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Fixing Shoulder Pain: Harvard Scientists Develop a Method To Restore Damaged Tendons and Muscles

The new complex tissue platform can restore damaged rotator cuffs

The typical office worker often has soreness throughout their body as a result of their sedentary desk jobs. Even young individuals may develop shoulder pain, which was previously primarily an issue for elderly people. Once shoulder pain creeps in, it is difficult to dress oneself, let alone move one's body freely. It is also difficult to fall asleep. While the rotator cuffs are often naturally harmed as we age, repairing them has shown to be difficult.

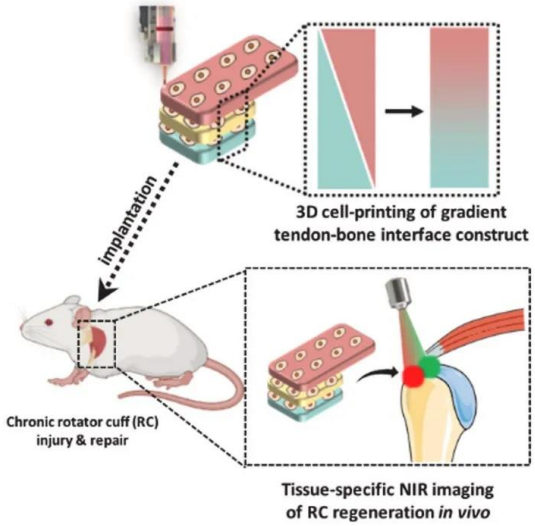
Through a collaboration with Professor Hak Soo Choi at the Harvard Medical School, a Pohang University of Science and Technology (POSTECH) research team made up of Professor Dong-Woo Cho, Dr. Suhun Chae, and Jinah Jang, as well as Professor Jinah Jang and Ph.D. candidate Uijung Yong, has developed a complex tissue platform that can repair damaged rotator cuffs. This platform, which can precisely replicate the intricate structure of rotator cuffs, is 3D-bioprinted using tissue-specific extracellular matrix bioink.

The international journal *Bioactive Materials* recently published the findings of this study, which could potentially provide patients with chronic shoulder pain renewed hope.

The study team transplanted this platform in rats that had full-thickness rotator cuff injuries. The researchers observed tissue regeneration and recovery in shoulder function. The results proved that the platform, which includes stem cells, can actually regenerate rotator cuffs.

Notably, the researchers combined tissue-specific bioimaging agents together with near-infrared fluorescence imaging to visualize this process. The researchers were able to use this technique to monitor anatomic change and regeneration processes in the animal model in real time and in a non-invasive fashion.

This platform offers a microenvironment and components similar to those of the actual tissue. Therefore, once applied to patients, it is expected to have high treatment benefits and eventual recovery of shoulder function. It is particularly beneficial for those patients who cannot use autologous tissues to regenerate rotator cuffs by providing a customized treatment option.



A graphic displaying how the researchers restored the shoulder's rotator cuffs. **Credit: POSTECH**

This study was supported by the Nano-materials Core Technology Development project of the National Research Foundation of Korea and the National Institute of Biomedical Imaging and Bioengineering (NIBIB) in the U.S.

Reference: "3D cell-printing of gradient multi-tissue interfaces for rotator cuff regeneration" by Suhun Chae, Uijung Yong, Wonbin Park, Yoo-mi Choi, In-Ho Jeon, Homan Kang, Jinah Jang, Hak Soo Choi and Dong-Woo Cho, 11 May 2022, Bioactive Materials. DOI: 10.1016/j.bioactmat.2022.05.004

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Breast cancer drug trial: Woman given months to live gets all-clear

A woman with cancer who was given less than a year to live has been told she is clear of the disease after taking part in a clinical trial.

Jasmin David, 51, of Manchester, was diagnosed with an aggressive form of breast cancer in 2017. Two years later it had spread and she

started a trial, using an experimental medicine combined with an immunotherapy drug, at The Christie hospital.

She said she felt "reborn" after scans showed no evidence of cancer.

The Christie said Ms David had found a lump above her nipple in November 2017.

She underwent six months of chemotherapy and a mastectomy in April 2018, followed by 15 cycles of radiotherapy which cleared her body of cancer.

But in October 2019 the cancer returned, and scans showed it had spread to her lung, lymph nodes and chest bone and she was told she had a poor prognosis.

'Horrible side effects'

Two months later, the mother-of-two was offered a two-year trial at The Christie of an experimental medicine combined with Atezolizumab, an immunotherapy drug.

Doctors have told her she is now showing no evidence of the disease.

"When I was offered the trial I didn't know if it would work for me, but I thought at least I could do something to help others and use my body for the next generation," Ms David said.

"At first I had many horrible side effects including headaches and spiking temperatures, so I was in hospital over Christmas and quite poorly. Then thankfully I started to respond well to the treatment.

"Two and a half years ago I thought it was the end and I now feel like I've been reborn."

Jasmin David says she has "so much to look forward to" including her 25th wedding anniversary

Ms David, who lives in Fallowfield, told BBC Radio Manchester: "I am here thanks to The Christie and to medical research."

She said after returning from India to visit her 97-year-old mother in April she decided to take early retirement and "live my life in gratitude to God and to medical science".

Ms David said it was "emotional" returning to India with the "good news" having gone two years before to say her goodbyes.

She said that she she had "so much to look forward to" including her 25th wedding anniversary in September, adding that she relished each day as "everything is a bonus".

Treatment on the clinical trial will continue until December 2023.

Prof Fiona Thistlethwaite, medical oncologist and clinical director at The Christie, who is leading the trial, said: "It is fantastic for everyone when someone responds as well to treatment as Jasmin has."

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AI Seems to Be Better at Distributing Wealth Than Humans Are, Study Hints

Artificial intelligence (AI) can devise methods of wealth distribution that are more popular than systems designed by people, new research suggests.

Peter Dockrill

The findings, made by a team of researchers at UK-based AI company DeepMind, show that machine learning systems aren't just good at solving complex physics and biology problems, but may also help deliver on more open-ended social objectives, such as the goal of realizing a fair, prosperous society.

Of course, that's not an easy task. Building a machine that can deliver beneficial results humans actually want – called "value alignment" in AI research – is complicated by the fact that people often disagree on the best method to resolve all kinds of things, and especially social, economic, and political issues.

"One key hurdle for value alignment is that human society admits a plurality of views, making it unclear to whose preferences AI should align," researchers explain in a new paper, led by first author and DeepMind research scientist Raphael Koster.

"For example, political scientists and economists are often at

loggerheads over which mechanisms will make our societies function most fairly or efficiently."

To help bridge the gap, the researchers developed an agent for wealth distribution that had people's interactions (both real and virtual) built into its training data – in effect, guiding the AI towards human-preferred (and hypothetically fairer overall) outcomes.

While AIs can produce truly amazing results, they can also arrive at far-from-desirable social conclusions when left to their own devices; human feedback can help to steer neural networks in a better direction.

"In AI research, there is a growing realization that to build human-compatible systems, we need new research methods in which humans and agents interact, and an increased effort to learn values directly from humans to build value-aligned AI," the researchers write.

In experiments involving thousands of human participants in total, the team's AI agent – called 'Democratic AI' – studied an investment exercise called the public goods game, in which players receive varying amounts of money, and can contribute their money to a public fund, and then draw a return from the fund corresponding to their level of investment.

In a series of different game styles, wealth was redistributed to players via three traditional redistribution paradigms – strict egalitarian, libertarian, and liberal egalitarian – each of which rewards player investments differently.

A fourth method was also tested, called the Human Centered Redistribution Mechanism (HCRM), developed using deep reinforcement learning, using feedback data from both human players and virtual agents designed to imitate human behavior.

Subsequent experiments showed that the HCRM system for paying out money in the game was more popular with players than any of the traditional redistribution standards, and also more popular than new redistribution systems designed by human referees who were incentivized to create popular systems by receiving small per-vote payments.

"The AI discovered a mechanism that redressed initial wealth imbalance, sanctioned free riders, and successfully won the majority vote," the researchers explain.

"We show that it is possible to harness for value alignment the same democratic tools for achieving consensus that are used in the wider human society to elect representatives, decide public policy or make legal judgements."

It's worth noting that the researchers acknowledge their system raises a number of questions – chiefly, that value alignment in their AI revolves around democratic determinations, meaning the agent could actually exacerbate inequalities or biases in society (provided they are popular enough to be voted for my a majority of people).

There's also the issue of trust. In the experiments, players didn't know the identity behind the wealth redistribution model they were paying for. Would they have voted the same way, knowing they'd be picking an AI over a person? For now, it's unclear.

Lastly, the team says its research should not be construed as a radical technocratic proposal to overthrow how wealth is actually redistributed in society – but it is a research tool that could help humans to engineer potentially better solutions than what we have now.

