSV-1 in infants, Ramos said, the baby catches the virus from its mother during delivery, and in 60 percent of such cases, the mother had no signs or symptoms of infection, Ramos told Live Science.

Indeed, according to a study published in March in the journal The Lancet Global Health, about 85 percent of newborns with herpes simplex infection catch the virus during delivery, while only 10 percent catch the virus after birth from someone with an infection. The other 5 percent catch the virus in utero.

Herpes simplex viruses can cause serve complications in newborns, and left untreated, the infection results in death in 60 percent of cases, The Lancet study said. These viruses can infect the brain, leading to a condition called herpes encephalitis, which can result in seizures, intellectual disabilities, vision and hearing loss, according to the March of Dimes. The viruses can also infect multiple organs at the same time, including the liver, lungs and kidneys, and about 30 percent of infants with these widespread infections die, the March of Dimes said.

About 1 of every 3,500 babies born in the United States, or less than 1 percent, contracts herpes simplex virus each year, according to the March of Dimes.

Ramos said newborns are particularly vulnerable to herpes simplex virus infections because their immune system is not mature enough to thwart the virus. "The baby doesn't have an immune system that can fight it off," Ramos said.

New parents should be extremely careful not to let people with any kind of infection have close contact with their baby, Ramos said.

"You have to be very careful and very vigilant that no one who has any kind of infection is around the baby," Ramos said. "People should not be kissing babies if they have any kind of infection," he said.

To prevent HSV-1 infections in babies after birth, the National Institutes of Health says that people with cold sores should not come into contact with newborn infants. Parents and caregivers with cold sores should wear a mask and wash their hands carefully before coming into contact with their baby, the NIH said. Good handwashing is also important for anyone who has contact with a newborn, Ramos said.

http://bit.ly/2vv5BU5

New research uncovers a cause of schizophrenia

Genetic defects may damage glial cells, which may lead to a number of brain disorders, including schizophrenia

A new study from the University of Copenhagen shows that genetic defects may damage the supporting cells of the brain - the glial cells - which may lead to a number of brain disorders, including schizophrenia. The study is based on ground-breaking tests with mice whose brains were colonized with human glial cells.

When the brain is formed in the embryonic stage, this happens partly according to a recipe from a particular type of stem cells - the progenitor cells. They develop into brain support cells, called glial cells, which include astrocytes and oligodendrocytes. These contribute

to the important formation and maintenance of neural networks throughout life.

Now, new research shows that distinct genetic dispositions may lead to disease in the progenitor cells, which may harm the maturation of the support cells. This in turn may impair the production by oligodendrocytes of myelin, the important protective fat layer surrounding the nerve pathways of the brain. The resultant lack of myelin is a significant contributor to the development of schizophrenia.

The researchers have identified a number of the decisive genes that trigger the defects in the progenitor cells, and this may be the first step in the development of targeted drugs and stem cell treatment against schizophrenia.

"It was through studies of mice with human glial cells that we succeeded in testing how dysfunctional glial cells may cause abnormalities in the formation of the brain's neural networks, which may in turn cause severe anxiety, anti-social behaviour and severe sleep problems. We see these problems in the mice, just as in human patients. This is an important discovery because it will now enable us to develop methods that can counteract the unwanted development of progenitor cells ", says Professor Steven Goldman of the Center for Translational Neuromedicine, at both the University of Copenhagen and the University of Rochester.

Mouse Studies with Stem Cells from Patients with Schizophrenia

Modern research into schizophrenia has pointed to different types of genetic defects in the brain's primary nerve cells (neurons), but the new research shows that one major cause is defects in the support cells - the glial cells. It is the task of the glial cells to ensure and coordinate the synaptic communication between the nerve cells, so that their dysfunction in schizophrenia can result in miscommunication among neurons.

The research is based on tests where glial cells - produced from progenitor cells from patients suffering from schizophrenia - have been incorporated into mouse brains. This revolutionary type of model is called a chimera (concept of Greek origin) because it combines human cells with those of mice. In practical terms, scientists have thus succeeded in creating a type of human brain network in living mice.

The new research results indicate that the defective glial cells contribute to an abnormal maturation of the brain. This is manifested as diminished development of the brain's white matter, and abnormal astrocyte development, each of which plays a central role in information processing in the brain.

These brain changes resulted in behavioural changes in the chimeric mice, which exhibited diminished sensory-motor coordination, excessive anxiety, anti-social behaviour and sleep disorders, all typical of schizophrenic patients as well.

Replacing Sick Brain Cells with Healthy Cells

According to Professor Goldman, the continued research into the significance of glial cells for the development of schizophrenia and brain disorders will be moving in several directions. One of the more dramatic prospects is that it may be attempted to replace defective glial cells with healthy ones to see if it is possible to reverse the progression of the disease.

Fact box:

Worldwide, more than 21 million people suffer from schizophrenia. It is a serious mental disorder characterised by thought and language disorders as well as problems with perception and self-awareness. One in two does not receive adequate treatment for the disorder. Source: WHO 2017

Glial cells are nerve cells that constitute the brain's supportive tissue in the central nervous system and the peripheral nervous system. Glial cells constitute the largest group of nerve cells and their volume accounts for more than half of the human brain with 9-10 glial cells for each nerve cell.