"Our results do not imply support for a form of 'AI government', whereby autonomous agents make policy decisions without human intervention," the authors write.

"We see Democratic AI as a research methodology for designing potentially beneficial mechanisms, not a recipe for deploying AI in the public sphere."

The findings are reported in *Nature Human Behaviour*.

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Physicists Are Startled by This Magnetic Material That 'Freezes' When Heated

Fractionally heating, the naturally occurring magnetic element neodymium freezes it

Michelle Starr

When disordered magnetic materials are cooled to just the right temperature, something interesting happens. The spins of their atoms 'freeze' and lock into place in a static pattern, exhibiting cooperative behavior not usually displayed.

Now for the first time, physicists have seen the opposite. When fractionally heated, the naturally occurring magnetic element neodymium freezes, turning all our expectations topsy turvy.

"The magnetic behavior in neodymium that we observed is actually the opposite of what 'normally' happens," said physicist Alexander Khajetoorians of Radboud University in the Netherlands.

"It's quite counterintuitive, like water that becomes an ice cube when it's heated up."

In a conventional ferromagnetic material, such as iron, the magnetic spins of the atoms all align in the same direction; that is, their north and south magnetic poles are oriented the same way in three-dimensional space. But in some materials, such as some alloys of copper and iron, the spins are instead quite random. This state is what is known as a spin glass.

You might be thinking "but neodymium is well known for making excellent magnets" and you'd be right… but it has to be mixed with iron in order for the spins to align. Pure neodymium doesn't behave like other magnets; it was only two years ago that physicists determined this material is, in fact, best described as a self-induced spin glass.

Now, it seems, neodymium is even stranger than we thought.

When you heat a material, the rise in temperature increases the energy in that material. In the case of magnets, this increases the motion of the spins. But the opposite also occurs: When you cool down a magnet, the spins slow.

For spin glasses, freezing temperature is the point at which the spin glass behaves more like a conventional ferromagnet.

Led by physicist Benjamin Verlhac of Radboud University, a team of scientists wanted to probe how neodymium behaves under changing temperatures. Interestingly, they found that raising the temperature of neodymium from -268 degrees Celsius to -265 degrees Celsius (-450.4 to -445 Fahrenheit) induced the freeze state usually seen when cooling a spin glass.

When the scientists cooled the neodymium back down, the spins once again fell into disarray.

It's unclear why this occurs, since it's very rare that a natural material behaves in the 'wrong' way, contrary to how all the other materials of its kind behave. However, the scientists believe that it may have to do with a phenomenon called frustration.

This is when a material is unable to attain an ordered state, resulting in a disordered ground state, such as we see in spin glasses.

It's possible, the researchers said, that neodymium has certain correlations in its spin glass state that are dependent on temperature. Raising the temperature weakens these, and also therefore the frustration, allowing the spins to settle into an alignment.

Further investigation could reveal the mechanism behind this odd behavior in which order emerges from disorder with the addition of energy; the researchers note this has implications ranging far beyond physics.

"This 'freezing' of the pattern does not normally occur in magnetic material," Khajetoorians explained. "If we ultimately can model how these materials behave, this could also be extrapolated to the behavior of a wide range of other materials."

The research has been published in *Nature Physics*.

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Scientists Discover First Effective Drug Treatment Against Hepatitis A

Scientists Discover Key to Hepatitis A Virus Replication, Show Drug Effectiveness

With no current treatments for hepatitis A, scientists at the University of North Carolina School of Medicine led by Stanley M. Lemon, MD, discovered how a protein and enzymes interact to allow hepatitis A virus to proliferate, and they used a known drug to stop viral replication in an animal model.

The viral replication cycle is essential for a virus to spread inside the body and cause disease. Focusing on that cycle in the hepatitis A virus (HAV), University of North Carolina (UNC) School of Medicine scientists discovered that replication requires particular interactions between the human protein ZCCHC14 and a group of enzymes called TENT4 poly(A) polymerases. They also discovered that the oral compound RG7834 stopped viral replication at a key step, preventing liver cell infection.

These findings are the first to demonstrate an effective drug treatment against HAV in an animal model of the disease. The study was published today (July 4, 2022) in the *Proceedings of the National Academy of Sciences*.

"Our research demonstrates that targeting this protein complex with an orally delivered, small-molecule therapeutic halts viral replication and reverses liver inflammation in a mouse model of hepatitis A, providing proof of principle for antiviral therapy and the means to stop the spread of hepatitis A in outbreak settings," said senior author Stanley M. Lemon, MD, professor in the UNC Department of Medicine and UNC Department of Microbiology & Immunology, and member of the UNC Institute for Global Health and Infectious Diseases.

Lemon, who in the 1970s and 80s was part of a Walter Reed Army Medical Center research team that developed the first inactivated HAV vaccine administered to humans, said research on HAV tapered off after the vaccine became widely available in the mid-1990s. Cases plummeted in the 2000s as vaccination rates skyrocketed. Researchers turned their attention to hepatitis B and C viruses, both of which are very different from HAV and cause chronic disease. "It's like comparing apples to turnips," Lemon said. "The only similarity is that they all cause inflammation of the liver." HAV is not even part of the same virus family as hepatitis B and C viruses.

Hepatitis A outbreaks have been on the rise since 2016, even though the HAV vaccine is very effective. Not everyone gets vaccinated, Lemon pointed out, and HAV can exist for long periods of time in the environment – such as on our hands and in food and water – resulting in more than 44,000 cases, 27,000 hospitalizations, and 400 deaths in the United States since 2016, according to the CDC.

Several outbreaks have occurred over the past several years, including in San Diego in 2017 driven largely by homelessness and illicit drug use, causing severe illness in about 600 people and killing 20. In 2022, there was a small outbreak linked to organic strawberries in multiple states, leading to about a dozen hospitalizations. Another outbreak in 2019 was linked to fresh blackberries. Globally, tens of millions of HAV infections occur each year. Symptoms include fever, abdominal pain, jaundice, nausea, and loss of appetite and sense of taste. Once sick, there is no treatment.

In 2013, Lemon and colleagues discovered that the hepatitis A virus changes dramatically inside the human liver. The virus hijacks bits of cell membrane as it leaves liver cells, cloaking itself from antibodies that would have otherwise quarantined the virus before it spread widely through the bloodstream. This work was published in

Nature and provided insight into how much researchers had yet to learn about this virus that was discovered 50 years ago and has likely caused disease dating back to ancient times.

A few years ago, researchers found that hepatitis B virus required TENT4A/B for its replication. Meanwhile, Lemon's lab led experiments to search for human proteins that HAV needs in order to replicate, and they found ZCCHC14 – a particular protein that interacts with zinc and binds to RNA.

"This was the tipping point for this current study," Lemon said. "We found ZCCHC14 binds very specifically to a certain part of HAV's RNA, the molecule that contains the virus's genetic information. And as a result of that binding, the virus is able to recruit TENT4 from the human cell."

In normal human biology, TENT4 is part of an RNA-modification process during cell growth. Essentially, HAV hijacks TENT4 and uses it to replicate its own genome.

This work suggested that stopping TENT4 recruitment could stop viral replication and limit disease. Lemon's lab then tested the compound RG7834, which had previously been shown to actively block Hepatitis B virus by targeting TENT4. In the *PNAS* paper, the researchers detailed the precise effects of oral RG7834 on HAV in liver and feces and how the virus's ability to cause liver injury is dramatically diminished in mice that had been genetically modified to develop HAV infection and disease. The research suggests the compound was safe at the dose used in this research and the acute timeframe of the study.

"This compound is a long way from human use," Lemon said, "But it points the path to an effective way to treat a disease for which we have no treatment at all."

The pharmaceutical company Hoffmann-La Roche developed RG7834 for use against chronic hepatitis B infections and tested it in humans in a phase 1 trial, but animal studies suggested it may be too toxic for use over long periods of time.

"The treatment for Hepatitis A would be short term," Lemon said, "and, more importantly, our group and others are working on compounds that would hit the same target without toxic effects."

Reference: "The ZCCHC14/TENT4 complex is required for hepatitis A virus RNA synthesis" 4 July 2022, Proceedings of the National Academy of Sciences.
DOI: 10.1073/pnas.2204511119

This research was a collaboration between the Lemon lab and the lab of Jason Whitmire, professor of genetics at the UNC School of Medicine. Lemon and Whitmire are members of the UNC Lineberger Comprehensive Cancer Center.
First authors of the PNAS paper are You Li and Ichiro Misumi. Other authors, all at UNC, are Tomoyuki Shiota, Lu Sun, Erik Lenarcic, Hyejeong Kim, Takayoshi Shirasaki, Adriana Hertel-Wulff, Taylor Tibbs, Joseph Mitchell, Kevin McKnight, Craig Cameron, Nathaniel Moorman, David McGivern, John Cullen, Jason K. Whitmire, and Stanley M. Lemon.
This work was supported by grants from the National Institute of Allergy and Infectious Diseases (R01-AI131685), (R01-AI103083), (R01-AI150095), (R21-AI163606), (R01-AI143894), (R01-AI138337). The UNC Pathology Services Core and UNC High-Throughput Sequencing Facility were supported in part by a National Cancer Institute Center Core Support Grant (P30CA016086) to the UNC Lineberger Comprehensive Cancer Center.