Astrocytes constitute the largest glial cell type surrounding the synapses (the nerve cell contact point). They regulate the communication between nerve cells and ensure the elimination of excess transmitter substances so they do not accumulate in the brain

Oligodendrocytes produce and maintain myelin sheaths in the central nervous system.

This international project was done with collaborators at the University of Rochester, Case Western Medical School, George Washington University, and Johns Hopkins Medical School in the US.

http://bit.ly/2tPsz64

Gene drives likely to be foiled by rapid rise of resistance

Gene drives using CRISPR/Cas9 will be derailed by development of mutations that give resistance to the drive

A study in fruit flies suggests that existing approaches to gene drives using CRISPR/Cas9, which aim to spread new genes within a natural population, will be derailed by the development of mutations that give resistance to the drive.

Jackson Champer, Philipp W. Messer, and colleagues at Cornell University in Ithaca, New York report these findings July 20, 2017 in *PLOS Genetics*.

Fruit flies with a CRISPR gene drive carrying a red fluorescent protein as payload. **Jackson Champer**

Gene drives offer tremendous hope for preventing the spread of mosquito-borne diseases and controlling invasive species. Newly developed approaches that use CRISPR/Cas9 gene editing technology can generate offspring that carry copies of the altered gene on both chromosomes - a phenomenon called super-Mendelian inheritance that, in theory, should quickly convert an entire population.

This process, however, can also create resistant genetic sequences and organisms that cannot be converted.

In the current study, researchers tested two different CRISPR gene drive constructs in the model fruit fly, *Drosophila melanogaster*, to investigate the rise of resistance. They saw that resistant gene variations formed frequently, both before fertilization in the germline and within the embryo.

Further analysis showed that in insects with genetically diverse backgrounds, as found in wild populations, there was considerable variation in terms of how efficiently the offspring converted, and how often resistance genes arose.

The study demonstrates that the evolution of resistance will likely be a severe roadblock for existing CRISPR gene drive approaches, which must be addressed before scientists could successfully employ them in the wild.

In the coming years, research groups have planned gene drives in mice on islands off the coast of Massachusetts to prevent the spread of Lyme disease, and in tree snakes in Guam to control these invasive species.

New gene drive approaches will be necessary to overcome the challenge posed by resistance, especially in genetically diverse, natural populations.

James J. Bull and Harmit S. Malik further discuss the research in an accompanying Perspective entitled "The Gene Drive Bubble: new realities", also published July 20th, 2017 in conjunction with this primary Research Article.

More information: *Champer J, Reeves R, Oh SY, Liu C, Liu J, Clark AG, et al. (2017) Novel CRISPR/Cas9 gene drive constructs reveal insights into mechanisms of resistance allele formation and drive efficiency in genetically diverse populations. PLoS Genet 13(7): e1006796. doi.org/10.1371/journal.pgen.1006796*

Bull JJ, Malik HS (2017) The gene drive bubble: New realities. PLoS Genet 13(7): e1006850. doi.org/10.1371/journal.pgen.1006850

http://bit.ly/2qSm2Xa

In saliva, clues to a 'ghost' species of ancient human

The evolutionary history of a salivary protein may point to interbreeding between humans and an enigmatic ancient relative

BUFFALO, N.Y. -- In saliva, scientists have found hints that a "ghost" species of archaic humans may have contributed genetic material to ancestors of people living in Sub-Saharan Africa today. The research adds to a growing body of evidence suggesting that sexual rendezvous between different archaic human species may not have been unusual.

Past studies have concluded that the forebears of modern humans in Asia and Europe interbred with other early hominin species, including Neanderthals and Denisovans. The new research is among more recent genetic analyses indicating that ancient Africans also had trysts with other early hominins.

"It seems that interbreeding between different early hominin species is not the exception -- it's the norm," says Omer Gokcumen, PhD, an assistant professor of biological sciences in the University at Buffalo College of Arts and Sciences.

"Our research traced the evolution of an important mucin protein called MUC7 that is found in saliva," he says. "When we looked at the history of the gene that codes for the protein, we see the signature of archaic admixture in modern day Sub-Saharan African populations."

The research was published on July 21 in the journal Molecular Biology and Evolution. The study was led by Gokcumen and Stefan Ruhl, DDS, PhD, a professor of oral biology in UB's School of Dental Medicine.

A tantalizing clue in saliva

The scientists came upon their findings while researching the purpose and origins of the MUC7 protein, which helps give spit its slimy consistency and binds to microbes, potentially helping to rid the body of disease-causing bacteria.

As part of this investigation, the team examined the MUC7 gene in more than 2,500 modern human genomes. The analysis yielded a surprise: A group of genomes from Sub-Saharan Africa had a version of the gene that was wildly different from versions found in other modern humans.

The Sub-Saharan variant was so distinctive that Neanderthal and Denisovan MUC7 genes matched more closely with those of other modern humans than the Sub-Saharan outlier did.

"Based on our analysis, the most plausible explanation for this extreme variation is archaic introgression -- the introduction of genetic material from a 'ghost' species of ancient hominins," Gokcumen says. "This unknown human relative could be a species that has been discovered, such as a subspecies of Homo erectus, or an undiscovered hominin. We call it a 'ghost' species because we don't have the fossils."

Given the rate that genes mutate during the course of evolution, the team calculated that the ancestors of people who carry the Sub-Saharan MUC7 variant interbred with another ancient human species as recently as 150,000 years ago, after the two species' evolutionary path diverged from each other some 1.5 to 2 million years ago.

Why MUC7 matters

The scientists were interested in MUC7 because in a previous study they showed that the protein likely evolved to serve an important purpose in humans.

In some people, the gene that codes for MUC7 holds six copies of genetic instructions that direct the body to build parts of the corresponding protein. In other people, the gene harbors only five sets of these instructions (known as tandem repeats).

Prior studies by other researchers found that the five-copy version of the gene protected against asthma, but Gokcumen and Ruhl did not see this association when they ran a more detailed analysis.

The new study did conclude, however, that MUC7 appears to influence the makeup of the oral microbiome, the collection of bacteria within the mouth. The evidence for this came from an analysis of biological samples from 130 people, which found that different versions of the MUC7 gene were strongly associated with different oral microbiome compositions.

"From what we know of MUC7, it makes sense that people with different versions of the MUC7 gene could have different oral microbiomes," Ruhl says. "The MUC7 protein is thought to enhance the ability of saliva to bind to microbes, an important task that may help prevent disease by clearing unwanted bacteria or other pathogens from the mouth."

In addition to Ruhl and Gokcumen, the research team included Duo "Erica" Xu, the study's first author and a UB PhD student in biological sciences; Pavlos Pavlidis, PhD, and Nikolaos

Alachiotis, PhD, of the Foundation for Research and Technology -- Hellas in Greece; Colin Flanagan, a UB undergraduate who has completed his degree in biological sciences; Ran Blekhman, PhD, of the University of Minnesota; and Michael Degiorgio, Ph.D., of Pennsylvania State University.

The research was funded primarily by the University at Buffalo Research Foundation, with additional support from InnovCrete and the National Institute of Dental and Craniofacial Research.

http://bit.ly/2tPNNkc

Giant deep-sea worms may live to be 1000 years old or more

Some individuals of Escarpia laminata may be 1000 years old or more

By Karl Gruber

Set up for a long life **Chemo III project/BOEM/NOAA OER**

In the depths of the ocean, life can extend far beyond its usual limits. Take the tube worm Escarpia laminata: living in an environment with a year-round abundance of food and no predators, individuals seem to live for over 300 years.

And some may be 1000 years old or more – meaning they would have been around when William the Conqueror invaded England.

"E. laminata is pushing the bounds of what we thought was possible for longevity," says Alanna Durkin at Temple University in Philadelphia, Pennsylvania.

These tube worms live between 1000 and 3300 metres below sea level in aggregations from five to more than 200 individuals around cold seeps. This environment also provides a habitat for brittlestars, shrimps, crabs, mussels, clams, snails, limpets and a huge variety of smaller species of worms.

"The tube worms look like oversized plastic straws with a delicate pink flower at the end when the animal extends its petal-like plume – a gill-like organ for gas exchange – out of the top of its tube," says Durkin. They can measure more than 1.5 metres, and feed through a symbiotic relationship they form with bacteria that thrive in these seeps.

Growth model

Finding out exactly how old the worms were was tricky, says Durkin, given that they don't produce a hard, permanent skeleton or tissue with annual, countable "growth rings". Instead, her team had to rely on a growth model from an earlier study of a different worm species, which predicts how much a worm grows each year.

"The idea behind the growth model is that it lets us simulate how these tube worms grow and age without us having to wait hundreds of years to watch them grow in real time," says Durkin.

Researchers fed real-life data into the model by looking at how much worms of different sizes grew over a single year. This served to reveal how fast they grow at varying stages of their lives, Durkin explains.

"Then we can use that data to simulate tube worms growing over time to find out how many years it would take these animals to reach a particular size," she says.

According to the model, some of the tube worms have been around for hundreds of years – with some maybe even thousands of years old. It is hard to put an upper limit on their age, because they grow more slowly as they get older. "There may indeed be large E. laminata over 1000 years old in nature, but given our research we are more confident reporting a lifespan of at least 250 to 300 years," says Durkin.

Long-lived species of the deep

This suggests that the tube worms are the second-longest-living non-colonial species ever found in the depths of the ocean – the deep-sea clam Arctica islandica can live for 500 years or more. Colony-forming animals, including some corals, are estimated to live for over 4000 years. "It's possible that new record-breaking lifespans will be discovered in the deep sea, since we are finding new species and new habitats almost every time we send down a submersible," says Durkin.

Journal reference: The Science of Nature, DOI: 10.1007/s00114-017-1479-z

http://bit.ly/2tAHdTz

Missing Mutations Suggest a Reason for Sex

Sex might help natural selection purge excessive mistakes from our genes.