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Intense Exercise Can Increase Your Risk of Catching Infectious Diseases Like COVID-19

The relationship between exercise intensity and infection risk

The relationship between exercise intensity and the emission and concentration of aerosol particles in exhaled air has not been well understood up to this point. A Munich research team has shown using a unique experimental setup that aerosol emissions rise exponentially with high levels of physical activity. This means indoor athletic events have an increased risk of infectious diseases like COVID-19.

Before the research, it was known that untrained individuals' respiratory volumes rise during exercise from 5 to 15 liters per minute at rest to over 100 liters per minute. In fact, well-trained athletes can reach 200 l/min levels. It was also recognized that a lot of individuals had contracted the SARS-CoV-2 virus while working

out indoors.

However, it was unclear how exercise intensity was related to the number of aerosols that a person actually inhaled per minute and the concentration of aerosol particles in exhaled air, and thus the potential danger of transmitting infectious diseases like SARS-CoV-2. However, this knowledge is urgently required, for instance, to build mitigation measures for school gyms and other indoor sports facilities, fitness studios, or discos to prevent a shutdown in case of major waves of infection.

The new methodology delivers individually measurable aerosol values

A team led by Henning Wackerhage, a Professor of Exercise Biology at the Technical University of Munich (TUM), and Prof. Christian J. Kähler, the Director of the Institute of Fluid Mechanics and Aerodynamics at the Universität der Bundeswehr München, has developed a new investigative method for studying these questions.

Their experimental apparatus initially filtered out the aerosols already present in the ambient air. In the subsequent ergometer stress test, the test subjects inhaled the purified air through a special mask covering the mouth and nose. The exercise intensity was gradually increased from rest to the point of physical exhaustion. The mask was connected to a two-way valve through which only the exhaled air can escape.

The number of aerosol particles emitted per minute was then measured and directly linked to the current performance of the healthy, 18-40-year-old test subjects.

Moderate aerosol emissions at medium exertion

The researchers were thus able to investigate for the first time how many aerosol particles are exhaled per minute by an individual at various levels of exercise intensity. The result: aerosol emissions during exercise initially increased only moderately up to an average workload of around 2 watts per kilogram of body weight. Above that point, however, they rose exponentially. That means that an individual who weighs 75 kilograms reaches that threshold at an ergometer reading of around 150 watts. This corresponds to moderate effort for a casual athlete, perhaps comparable to the exercise intensity of moderate jogging.

The aerosol emissions of well-trained athletes were significantly higher than those of untrained test subjects at maximum effort due to their much higher minute ventilation. The researchers did not find significant differences in particle emissions between genders.

Protective measures are important for high-intensity training

Although the aerosol experiments provide only indirect knowledge on the number of viruses in exhaled air, the study suggests useful starting points for managing indoor activities when a wave of infection combined with a poorly immunized population threatens to overwhelm the healthcare system.

“Based on our results, we distinguish between moderate endurance training with an intensity of up to 2 watts per kilogram of body weight and training at high to maximum intensity. Due to the sharp rise in aerosol emissions at high-intensity workloads above that initial benchmark, special protective measures are needed in case of a high risk of infections with serious consequences,” says study leader Prof. Wackerhage: “Ideally, that kind of training would be moved outdoors. If that is not possible, testing should be done to ensure that no infected individuals are in the room. The participants should also maintain a proper distance and a high-efficiency ventilation system should be running. In addition, infection risks are reduced by training at lower intensities and keeping sessions shorter. It might also be possible for fit, young athletes to wear masks while training.” At low workloads such as easy to moderately intense endurance training, adds Prof. Wackerhage, less protection is needed and the infection risk can be controlled through

distancing and ventilation systems.

The research team is currently conducting experiments to compare aerosol emissions in strength and endurance training and to correlate them with test subjects' ages and physical characteristics.

The study was funded by the German Federal Institute of Sports Science (BISp) and the German Research Foundation (DFG).

Reference: "Aerosol particle emission increases exponentially above moderate exercise intensity resulting in superemission during maximal exercise" by Benedikt Mutsch, Marie Heiber, Felix Grätz, Rainer Hain, Martin Schönfelder, Stephanie Kaps, Daniela Schranner, Christian J. Kähler and Henning Wackerhage, 23 May 2022, Proceedings of the National Academy of Sciences.

DOI: 10.1073/pnas.2202521119

https://go.nature.com/3OV2vkn

Revealed: the pay bump for being a straight, white man in US science

Study reveals the vast disparity in salary, respect and opportunities between people from marginalized groups and their privileged peers.

Clare Watson

A large, comprehensive study reveals what privilege looks like in science: straight, white men who are not disabled get more pay, greater respect and a wealth of career opportunities compared with all other groups.

Past studies have shown how sexism, racism and other types of discrimination separately contribute to inequality in academia. But sociologist Erin Cech at the University of Michigan in Ann Arbor compared the experiences of researchers who fit along a spectrum of 32 intersecting identities. She analysed data from a survey of roughly 25,300 researchers working in sectors including academia, industry and government in the United States, conducted between 2017 and 2019. The study was published in *Science Advances* last month[1].

Cech, who describes herself as a white, queer cisgender woman, says the results reveal consistent, striking patterns of privilege that persist after adjustment for differences in education, experience, hours worked, family responsibilities and more than a dozen other confounding factors. Heterosexual, white men without disabilities enjoy a raft of unearnt benefits that cannot be accounted for by such differences, the analysis shows. They get paid an average of US$7,831 a year more than other groups, adjusting for confounding factors. They are also granted more career opportunities, feel more respected at work and experience less harassment than people in every other intersecting demographic group that Cech studied, and so are less likely to leave science.

"Time and time again, I've heard [people say] there's no data to prove" that privilege exists, says Jessica Esquivel, a particle physicist at Fermi National Accelerator Laboratory in Batavia, Illinois. Now, marginalized groups have hard data that they can point to and say, "here, this is what you've been asking for. Now what?" says Esquivel, a Black, queer, neurodivergent, Mexican woman.

More money, more respect

Straight, white men without disabilities received at least an extra US$32,000 each year compared with queer people of colour who had the same level of experience, tenure, hours worked, family responsibilities, education and other factors, Cech found. The most privileged group also earnt US$20,000 a year more than disabled people of any gender, ethnicity or sexual identity.

Kelsey Byers, an agender, asexual and multiply disabled plant biologist, who works at the John Innes Centre in Norwich, UK, says the disadvantage that marginalized groups face is distressing, and the salary gap shocking: "As someone who has struggled to literally get in the door, [the findings] were a gut punch, but one I know is true."

Cech found that the groups that are most disadvantaged are LGBTQ-identifying women of colour, and people with a physical

disability, chronic illness or mental-health condition. People in these groups had lower salaries and fewer career opportunities, garnered less respect from colleagues and often felt excluded — even when their education, experience and job characteristics equalled those of their straight, white, male, non-disabled peers.

Christopher Jackson, a Black geoscientist based in the United Kingdom, says Cech's study shows how identity and circumstance determines who gets to participate in science. "Being smart isn't enough," he says, because not everyone is given the same access to opportunities or peer support to help them to achieve what they wish. Many of the barriers that some people have to contend with also go mostly unseen, adds Jackson, who left academia in March to join a scientific consulting firm.

Esquivel hopes the data from Cech's study will help to counter something she has experienced — researchers from privileged groups questioning whether marginalized scientists hired under diversity initiatives deserve their places in academia. People who are not marginalized need to reflect on how privilege has made their careers easier, she says.

Culture change

Structural and cultural changes are needed to rectify the inequalities that contribute to people from minority groups leaving science, says sociologist Meredith Nash at the Australian National University in Canberra. "You can't bring people from historically excluded groups into these fields [and expect them to stay] without creating an environment for them to thrive," she says.

To create more equitable workplaces, Nash says, institutions and their leaders must overhaul processes that give unfair advantage to particular groups of people. She says that white, cisgender women such as herself often benefit from equity initiatives, also need to reflect on their privilege and use it to advocate in favour of greater diversity. That means taking a critical eye to hiring and promotion practices, and rethinking how academia recognizes and rewards research excellence, says Cech. Given that systemic advantages are anchored in the historical over-representation of white men in science, structural and cultural change starts with that group, she adds. White men who are willing to reflect on and discuss these forms of privilege wield real influence, she says.

But past research has found that many white males in some fields claim to be unaware of racism or sexism around them, despite evidence that their field can be a particularly hostile environment for women and people from minority groups. In a survey of physicists, white men often distanced themselves from the problem, saying that it didn't occur in their laboratories, and that the solutions lay outside their sphere of influence.

That attitude propagates inequalities, says Timothy O'Connor, a disabled, white man and an evolutionary geneticist at the University of Maryland School of Medicine in Baltimore. "We need to constantly be vigilant in addressing bias wherever we see it, even and especially in ourselves." He adds, however, that more work needs to be done to appreciate the manifold experiences of researchers with diverse identities within groups that were "lumped together" in Cech's study. For example, in its main analyses, the study did not distinguish between people with different types of disability or between those with varying LGBTQ identities. It also used broad ethnic divisions with little nuance, such as "Asian". Cech says this was to protect respondent confidentiality.

Patterns of disadvantage and privilege are seeded long before people embark on careers in science, says Mohammad Taha, a materials engineer at the University of Melbourne, Australia, who identifies as a non-binary, transgender, queer person of colour. Academia needs to do a better job of measuring the performance of people who have experienced disadvantage. Many of these people

will not have had the same opportunities as their majority-group peers, and need to be judged accordingly when applying for jobs and funding, Taha says.

They add that many researchers have a genuine interest in making academia more inclusive, but fail to act. “Your inaction isn’t neutral; your inaction is contributing to this problem.”

doi: https://doi.org/10.1038/d41586-022-01851-4

References *1. Cech, E. A. Sci. Adv.* ***8****, eabo1558 (2022).* *PubMed* *Article* *Google Scholar*

https://bit.ly/3nN4HP3

Ozone Destruction Over North Pole Produces Weather Anomalies Across the Entire Northern Hemisphere

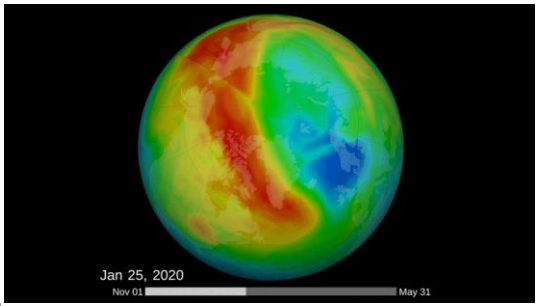
Weather abnormalities occur over the whole northern hemisphere whenever the ozone layer over the north pole thins out

Many people are aware of the hole in the ozone layer over Antarctica, but what is less widely known is that the protective ozone in the stratosphere over the Arctic is periodically destroyed as well, thinning the ozone layer there. This last happened in the spring of 2020, and before that, in the spring of 2011.

Climate scientists have seen weather abnormalities over the whole northern hemisphere every time the ozone layer over the north pole has been thinned out. Those spring seasons were unusually warm and dry throughout central and northern Europe, Russia, and especially in Siberia. However, in other areas, such as polar regions, wet conditions prevailed. These weather anomalies were particularly pronounced in 2020. That spring in Switzerland was also abnormally warm and dry.

In climate research, it is a matter of debate whether there is a causal relationship between stratospheric ozone destruction and the observed weather anomalies. A role is also played by the polar vortex in the stratosphere, which forms in winter and decays in spring. Researchers who have investigated the phenomenon so far have arrived at contradictory results and different conclusions.

New findings are now shining light on the situation, thanks to doctoral student Marina Friedel and Swiss National Science Foundation Ambizione Fellow Gabriel Chiodo. Both are members of the research group headed by Thomas Peter, Professor of Atmospheric Chemistry at ETH Zurich, and are collaborating with Princeton University and other institutions.



False-color view of total ozone over the Arctic pole during the beginning of 2020. The purple and blue colors are where there is the least ozone, and the yellows and reds are where there is more ozone. **Credit: NASA Ozone Watch**

Simulations reveal correlation

To uncover a possible causal relationship, the scientists ran simulations that integrated ozone depletion into two different climate models. Most climate models consider only physical factors, not fluctuations in stratospheric ozone levels, in part because this would require much more computing power.

However, the new calculations make it clear: the cause of the weather anomalies observed in the northern hemisphere in 2011 and 2020 is mostly ozone depletion over the Arctic.

The simulations the scientists ran with the two models largely coincided with observational data from those two years, as well as eight other such events that were used for comparison purposes. But when the scientists “turned off” ozone destruction in the models, they could not reproduce those results.

“What surprised us most from a scientific point of view is that, even though the models we were using for the simulation are utterly different, they produced similar results,” says co-author Gabriel Chiodo, SNSF Ambizione Fellow at the Institute for Atmospheric and Climate Science.

The mechanism explained

According to the researchers' new understanding, the phenomenon begins with ozone depletion in the stratosphere. For ozone to be broken down there, temperatures in the Arctic must be very low. "Ozone destruction occurs only when it is cold enough and the polar vortex is strong in the stratosphere, about 30 to 50 kilometers above the ground," Friedel points out.

Normally, ozone absorbs UV radiation emitted by the sun, thereby warming the stratosphere and helping to break down the polar vortex in spring. But if there is less ozone, the stratosphere cools and the vortex becomes stronger. "A strong polar vortex then produces the effects observed at the Earth's surface," Chiodo says. Ozone thus plays a major role in temperature and circulation changes around the North Pole.

Greater accuracy possible for long-term forecasts

The new findings could help climate researchers make more accurate seasonal weather and climate forecasts in the future. This allows for better prediction of heat and temperature changes, "which is important for agriculture," Chiodo says.

Friedel adds, "It will be interesting to observe and model the future evolution of the ozone layer." This is because ozone depletion continues, even though ozone-depleting substances such as chlorofluorocarbons (CFCs) have been banned since 1989. CFCs are very long-lived and linger in the atmosphere for 50 to 100 years; their potential to cause ozone destruction lasts for decades after they have been taken out of circulation. "Yet CFC concentrations are steadily declining, and this raises the question of how quickly the ozone layer is recovering and how this will affect the climate system," she says.

Reference: "Springtime arctic ozone depletion forces northern hemisphere climate anomalies" 7 July 2022, Nature Geoscience. DOI: 10.1038/s41561-022-00974-7

https://wb.md/3ysRCiG

Scientists Find Brain Mechanism Behind Age-Related Memory Loss

Discovery expands our knowledge of inner workings of the aging brain and possibly opens the door to new Alzheimer's treatments

Lisa Jhung

Scientists at Johns Hopkins University have identified a mechanism in the brain behind age-related memory loss, expanding our knowledge of the inner workings of the aging brain and possibly opening the door to new Alzheimer's treatments.

The researchers looked at the hippocampus, a part of the brain thought to help store long-term memories.

Neurons there are responsible for a pair of memory functions – called pattern separation and pattern completion – that work together in young, healthy brains. These functions can swing out of balance with age, impacting memory.

The Johns Hopkins team may have discovered what causes this imbalance. Their findings – reported in a new paper in the journal *Current Biology* – may not only help us improve dementia treatments, but even prevent or delay a loss of thinking skills in the first place, the researchers say.

Pattern Separation vs Pattern Completion

To understand how the hippocampus changes with age, the researchers looked at rats' brains. In rats and in humans, pattern separation and pattern completion are present, controlled by neurons in the hippocampus.

As the name suggests, pattern completion is when you take a few details or fragments of information – a few notes of music, or the start of a famous movie quote – and your brain retrieves the full memory. Pattern separation, on the other hand, is being able to tell similar observations or experiences apart (like two visits to the same restaurant) to be stored as separate memories.

These functions occur along a gradient across a tiny region called CA3. That gradient, the study found, disappears with aging, says lead study author Hey-Kyoung Lee, PhD, an assistant research scientist at the university's Zanvyl Krieger Mind/Brain Institute. "The main consequence of the loss," Lee says, "is that pattern completion becomes more dominant in rats as they age."

What's Happening in the Brain

Neurons responsible for pattern completion occupy the "distal" end of CA3, while those in charge of pattern separation reside at the "proximal" end. Lee says prior studies had not examined the proximal and distal regions separately, as she and her team did in this study.

What was surprising, says Lee, "was that hyperactivity in aging was observed toward the proximal CA3 region, not the expected distal region." Contrary to their expectations, that hyperactivity did not enhance function in that area but rather *dampened* it. Hence: "There is diminished pattern separation and augmented pattern completion," says Lee.

As pattern completion dominates, pattern separation fades, Lee says. This may make it harder for older adults to separate memories – they may recall a certain restaurant they'd been to but not be able to separate what happened during one visit versus another.