Veronique Greenwood *Contributing Writer*

For a species whose numbers show no signs of collapsing, humans have a shockingly high mutation rate. Each of us is born with about 70 new genetic errors that our parents did not have. That's much more than a slime mold, say, or a bacterium. Mutations are likely to decrease an organism's fitness, and an avalanche like this every generation could be deadly to our species. The fact that we haven't gone extinct suggests that over the long term, we have some way of taking out our genetic garbage. And a new paper, recently published in *Science*, provides evidence that the answer may be linked to another fascinating procedure: sex.

For about three decades, one of the senior authors of that paper, Alexey Kondrashov, a biologist at University of Michigan, has explored how populations might shed such mutations. The question poses more of a conundrum than you might think. One model of natural selection is that it acts on mutations one by one: letting this one stay, forcing that one out. Another, though, is that the fates of mutations can be linked — an effect that population geneticists call synergistic, or narrowing, epistasis. This might happen if having one mutation can compound the effects of another: for instance, a system that's able to limp along with one defective piece will fail with the loss of a second or a third. In this way of thinking, for an individual, having more mutations is not just additively worse, but closer to exponentially worse.

To Kondrashov and others, that prediction suggests an escape route from the trap of rapidly accumulating mistakes, both for humans and other multicellular organisms prone to mutations: As the number of nasty genetic errors in a population rises, natural selection will sweep large rafts of them out of the genome together. And in sexual organisms, because of the ways that mutations from each parent can recombine randomly onto the same chromosomes, the synergistic elimination of bad mutations can happen even faster.

Kondrashov has investigated the implications of synergistic epistasis with theoretical studies. Other researchers have taken the experimental route, trying to detect whether, in real life, mutations can interact with each other this way. Those tests yielded mixed results, though, perhaps because the effect would not have to be very large to keep a population from succumbing.

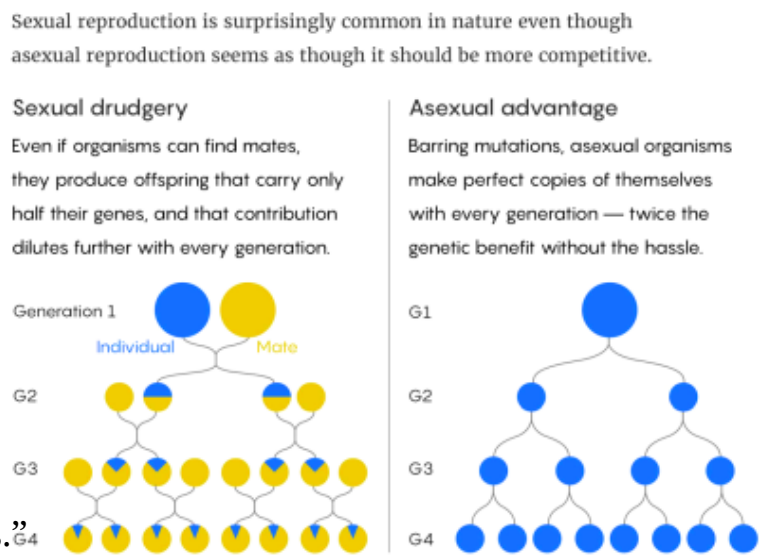
Now, however, Kondrashov and his co-authors have put together a statistical case, pulled from the genomes of about 2,000 people and about 300 wild fruit flies, that the effect has been quietly acting on us and other organisms all along. Drawing on knowledge of the species' mutation rates and other factors, Mashaal Sohail, a doctoral candidate in systems biology at Harvard Medical School, and the rest of the team began by calculating what the distribution of mutations in populations of humans and flies ought to be in the absence of this purging effect. Certain numbers of individuals in the group, for example, ought to show 100, 50 or 30 mutations. Then the scientists turned to the genomic data, looking for the distribution of mutations in real-world populations.

What they found was that significantly fewer individuals than expected had large numbers of dangerous mutations. They are missing from the population, "suggesting that at the high end, at the end where people have many deleterious mutations, there's stronger selection against these people," said Arjan de Visser, an evolutionary geneticist at University of Wageningen who was not involved in the work. This observation fits well with what should happen if mutations are not acting independently.

That finding comes with some caveats. There does not seem to be any shrinkage in the number of individuals with less-than-devastating mutations, cautioned both Kondrashov and Shamil Sunyaev, a computational geneticist at Harvard Medical School and another

senior author of the paper. “We don’t see it for the whole genome,” Sunyaev said, although the decrease is there “at least for mutations that are undoubtedly deleterious in effect.” The team would also like to get better data on the consequences of mutations in parts of the genome that don’t make proteins. That would let them run their statistical tests again with more confidence that the interactions are occurring more broadly.

Still, the evidence is provocative, and the idea elegant. “I always found it quite attractive, biologically,” said Brian Charlesworth, an evolutionary geneticist at University of Edinburgh who was not involved in the study. “If you think about someone getting hit on the head with a hammer, the first few blows might not do you too much harm, but after a while it will finish you off.” Of the new work, he said, “It’s really the first study which comes up with evidence from what’s going on actually out there in natural populations.”