Why Do Some Older Adults Stay Sharp?

But that memory impairment does not happen to everyone, and it doesn't happen to all rats either. In fact, the researchers found that some older rats performed spatial-learning tasks as well as young rats did – even though their brains were already beginning to favor pattern completion.

If we can better understand why this happens, we may uncover new therapies for age-related memory loss, Lee says.

Co-author Michela Gallagher's team previously demonstrated that the anti-epilepsy drug levetiracetam improves memory performance by reducing hyperactivity in the hippocampus.

The extra detail this study adds may allow scientists to better aim such drugs in the future, Lee speculates. "It would give us better control of where we could possibly target the deficits we see."

Sources

Hey-Kyoung Lee, PhD, assistant research scientist, Zanvyl Krieger Mind/Brain Institute, Johns Hopkins University. -- Current Biology: "Loss of functional heterogeneity along the CA3 transverse axis in aging."

https://bit.ly/3IvDkmq

Researchers seem to stumble across an electrolyte for a sodium battery

Sodium is cheap and plentiful, but its use in batteries brings some challenges.

John Timmer

Lithium-based batteries are great, with different electrode chemistries allowing them to be slotted into a variety of uses. The problem with them has nothing to do with their performance. The challenge we face is that we want to make a *lot* of batteries; if all of them use lithium, we're undoubtedly going to face supply crunches.

One potential solution to that is to simply replace lithium with a different ion. Alternative batteries may not be as good as lithium variants in all the different places we currently use them. They just have to be good enough at one task to take away some of the need to stick lithium everywhere.

That's the reasoning behind some interest in sodium-based batteries. Sodium is very plentiful and correspondingly cheap and can be made to behave a bit like lithium when used in a battery. But sodium batteries always carry risks associated with sodium's tendency to react explosively. But a recently developed solid electrolyte suggests that at least some of the challenges associated with sodium could be overcome.

An accidental electrolyte

There are a number of battery technologies that are based on

sodium, like sodium-sulfur batteries, that have little in common with lithium batteries. But sodium-ion batteries work based on more or less the same principles as lithium-ion and can even use some of the same materials, like carbon-based electrodes. Sodium is heavier, so sodium-ion batteries can't really reach the same energy-per-weight levels that lithium can. But again, sodium is plentiful and cheap, so sodium batteries might make sense in cases where weight isn't critical, like home- and grid-level storage.

The big hang-up here is the sodium itself. Many lithium-based batteries use an aqueous electrolyte to get the ions between the two electrodes. And sodium is not noted for getting along well with water. In fact, it reacts energetically to release hydrogen, which then explodes. Fire hazards are problematic with the non-aqueous electrolytes in lithium batteries; add sodium's reactivity with the environment, and the hazards are severe.

So, the electrolyte appears to be a reasonable target for research. This is somewhat surprising because the research team seems to have stumbled across the electrolyte by accident. The researchers reference their work for the synthesis of the electrolyte and, if you chase that reference down, you'll find it's talking about an MRI contrast agent. It's not exactly clear how someone came up with the idea of trying it in batteries, but here we are.

The electrolyte itself is what's called a block copolymer. These are molecules that are built out of two different classes of subunits. The polymerization process is controlled in such a way that you end up with stretches of the polymer made of repeats of one subunit alternating with stretches composed of the other. (Those stretches are called blocks, giving the material its name.)

In this case, one of the two blocks was based on a carbon/sulfur compound; this polymer alone served as a control material. For the block copolymer, the second block was a hydrocarbon with most of the hydrogens swapped out for fluorine atoms. The idea behind the fluorine was to avoid a situation that occurred with related electrolytes, where the sodium ended up interacting with oxygens in the polymer and therefore getting stuck in it instead of moving through.

While the block copolymer is solid, it does undergo a transition from glass to plastic at temperatures that are likely to occur during battery operations. In either state, it tends to form distinct domains based on the two different blocks, with the fluorinated material creating internal channels that can accommodate sodium and the other blocks providing structural integrity.

How's it work?

The researchers spend a lot of the paper simply cycling sodium into and out of the polymer and seeing what happens. This tended to create a layer of sodium on the surface of the material—a bit like electroplating it. It's important to note that the sodium formed a smooth surface on the polymer. On the control polymer, by contrast, dendrites of sodium with sharp edges formed. That's significant because dendrite formation is a major point of failure for lithium-ion batteries.

The key thing is that this process remained reversible; the plating of sodium on the polymer could be reversed and then plated again. Performance remained good for over 200 cycles of sodium in and out.

So, they went ahead and built two different batteries. For both batteries, one electrode was simply sodium metal (an approach that's being developed for lithium, as it'll greatly increase the charge per weight). The other electrode stored sodium in either a sodium-vanadium phosphate material or sodium iron phosphate. Both batteries worked. Performance dropped slightly as the charge/discharge current was boosted, but this didn't result in permanent damage to the polymer; dropping the current restored the previous performance.

But the main thing was the stability. After over 900 cycles, it still had over 97 percent of the battery's initial capacity.

None of which is to say that sodium batteries are guaranteed to be the next big thing. Any battery that involves a sodium metal electrode is going to involve some pretty significant engineering costs to maintain safety—engineering that might offset some of the cost savings of using sodium and weight savings of having a metal electrode. But the important thing is less about having mature technology now, so much as having a variety of battery chemistries under development by the time existing battery production scales to the point where lithium becomes a limiting factor.

Nature Materials, 2022. DOI: 10.1038/s41563-022-01296-0 (About DOIs).

https://wb.md/3OV87er

Can Bone Density Scans Help Predict Dementia Risk?

Bone densitometry scans may be a novel, noninvasive, and scalable way to identify older women at risk of developing dementia, new research suggests.

Megan Brooks

In an analysis of more than 900 study participants, women in their 70s with more advanced abdominal aortic calcification (AAC) seen on lateral spine images during dual-energy x-ray absorptiometry (DEXA) had a two- to fourfold higher risk for late-life dementia than those with low AAC. This finding was independent of cardiovascular risk factors and apolipoprotein E (*APOE*) genotype.

"While these results are exciting, we now need to undertake further large screening studies in older men and women using this approach to show that the findings are generalizable to older men and can identify people with greater cognitive decline," co-investigator Marc Sim, PhD, Edith Cowan University, Joondalup, Australia, told *Medscape Medical News*.

"This will hopefully open the door to studies of early disease-modifying interventions," Sim said. The findings were published online June 26 in *Lancet Regional Health — Western Pacific.*

AAC and Cognition

Late-life dementia occurring after age 80 is increasingly common because of both vascular and nonvascular risk factors.

Two recent studies in middle-aged and older men and women showed that AAC identified on bone densitometry was associated with poorer cognition, suggesting it may be related to cognitive decline and increased dementia risk.

This provided the rationale for the current study, Sim noted.

The researchers assessed AAC using DEXA lateral spine images captured in the late 1990s in a prospective cohort of 958 older women who were participating in an osteoporosis study.

AAC was classified into established low, moderate, and extensive categories. At baseline, all women were aged 70 and older, and 45% had low AAC, 36% had moderate AAC, and 19% had extensive AAC. Over 14.5 years, 150 women (15.7%) had a late-life hospitalization and/or died.

Improved Risk Prediction

Results showed that, compared with women who had low AAC, women with moderate and extensive AAC were more likely to experience late-life dementia hospitalization (9.3% low, 15.5% moderate, and 18.3% extensive) and death (2.8%, 8.3%, and 9.4%, respectively).

After multivariable-adjustment, women with moderate AAC had a two- and threefold increased relative risk for late-life dementia hospitalization or death compared with their peers who had low AAC. Women with extensive AAC had a two- and fourfold increase in the adjusted relative risk for late-life dementia hospitalization or death.

"To our knowledge this is the first time it has been shown that AAC from these scans is related to late-life dementia," Sim said.

"We demonstrated that AAC improved risk prediction in addition to cardiovascular risk factors and *APOE* genotype, a genetic risk factor for Alzheimer's disease, the major form of dementia," he added. Sim noted "these additional lateral spine images" can be taken at the same time that hip and spine bone density tests are done. "This provides an opportunity to identify AAC in large numbers of people," he said.

He cautioned, however, that further studies with detailed dementia-related phenotypes, brain imaging, and measures of cognition are needed to confirm whether AAC will add value to dementia risk prediction.

"Not Surprising"

Commenting on the findings for *Medscape Medical News*, Claire Sexton, DPhil, senior director of scientific programs and outreach at the Alzheimer's Association, noted that AAC is a marker of atherosclerosis and is associated with vascular health outcomes.

Therefore, it is "not surprising it would be associated with dementia too. There's been previous research linking atherosclerosis and Alzheimer's disease," Sexton said.

"What's novel about this research is that it's looking at AAC specifically, which can be identified through a relatively simple test that is already in widespread use," she added.

Sexton noted that "much more research" is now needed in larger, more diverse populations in order to better understand the link between AAC and dementia — and whether bone density testing may be an appropriate dementia screening tool.

"The good news is vascular conditions like atherosclerosis can be managed through lifestyle changes like eating a healthy diet and getting regular exercise. And research tells us what's good for the heart is good for the brain," Sexton said.

The study was funded by Kidney Health Australia, Healthway Health Promotion Foundation of Western Australia, Sir Charles Gairdner Hospital Research Advisory Committee Grant, and the National Health and Medical Research Council of Australia.

Sim and Sexton have reported no relevant financial relationships.

Lancet Reg Health West Pac. Published online June 26, 2022. Full text

https://bit.ly/3uzNUme

Mass layoff looms for Japanese researchers

Thousands could see their jobs axed in the wake of labor law adopted a decade ago

By Dennis Normile

Thousands of researchers at Japanese institutes and universities may see their jobs disappear by next spring, an unintended result of labor legislation adopted a decade ago that gave researchers who have worked under fixed-term contracts for more than 10 years the right to permanent employment. Japan's science system has many such temporary workers—but rather than fully hire them, institutions are terminating their jobs.

Scientists are trying to head off the lay-offs; the union for RIKEN, Japan's network of nationally supported laboratories, filed a protest with a Tokyo labor board last month and may take legal action. Regardless of the outcome, the dispute could create more upheaval in a research system whose global impact is already waning. "We are on the verge of seeing a possible mass dismissal of researchers this year," Tomoko Tamura, a member of the legislature's upper house, said during a May parliamentary question time on the issue. Tamura's analysis of government data suggests up to 4500 researchers are at risk, which "could have a serious long-term impact on Japan's research and development," she said.

Japan's R&D funding grew rapidly in the 1990s and 2000s, but many newly recruited researchers were hired under fixed-term contracts, which offer lower pay, fewer benefits, and less job security than permanent jobs. The scheme gave research institutions more flexibility—but in practice, most fixed-term contracts were renewed indefinitely.

RIKEN is a prime example. Thirty years ago, it had about 400

researchers, most of them permanent employees working on basic physics and chemistry at the main campus near Tokyo. In the mid-1990s, Japan set out to roughly double government spending on research within 5 years, but the National Personnel Authority resisted increasing the number of employees on the national government payroll. Instead, RIKEN used project funds to hire many fixed-term employees. Today RIKEN has programs in brain science, quantum computing, and preventive medicine scattered among 10 branches and campuses, and it runs a powerful synchrotron and a petascale supercomputer. But 77% of its 2893 current researchers are fixed-term workers.

Legislation adopted in 2013 and amended in 2014 gave most contract employees the right to request permanent employment after working for the same employer for 5 years; for researchers, the term was set to 10 years. Many employers have responded by making sure contract workers never accumulate that duration of service.

RIKEN took that step in 2016, specifying that the count of years served starts in 2013. That means contract researchers who have already worked for RIKEN for more than 10 years may face termination next year. In an email to *Science*, RIKEN says 203 fixed-term researchers will reach the end of their final contracts before the end of March 2023. The institute is currently screening them and expects to make an unspecified number permanent employees, but many will have to leave. Among the vulnerable scientists are 42 team leaders whose groups will be disbanded if they go, which puts another 177 positions at risk. RIKEN says it hopes those who are forced out "will be able to continue their research activities at universities, research institutes, and private companies in Japan and overseas."

Applying an employment policy adopted in 2016 retroactively to those who have already worked under contract for 10 or more years, is "illegal," says Yasuyuki Kanai, the executive committee chairman of RIKEN's labor union. He says the researchers have a right to continued employment. Unhappy with the way RIKEN negotiated, the union on 20 June formally asked a governmental labor relations board to order the agency to bargain in good faith. With union support, "researchers are now preparing to take the matter to court," Kanai says. The union notes that fresh cohorts of several dozen fixed-term researchers annually will reach the term limit in the years ahead.

Other institutions face similar problems, although few have as many temporary contracts as RIKEN. Some are trying to find ways to retain their workers. The National Institute of Advanced Industrial Science and Technology has converted to permanent status all 245 fixed-term contractors who applied for it, according to press reports. Tohoku University is reportedly screening 275 fixed-term researchers for possible permanent employment. At the University of Tokyo, which has 588 fixed-term employees approaching 10 years of service, some might be moved to new projects, a spokesperson says, without providing details.

The broader problem is a scarcity of opportunities for researchers to change jobs in Japan, says Eisuke Enoki, who heads an Osaka-based organization that studies science policy. "The originally envisioned ideal was for academics to become assistant professors after one or two postdocs and to gain a permanent position if tenure is approved," he says. But a tenure system has never taken hold, and there are few permanent positions, even for team leaders with good track records, Enoki says.

A senior scientist at RIKEN who asked not to be identified agrees. His final contract is ending and it's "very difficult to find a new position," he says: "If I get a job in China, Korea, or Taiwan, I will move." The crisis underscores that for young people, in Japan "being a researcher is not an attractive profession," he adds.

https://wb.md/3yr5XfO

Virus Evolved in Patient Who Had COVID for 471 Days

A Connecticut cancer patient had COVID-19 for at least 471 days, and the virus appeared to evolve into several new lineages, researchers at Yale University say in a new study.

Jay Croft

The findings show that "untreated chronic infections accelerate SARS-CoV-2 evolution, ultimately providing opportunity for the emergence of genetically divergent and potentially highly transmissible variants as seen with Delta and Omicron," the study says.

Scientists following COVID-19 variants found a lineage called B.1.517 in Connecticut after it stopped appearing much elsewhere. They traced it back to the cancer patient, in his or her 60s, who has lymphoma.

That person tested positive for COVID-19 from November 2020 through at least March of this year, the study says.

The patient had only a few mild symptoms at the beginning and was almost entirely free of Covid-19 symptoms during the period.

The patient was infectious with high viral loads throughout most of the period, according to NBC News.

"The patient continues to test positive for SARS-CoV-2 471 days and counting after the initial diagnosis," the study says.

During the observed time, the virus evolved in the patient, presenting three distinct lineages.

Researchers found the virus evolving at two times the speed inside this patient as it does generally.

The study has not been peer reviewed.

Sources:

MedRxiv: "Accelerated SARS-CoV-2 intrahost evolution leading to distinct genotypes during chronic infection"

NBC: "Connecticut Patient Had COVID for 471 Days, Evolved 3 New Lineages: Study"

https://lat.ms/3OVtj4c

Multipronged vaccine protects against COVID virus family members — even some still in hiding

Researchers at Caltech have devised an experimental vaccine that targets an array of coronaviruses and variants in a single shot.

By Corinne Purtill, Melissa Healy

Long before COVID-19 transformed daily life, scientists were aware of the possibility that a coronavirus could make the leap from an animal species to the human population.

How different the last few years might have been had a vaccine capable of blocking the SARS-CoV-2 virus been administered to workers at the Huanan Market in Wuhan, China — where, scientists suspect, a raccoon dog infected a vendor and set off a pandemic that has killed more than 6.3 million people around the globe.

A new type of vaccine developed at Caltech aims to ward off novel coronaviruses even before health officials are aware that they exist. When tested in mice and monkeys, it trained the animals' immune systems to recognize eight viruses at once — and induced immunity to viruses they had never encountered.

The findings, published Tuesday in the journal Science, could lead to a powerful tool against a virus that mutates too quickly to be contained with current vaccines. An international vaccine foundation has pledged $30 million to begin clinical trials of the experimental vaccine in humans.

"We've had three pandemics or epidemics in the past 20 years: first SARS, then MERS, then SARS-CoV-2," said Caltech biochemist Pamela Bjorkman, who led the new work. More outbreaks sparked by "spillover events" are inevitable, she said, and "we want to protect now against the future spillover."

Dr. Anthony Fauci, President Biden's chief advisor on the COVID-19 pandemic, praised the research as "a major conceptual step

toward a pan-coronavirus vaccine."

"It's a very, very important proof of concept," he said, noting that it remains to be seen whether it works as well in humans as it has in lab animals. "That's why you do the experiment."

The new vaccine doesn't block all coronaviruses, an ambitious goal not yet within science's grasp. Instead, it focuses on the group known as betacoronaviruses, which includes those that cause COVID-19, severe acute respiratory syndrome and Middle East respiratory syndrome, among other diseases.

Rather than using a piece of inactivated virus or a lab-created molecule designed to mimic one found in nature, the Caltech researchers created a microscopic speck of matter that they could adorn as they pleased. Their nanoparticle is composed of proteins with sticky bits on their surfaces, to which researchers can attach even tinier bits of viruses.