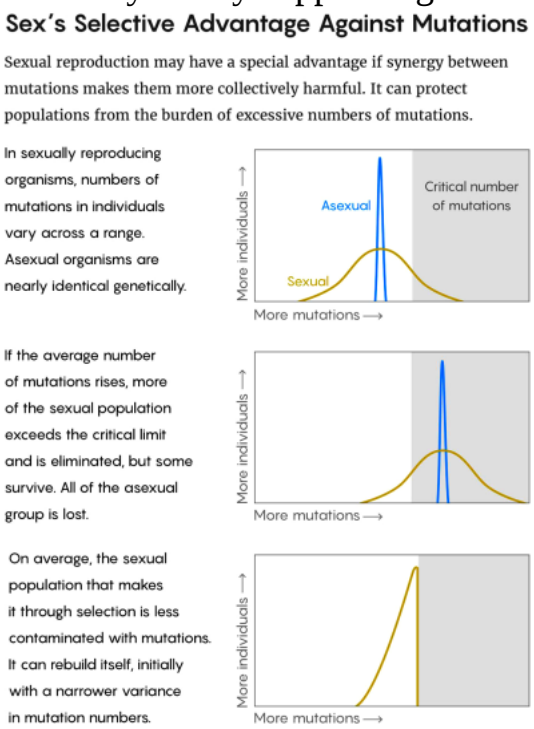
Lucy Reading-Ikkanda/Quanta Magazine

Perhaps the most interesting corollary of this finding, however, is that it might help explain the persistence of sex. Among population geneticists, sexual reproduction is notoriously difficult to justify as an evolutionary strategy. As a sexual organism, even if everything goes well — if you manage to find a mate who accepts you, if you manage to conceive — you will still be passing on only half of your genes. An asexually reproducing organism, having daughters by making perfect copies of itself, gets double the benefit, none of the hassle. Yet clearly, sex continues.

The redeeming feature of sex, when it comes to evolution, seems to be that it shuffles the parents’ genes together in endlessly new combinations. Unless you have an identical twin, none of your siblings are just like you. And each of your sperm or egg cells carries a mish-mash of your own genes, so none of your children will get the same thing. Sex leads to greater variety for natural selection to work with, a wider palate of quirks, abilities, shapes and sizes that might be fitted to the situation at hand.

The benefits of this arrangement may exceed the costs, though, when there is some efficient way to get rid of the real genetic disasters. And that’s where this new work comes in. Dangerous mutations can be wiped out from the population en masse only if they happen to get shuffled together, thanks to sex, into the same individual. That unlucky “individual” loaded with bad mutations could be a sperm cell that’s not fit enough to ever reach an egg, or an organism that is not healthy enough to ever reproduce. Either way, that combination of mutations would drop out of the population, never to be passed on.

At one stroke, then, a large mass of worrisome problems — brought together by sex, then doomed by their associations with one another — would be culled from the gene pool.



Lucy Reading-Ikkanda/Quanta Magazine

Nearly 30 years ago, Kondrashov, then a scientist in the Soviet Union, wrote a paper for *Nature* that pointed out this process, now called the deterministic mutation hypothesis, could help to justify sex. "The [genetic profiles] that are eliminated can contain many mutations, which may give a sexual population an enormous advantage," he mused in the paper. In an asexual population, because the members are genetically identical, natural selection can't purge bad mutations rapidly without killing everyone.

Speaking from his summer research base near Moscow, Kondrashov said he hopes to see more experimental verification of the interactions between mutations. "Before it's replicated on a number of species, I'm reluctant to say that we made a discovery," he said dryly. "But I can't think of any other explanation." Next he plans to raise a carefully controlled population of fruit flies in which the genetic variation among individuals is known from the beginning, and then to run selection experiments to see in more precise detail exactly how it changes over time.

Furthermore, the statistical test the group uses should be applicable to any population where researchers have some basic information to plug in, de Visser noted. It would be relatively straightforward for other scientists to apply it and see if they can uncover similar interactions in other human or animal populations.

It is easy to assume that, in an era with modern medicine and agriculture, we humans have somehow escaped the grasp of natural selection. But this glimpse into the mutational landscape of the human genome shows selection may still be acting on us without our noticing it, even as our numbers boom. These absences in the population, these empty places at the high end of the mutational distribution — these may be selection's fingerprints on our DNA.

Correction: This article was updated on July 18, 2017, to clarify the caption of the opening image, and on July 20, 2017, to acknowledge the contribution of Mashaal Sohail.

http://bit.ly/2vxGDn1

Cancer patients' grey hair unexpectedly darkens in drug study

Spanish study suggests side effects of new immunotherapy drugs may include restoring hair pigment

A group of cancer patients' grey hair has unexpectedly darkened after they took new types of drugs, researchers have revealed.

Chemotherapy is known to make patients' hair fall out, but the 14 people involved were all being treated with new immunotherapy drugs that work differently and have different side effects from chemotherapy. A Spanish study suggests those may include restoring hair pigment, at least in patients with lung cancer.