The team tested three versions of the nanoparticle. One was covered with pieces of SARS-CoV-2. A "mosaic" version had SARS-CoV-2 plus samples of seven other coronaviruses, including one that causes MERS and other strains found in bats and pangolins. The last one was bare, to serve as a control.

When looking for pieces of viruses to clip and attach, the team zeroed in on a section of the spike protein called the receptor binding domain, or RBD. This is the part that's typically targeted by the immune system's neutralizing antibodies, whether they've been generated in response to a vaccine or a previous infection.

Given that the RBDs of betacoronaviruses share many characteristics, the researchers hoped that the mosaic version would prompt the immune system to focus on parts common to all eight viruses. They further theorized that if these parts were shared across most or all betacoronaviruses, the vaccine would trigger an immune response when presented with any member of the viral group — even those that weren't among the samples.

They were right.

As they designed their mosaic nanoparticle, they deliberately left out SARS-CoV, the virus responsible for severe acute respiratory syndrome. If the vaccine worked as intended, animals vaccinated with the mosaic nanoparticle, then exposed to SARS-CoV, would mount an immune response.

They did. In fact, the vaccinated mice and monkeys had little to no detectable virus in their systems despite attempts to infect them with either SARS-CoV or SARS-CoV-2.

"We're very excited about that," Bjorkman said.

That wasn't the case with the animals injected with the bare nanoparticle — they weren't able to fight off any viruses and died. The animals that received the vaccine with pieces of SARS-CoV-2 only were protected against that virus but had no protection against any other coronavirus, and most of them died as well.

If the mosaic vaccine works as well in humans as it did in animals, it could offer protection against the betacoronaviruses we know about, as well as related ones that have yet to make the leap to humans. That prospect is promising but far from certain.

The next step is a Phase 1 clinical trial in humans, the first hurdle to cross when bringing a new drug or vaccine to market in the U.S. That will take place at Oxford University, home to Bjorkman's collaborators on the project, and will likely take at least a year.

The Coalition for Epidemic Preparedness Innovations said Tuesday that it will foot the bill for the initial trial, with the goal of establishing evidence that the vaccine is safe in humans.

"It's certainly encouraging," said Dr. Paul Offit, a virologist and immunologist at the University of Pennsylvania. "But these are animal model studies, and as is well known among scientists, mice lie and monkeys exaggerate."

"It's hard to make universal vaccines work," Offit added. "It's not for want of money. It's not for want of desire or effort. It's just a

very hard thing to do."

This isn't the only team in the U.S. exploring nanoparticle vaccines for coronaviruses. Researchers at Duke University and the Walter Reed Army Institute of Research are investigating them as well.

"These general approaches all use the receptor binding domain to elicit strong antibody responses that can neutralize the virus, so they all have some promise," said Dr. Stanley Perlman, a virologist and immunologist at the University of Iowa who specializes in betacoronaviruses.

"This is a good approach based on what we know," he said, "and one has to hope that it'll be useful for viruses that we haven't identified yet."

https://bit.ly/3Iq4MBC

1.2-Billion-Year-Old Groundwater System Found in South African Mine

Geologists have discovered 1.2-billion-year-old groundwater about 3 km below surface in Moab Khotsong, a gold- and uranium-producing mine in South Africa.

This ancient groundwater is enriched in the highest concentrations of radiogenic products yet discovered in fluid. The discovery have implications beyond Earth, where on rocky planets such as Mars, subsurface water may persist on long timescales despite surface conditions that no longer provide a habitable zone.

Uranium and other radioactive elements naturally occur in the surrounding host rock that contains mineral and ore deposits.

These elements hold new information about the groundwater's role as a power generator for chemolithotrophic, or rock-eating, groups of co-habitating microorganisms previously discovered in the Earth's deep subsurface.

When elements like uranium, thorium and potassium decay in the subsurface, the resulting alpha, beta, and gamma radiation has ripple effects, triggering what are called radiogenic reactions in the surrounding rocks and fluids.

At Moab Khotsong, a gold and uranium mine located in the Witwatersrand Basin, within the Kaapvaal Craton, South Africa, University of Toronto researcher Oliver Warr and colleagues found large amounts of radiogenic helium, neon, argon and xenon, and an unprecedented discovery of krypton-86 — a never-before-seen tracer of this powerful reaction history.

The radiation also breaks apart water molecules in a process called radiolysis, producing large concentrations of hydrogen, an essential energy source for subsurface microbial communities deep in the Earth that are unable to access energy from the sun for photosynthesis.

Due to their extremely small masses, helium and neon are uniquely valuable for identifying and quantifying transport potential.

While the extremely low porosity of crystalline basement rocks in which these waters are found means the groundwaters themselves are largely isolated and rarely mix, accounting for their 1.2-billion-year age, diffusion can still take place.

"Solid materials such as plastic, stainless steel and even solid rock are eventually penetrated by diffusing helium, much like the deflation of a helium-filled balloon," Dr. Warr said.

"Our results show that diffusion has provided a way for 75-82% of the helium and neon originally produced by the radiogenic reactions to be transported through the overlying crust."

The authors stress that the insights on how much helium diffuses up from the deep Earth is a critical step forward, as global helium reserves run out, and the transition to more sustainable resources gains traction.

"Humans are not the only life forms relying on the energy resources of the Earth's deep subsurface," Dr. Warr said.

"Since the radiogenic reactions produce both helium and hydrogen, we can not only learn about helium reservoirs and transport, but

also calculate hydrogen energy flux from the deep Earth that can sustain subsurface microbes on a global scale."

"These calculations are vital for understanding how subsurface life is sustained on Earth, and what energy might be available from radiogenic-driven power on other planets and moons in the Solar System and beyond, informing upcoming missions to Mars, Titan, Enceladus and Europa."

The discovery is described in a paper published in the journal *Nature Communications*.

O. Warr et al. 2022. ^{86}Kr excess and other noble gases identify a billion-year-old radiogenically-enriched groundwater system. Nat Commun 13, 3768; doi: 10.1038/s41467-022-31412-2

https://bit.ly/3arjJad

Scientists Have Created Worms That Can Kill Cancer Cells

Osaka University researchers discovered that worms may be coated with hydrogel sheaths that contain useful cargo such as anti-cancer medications

James Bond's famed quartermaster Q provided the secret agent with an unlimited supply of equipment and gadgets to aid him on his missions. Now, scientists from Japan have shown that they are equally adept in providing microscopic worms with a surprising variety of useful and protective components.

Researchers from Osaka University have discovered that microscopic, free-living worms known as nematodes may be coated with hydrogel-based "sheaths" that can be further customized to transport functional cargo.

Nematodes are tiny, free-living worms that normally inhabit soil or other environmental niches and, under certain circumstances, may enter the human body. *Anisakis simplex*, a marine-dwelling nematode that may colonize humans when consumed, has shown an odd liking for cancer cells.

Naked Anisakis simplex and Anisakis simplex coated with hydrogel sheath containing fluorescence dye. Credit: Shinji Sakai

"*Anisakis simplex* has been reported to sense cancer, potentially by detecting cancer "odor," and to attach to cancerous tissues," says Wildan Mubarok, first author of the study. "This led us to ask whether it could be used to deliver anti-cancer treatments directly to cancer cells within the human body."

To investigate this possibility, the researchers first developed a system for applying hydrogel sheaths to nematodes by dipping them in a series of solutions containing chemicals that bind together to create a gel-like layer all over their surface. This process essentially custom-fits a suit about 0.01 mm thick to the worm in about 20 minutes.

"The results were very clear," says Shinji Sakai, senior author of the study. "The sheaths did not in any way interfere with the worms' survival and were flexible enough to maintain the worms' motility and natural ability to seek out attractive smells and chemical signals."

Next, the researchers loaded the sheaths with functional molecules and found that this protected the worms from ultraviolet light or hydrogen peroxide. What's more, the sheaths could be loaded with

anti-cancer agents that the nematodes, protected but unimpeded by their hydrogel armor, could transport and deliver to kill cancer cells in vitro.

“Our findings suggest that nematodes could potentially be used to deliver functional cargo to a range of specific targets in the future,” states Mubarok. Given the adaptability of the hydrogel sheaths, this worm-based delivery system holds promise not only for delivering anti-cancer drugs to tumor cells in patients, but it also has potential applications in other fields such as delivering beneficial bacteria to plant roots.