Noelia Rivera, a dermatologist at Autonomous University of Barcelona, said they thought it could be an isolated case when it happened with the first patient. But the research team found the same thing when they asked other patients for photographs of themselves from before treatment.

The 14 people were among 52 patients with lung cancer being followed to see whether they developed bad side effects from the drugs — Keytruda, Opdivo and Tecentriq.

While most patients did not have a hair colour change, the 14 cases suggest it is not an isolated finding. In 13 patients, hair turned darkish brown or black; in one patient, it turned black in patches.

The same drugs have been linked previously with hair losing colour in patients with another cancer, melanoma.

All but one of the 14 patients in the Spanish study responded better to treatment than other patients, suggesting that hair darkening might be an indication that the drugs are working, the researchers said.

Rivera said they were continuing with the study to search for an explanation.

"It's a fascinating report – one of those things that comes out of the blue," said June Robinson, a Northwestern University research professor in dermatology. Robinson is also editor of the medical

journal JAMA Dermatology, which published the study online this month.

She said the results deserved a deeper look but cautioned that it was too soon to suggest that they might lead to new treatments for unwanted grey hair.

Rivera noted that the drugs used in the study had serious side effects that made them unsafe for healthy people. But if it is confirmed that they do change hair colour, a different drug could be developed to treat grey hair, she said.

The pharmaceutical industry has previously capitalised on unexpected drug side effects. Examples include the male pattern baldness drug Propecia, the eyelash growing drug Latisse, and Botox anti-wrinkle injections. Active ingredients in these drugs were initially approved to treat enlarged prostates, eye pressure problems, and eye muscle spasms.

http://nyti.ms/2vQQkMF

Companies Rush to Develop 'Utterly Transformative' Gene Therapies

The approval of gene therapy for leukemia, expected in the next few months, will open the door to a radically new class of cancer treatments.

By DENISE GRADY JULY 23, 2017

Companies and universities are racing to develop these new therapies, which re-engineer and turbocharge millions of a patient's own immune cells, turning them into cancer killers that researchers call a "living drug." One of the big goals now is to get them to work for many other cancers, including those of the breast, prostate, ovary, lung and pancreas.

"This has been utterly transformative in blood cancers," said Dr. Stephan Grupp, director of the cancer immunotherapy program at the Children's Hospital of Philadelphia, a professor of pediatrics at the University of Pennsylvania and a leader of major studies. "If it can start to work in solid tumors, it will be utterly transformative for the whole field."

But it will take time to find that out, he said, at least five years.

This type of treatment is now also being studied in glioblastoma, the aggressive brain tumor that Senator John McCain was found to have this week. Results of a study at the University of Pennsylvania, published Wednesday, were mixed. In the first 10 patients treated there, one has lived more than 18 months with what the researchers called "stable disease." Two other survivors have cancer that has progressed, and the rest have died.

Studies are forging ahead on many fronts. Researchers plan to try giving the cell treatment to children with earlier stages of leukemia than in the past, combining it with other treatments and developing new types of cell therapy. One new version, with human trials just starting, uses immune cells extracted not from the patient, but from samples of umbilical-cord blood donated by mothers when they give birth.

The products closest to approval so far have a limited focus — to treat blood cancers like leukemia (for which an F.D.A. advisory panel recommended approval of the first treatment last week) and lymphoma, as opposed to the solid tumors that form in organs like the breasts and lungs and cause many more deaths. About 80,000 people a year have the kinds of blood cancers that the first round of new treatments can fight, out of the 1.7 million cases of cancer diagnosed annually in the United States.

The new treatments are expected to cost hundreds of thousands of dollars, and they come with risks. Patients in the earliest studies nearly died from side effects like raging fever, low blood pressure and lung congestion. Doctors have learned how to control those reactions, but experts also have concerns about possible long-term effects like second cancers that could in theory be caused by the disabled viruses used in genetic engineering. No such cancers have been seen so far, but it is too soon to rule them out.

The new leukemia treatment involves removing millions of white blood cells called T cells — often referred to as the soldiers of the immune system — from the patient's bloodstream, genetically engineering them to recognize and kill cancer, multiplying them and then infusing them back into the patient. The process is expensive because each treatment has to be made separately for each person.

Solid tumors are less amenable to treatment with these altered cells — which scientists call CAR-T cells — but studies at various centers are trying to find ways to use it against mesothelioma and cancers of the ovary, breast, prostate, pancreas and lung.

"These solid tumors are like Fort Knox," Dr. Grupp said. "They don't want to let the T cells in. We need combination approaches, CAR-T plus something else, but until the something else is defined we're not doing to see the same kind of responses."

The pioneering T-cell therapy for leukemia was created at the University of Pennsylvania, which licensed it to Novartis. The F.D.A. panel recommended approval of it for a narrow subset of severely ill patients, only a few hundred a year in the United States: those ages 3 to 25 who have B-cell acute lymphoblastic leukemia that has relapsed or not responded to the standard treatments. Those patients have poor odds of surviving, but in clinical trials, a single T-cell treatment has produced long remissions in many and possibly even cured some.

Novartis plans to request another approval later this year of the same treatment (which it calls CTL019 or tisagenlecleucel) for adults who have a type of lymphoma — diffuse large B-cell lymphoma that has relapsed or resisted treatment. A competitor, Kite Pharma, has also filed for approval of a T-cell treatment for lymphoma. Another competitor, Juno, suffered a setback when it shut down a T-cell study in adults after five patients died from brain swelling. Kite has also reported one such death.

Novartis is studying several other types of T-cells, with different genetic tweaks, to treat chronic lymphocytic leukemia, multiple myeloma as well as glioblastoma.

Some of the more promising work so far involves efforts to make the existing gene treatments even more effective in blood cancers. For lymphoma patients, the T cells are being given along with a drug, ibrutinib, and the combination seems to work better than either treatment alone.

At the Children's Hospital of Philadelphia, there are not enough study spots for all the patients who hope to receive T-cell treatment, and the waiting time can stretch to months, longer than some can afford to wait. Waiting times should decline after the treatment is approved and becomes more widely available.

Dr. Grupp said that one encouraging avenue of research involved giving the T-cells at an earlier stage of the disease, instead of very late, as rules now require. He said a study was being planned at multiple centers that he hoped would start within the next six months or so. The patients would be children with early signs that the usual chemotherapy — which cures many — is not working well for them.

"We could deploy the treatment considerably earlier and before they get so sick," he said. He added, "That is another big step in terms of trying to figure out how to use these cells appropriately."

Earlier treatment, he said, might help some patients avoid bone-marrow transplant, a grueling, last-ditch treatment. Children with less advanced disease also tend to have milder side effects from the T-cell treatment.

Studies in children are also underway to combine T-cell treatment with the immunotherapy drugs called checkpoint inhibitors, which help unleash the cancer-killing power of T cells. There will be many such studies, Dr. Grupp predicted, but, he said, "It's early days."

The T cells in the Novartis products, and in the earliest ones its competitors are developing, have been engineered to seek and destroy cells that display on their surfaces a protein called CD19 — a characteristic of many leukemias and lymphomas.

Identifying other targets would be a boon, Dr. Grupp said, because sometimes leukemic cells lacking CD19 proliferate, escape the

treatment and cause relapse. Another target is being studied, and Dr. Grupp said the next step, which he called “superimportant,” would be to attack two cellular targets in the same patient.

In the next year or so, he said, that approach will also be studied in both children and adults who have acute myeloid leukemia, which he described as a “tough disease.”

Researchers at the University of Texas MD Anderson Cancer Center in Houston are trying a completely different approach to engineering cells, one that they hope might eventually yield an “off the shelf” treatment that would not have to be tailored to each individual patient and that might be less expensive.

Instead of using T cells, the team uses natural killer cells, another component of the immune system, one that has a powerful ability to fight anything it recognizes as foreign. Instead of extracting the cells from patients, the researchers, Dr. Katy Rezvani and Dr. Elizabeth Shpall, remove the natural killers from samples of umbilical-cord blood donated by women who have just given birth.

They use natural killer cells because T cells from one person cannot be safely given to another, lest they attack the host’s tissue, causing graft-versus-host disease, which can be fatal. Natural killer cells do not cause that deadly reaction, so it is safe to use such cells from a newborn’s cord blood to treat patients.

The natural killer cells are genetically engineered to attack CD19, and also to produce a substance that activates them and helps them persist in the body. They also have an “off switch,” a gene that will let the researchers shut down the cells with a certain drug if they cause dangerous side effects that cannot be controlled.

After promising studies in mice, the researchers have opened a study for adults with relapsed or treatment-resistant chronic lymphocytic leukemia, acute lymphocytic leukemia or non-Hodgkin lymphoma. The first patient was to be treated this week, Dr. Rezvani said.

One unit of cord blood yields enough cells to treat five patients, she said, and in two weeks the natural killer cells can be expanded 500-fold, to a billion cells.

“We plan to make the product and infuse it fresh to the patient, but we are also working on optimizing the freezing process so we can make the product, freeze it and keep it, so that when patients need it, we can give it.”

http://bit.ly/2tSWaf8

Neuroticism may postpone death for some

Data indicate having higher levels of neuroticism may reduce the risk of death for individuals who report being in fair or poor health

Data from a longitudinal study of over 500,000 people in the United Kingdom indicate that having higher levels of the personality trait neuroticism may reduce the risk of death for individuals who report being in fair or poor health. The research, published in Psychological Science, a journal of the Association for Psychological Science, further revealed that a specific aspect of neuroticism related to worry and feelings of vulnerability was associated with lower mortality, regardless of self-reported health.

"Our findings are important because they suggest that being high in neuroticism may sometimes have a protective effect, perhaps by making people more vigilant about their health," says lead researcher Catharine R. Gale of the University of Edinburgh and University of Southampton.

By definition, people with high levels of neuroticism are more likely to experience negative emotions--including irritability, frustration, nervousness, worry, and guilt--compared with their peers who have lower levels of neuroticism. Studies investigating links between neuroticism and mortality have produced inconsistent results, with some showing higher risk of death and others showing no relationship or even lower risk of death.

Drawing from existing evidence, Gale and colleagues hypothesized that the relationship between neuroticism and risk of death may depend on how people rate their health.

The researchers examined UK Biobank data collected from 502,655 people ages 37 to 73. Participants completed a validated personality assessment measuring neuroticism and indicated whether they thought they were in excellent, good, fair, or poor health overall. The data also included information on participants' health behaviors (e.g., smoking, physical activity), physical health (e.g., body mass index, blood pressure), cognitive function, and medical diagnoses (e.g., heart problems, diabetes, cancer).

Examining death certificates from the National Health Service Central Registry, the researchers found that a total of 4,497 participants had died in the follow-up period (which was about 6.25 years, on average). In general, the data showed that mortality was slightly higher among participants with higher levels of neuroticism. However, when Gale and colleagues adjusted for participants' self-rated health, they found that the direction of the relationship reversed, with higher neuroticism being linked with slightly lower risk of death from all causes and from cancer.

"When we explored this further, we found that this protective effect was only present in people who rated their health as fair or poor," explains Gale. "We also found that people who scored highly on one aspect of neuroticism related to worry and vulnerability had a reduced risk of death regardless of how they rated their health."

Intriguingly, these relationships did not seem to vary according to participants' health behaviors or medical diagnoses at the time they completed the neuroticism questionnaire, a finding which surprised the researchers.

"Health behaviors such as smoking, exercise, diet and alcohol consumption did not explain any part of the link between high scores on the worry/vulnerability facet and mortality risk. We had thought that greater worry or vulnerability might lead people to behave in a healthier way and hence lower their risk of death, but that was not the case," Gale says.

Following on these findings, Gale and colleagues plan to further investigate the different facets of neuroticism to understand why worry and vulnerability may have specific protective effects.

Co-authors on the study include Iva Čukić (University of Edinburgh), G. David Batty (University of Edinburgh and University College London), Andrew M. McIntosh (University of Edinburgh), Alexander Weiss (University of Edinburgh), and Ian J. Deary (University of Edinburgh).

This work was undertaken in The University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, part of the cross-council Lifelong Health and Wellbeing Initiative (Grant MR/K026992/1), which supports I. J. Deary. Funding from the Biotechnology and Biological Sciences Research Council and the Medical Research Council (MRC) is gratefully acknowledged. I. J. Deary, C. R. Gale, and I. ?uki? are supported by the MRC (Grant MR/K025023/1). I. J. Deary and A. M. McIntosh are supported by the Wellcome Trust (Grant 104036/Z/14/Z).

http://bit.ly/2uoXbPH

Immune cells the missing ingredient in new bladder cancer treatment

New research offers a possible explanation for why a new type of cancer treatment hasn't been working as expected against bladder cancer.

The study finds that checkpoint immunotherapy, which is designed to activate the immune system, is not effective on some bladder cancers because there are no immune cells in the tumours. The finding explains what is happening at a cellular level to prevent the immune cells from getting into the tumour and points scientists in the right direction towards developing a combination therapy that could work.

"It's been a mystery for decades as to how tumours escape the immune system," said Mads Daugaard, an assistant professor of urologic science at UBC and a senior scientist at the Vancouver Prostate Centre and Vancouver Coastal Health Research Institute (VCHRI). "We've identified a cellular signaling pathway that regulates whether the body's immune cells are allowed to infiltrate the tumour."

Bladder cancer is the fifth most common cancer in Canada. There is only one line of chemotherapy available, cisplatin-based therapy, for

invasive tumours. Once cancers become resistant, only checkpoint immunotherapy is approved as second-line treatment.

Atezolizumab is a checkpoint immunotherapy drug that strengthens the body's immune response and recently became the first new bladder cancer drug to be approved in more than twenty years. Initial results were very promising but subsequent clinical trials have shown that only one in five patients showed an objective response to treatment. The reason for that has puzzled researchers, until now.

In this study, Daugaard and his colleagues, Dr. Peter Black, an associate professor in urologic sciences at UBC and a senior scientist at the Vancouver Prostate Centre and VCHRI, and a team of scientists from H3 Biomedicine headed by Ping Zhu, found that some invasive bladder cancer tumours block the immune cells from accessing it by activating a cell signaling pathway called the peroxisome proliferator-activated receptor gamma (PPAR-γ) pathway.

"With this pathway, the tumours close the door to the immune system," said Daugaard. "Without immune cells in the tumour, checkpoint immunotherapy has little effect. Now we know what door the tumours are closing and we can therefore focus our efforts on breaking down that door and let the immune system back in."

Daugaard and his team have taken the first steps to develop a drug able to target the PPAR-γ pathway. The rationale is to use such a drug in combination with checkpoint immunotherapy treatment.

"The most efficient way to combat a cancer would be to have the immune system take care of it itself. This is ultimately what we want to achieve," he said.

This research was published today in Nature Communications: http://www.nature.com/ncomms