Reference: “Nematode surface functionalization with hydrogel sheaths tailored in situ” by Wildan Mubarok, Masaki Nakahata, Masaru Kojima and Shinji Sakai, 16 June 2022, Materials Today Bio. DOI: 10.1016/j.mtbio.2022.100328

https://bit.ly/3yxO2DU

Researchers argue that long human lifespan is due in part to the contributions of elders

What could the force of selection be once you take into account the contributions of older adults

According to long-standing canon in evolutionary biology, natural selection is cruelly selfish, favoring traits that help promote reproductive success. This usually means that the so-called "force" of selection is well equipped to remove harmful mutations that appear during early life and throughout the reproductive years. However, by the age fertility ceases, the story goes that selection becomes blind to what happens to our bodies. After the age of menopause, our cells are more vulnerable to harmful mutations. In the vast majority of animals, this usually means that death follows shortly after fertility ends.

Which puts humans (and some species of whale) in a unique club: animals that continue to live long after their reproductive lives end. How is it that we can live decades in selection's shadow?

"From the perspective of natural selection, long post-menopausal life is a puzzle," said UC Santa Barbara anthropology professor Michael Gurven. In most animals, including chimpanzees—our closest primate brethren—this link between fertility and longevity is very pronounced, where survival drops in sync with the ability to reproduce. Meanwhile in humans, women can live for decades after their ability to have children ends. "We don't just gain a few extra years—we have a true post-reproductive life stage," Gurven said.

In a paper published in the *Proceedings of the National Academy of Sciences*, senior author Gurven, with former UCSB postdoctoral fellow and population ecologist Raziel Davison, challenge the longstanding view that the force of natural selection in humans must decline to zero once reproduction is complete.

They assert that a long post-reproductive lifespan is not just due to recent advancements in health and medicine. "The potential for long life is part of who we are as humans, an evolved feature of the life course," Gurven said.

The secret to our success? Our grandparents.

"Ideas about the potential value of older adults have been floating around for awhile," Gurven said. "Our paper formalizes those ideas, and asks what the force of selection might be once you take into account the contributions of older adults."

For example, one of the leading ideas for human longevity is called the Grandmother Hypothesis—the idea that, through their efforts, maternal grandmothers can increase their fitness by helping improve the survival of their grandchildren, thereby enabling their daughters to have more children. Such fitness effects help ensure that the grandmother's DNA is passed down.

"And so that's not reproduction, but it's sort of an indirect reproduction. The ability to pool resources, and not just rely on your own efforts, is a game changer for highly social animals like humans," Davison said.

In their paper, the researchers take the kernel of that idea—

intergenerational transfers, or resource sharing between old and young—and show that it, too, has played a fundamental role in the force of selection at different ages. Food sharing in non-industrial societies is perhaps the most obvious example.

"It takes up to two decades from birth before people produce more food than they're consuming," said Gurven, who has studied the economy and demography of the Tsimané and other indigenous groups of South America. A lot of food has to be procured and shared to get kids to the point where they can fend for themselves and be productive group members. Adults fill most of this need with their ability to obtain more food than they need for themselves, a provisioning strategy that has sustained pre-industrial societies for ages and also carries over into industrialized societies.

"In our model, the large surplus that adults produce helps improve the survival and fertility of close kin, and of other group members who reliably share their food, too," Davison said. "Viewed through the lens of food production and its effects, it turns out that the indirect fitness value of adults is also highest among reproductive-aged adults. But using demographic and economic data from multiple hunter-gatherers and horticulturalists, we find that the surplus provided by older adults also generates positive selection for their survival. We calculate all this extra fitness in late adulthood to be worth up to a few extra kids!"

"We show that elders are valuable, but only up to a point," contends Gurven. "Not all grandmothers are worth their weight. By about their mid-seventies, hunter-gatherers and farmers end up soaking up more resources than they provide. Plus, by their mid-seventies, most of their grandkids won't be dependents anymore, and so the circle of close kin who stand to benefit from their help is small."

But food isn't everything. Beyond getting fed, children are also taught and socialized, trained in relevant skills and worldviews. This is where older adults can make their biggest contributions: While they don't contribute as much to the food surplus, they have the accumulation of a lifetime of skills they can deploy to ease the burden of childcare on parents, as well as knowledge and training that they can pass on to their grandchildren.

"Once you take into account that elders are also actively involved in helping others forage, then it adds even more fitness value to their activity and to them being alive," Gurven said. "Not only do elders contribute to the group, but their usefulness helps ensure that they also receive from the surpluses, protections and care from their group. In other words, interdependence runs both ways, from old to young, and young to old."

"If you're part of my social world, there might be some kickback," Davison explained. "So to the extent that we're interdependent, I'm vested in your interest, beyond just simple kinship. I'm interested in getting you to be as skilled as possible because some of your productivity could help me down the road."

Gurven and Davison found that rather than our long lifespans opening up opportunities that led to a human-like foraging economy and social behavior, the reverse is more likely—our skills-intensive strategies and long-term investments in the health of the group preceded and evolved with our shift to our particular human life history, with its extended childhood and unusually long post-reproductive stage.

In contrast, chimpanzees—who represent our best guess as to what humans' last common ancestor may have been like—are able to forage for themselves by age 5. However, their foraging activities require less skill, and they produce minimal surplus. Even so, the authors show that if a chimpanzee-like ancestor would share their food more widely, they could still generate enough indirect fitness contributions to increase the force of selection in later adulthood.

"What this suggests is that human longevity is really a story about cooperation," said Gurven. "Chimpanzee grandmothers are rarely

observed doing anything for their grandkids."

Though the authors say their work is more about how the capacity for long life came to first exist in the Homo lineage, the implication that we owe it to elders everywhere is an important reminder looking forward.

"Despite elders being far more numerous today than ever before in the past, there's still much ageism and underappreciation of older adults," Gurven said. "When COVID seemed to be most deadly just for older adults, many shrugged their shoulders about the urgency of lockdown or other major precautions.

"Much of the huge value of our elders goes untapped," he added. "It's time to think seriously about how to reconnect the generations, and harness some of that elder wisdom and expertise."

More information: *Raziel Davison et al, The importance of elders: Extending Hamilton's force of selection to include intergenerational transfers, Proceedings of the National Academy of Sciences (2022).* *DOI: 10.1073/pnas.2200073119*

https://bit.ly/3OX6NYC

Yet another omicron subvariant is raising concern as BA.5 sweeps the US

BA.2.75 is spreading quickly and widely. Three cases detected in US so far.

Beth Mole

As the omicron coronavirus subvariant BA.5 blazes through the US—accounting for an estimated 54 percent of cases in the country—experts are eyeing another subvariant that threatens to follow hot on its heels.

The subvariant is referred to as BA.2.75 and was first detected in India in late May. Amid a backdrop of BA.2 and BA.5 circulating in India, the newcomer BA.2.75 began quickly gaining ground in June. This week it reached 23 percent of recent virus samples there. Meanwhile, BA.2.75 spread beyond India's borders. It is now present in about 10 other countries, including the US, according to the World Health Organization.

Experts are concerned about the new subvariant, not just because of its rapid rise. It has several mutations in its spike protein—the critical protein that allows the virus to latch onto human cells and the protein that acts as a prime target for immune responses. In particular, BA.2.75 has key mutations that suggest it could be good at evading antibody responses in people who have been vaccinated and/or previously infected with earlier omicron subvariants.

"This subvariant seems to have a few mutations on the receptor binding domain of the spike protein, so obviously, that's a key part of the virus that attaches itself to the human receptor, so we have to watch that," Dr. Soumya Swaminathan, the chief scientist for the World Health Organization, said in a video explainer this week.

Swaminathan notes that, for now, the number of samples and sequences is still low, and our understanding of this version of the virus is limited. "It's still too early to know if this subvariant has properties of additional immune evasion or, indeed, of being more clinically severe. We don't know that. So, we have to wait and see," she said, adding that WHO is monitoring the subvariant closely.

US situation

So far, three cases of BA.2.75 have been detected in the US, which were identified in California and Washington state. Helix—a California-based viral surveillance company that works with the Centers for Disease Control and Prevention to track emerging coronavirus variants—confirmed the third US case to Ars in an email Friday. Samples for the three US cases were collected on June 14, June 15, and June 27.

Helix said it's still too early to predict how BA.2.75 will play out in the US, but the subvariant is worth keeping an eye on—which echoes warnings from outside experts.

In the meantime, BA.5 is sweeping the US. The prevalence of the

previous reigning omicron subvariant, BA.2.12.1, has fallen to an estimated 27 percent. BA.4—a subvariant that shares the same spike mutations as BA.5 and has spread alongside BA.5 elsewhere—appears to have stalled out, accounting for just 16.5 percent of US cases.

Amid BA.5's rise, cases have maintained a high plateau, though many cases detected by rapid tests at home are not being reported. According to tracking by The New York Times, the country is averaging around 108,000 new cases per day. Some experts are anxiously waiting to see if there will be a bump following Independence Day celebrations. Just before the holiday, the positivity rate of reported tests reached a concerning 17.5 percent.

Otherwise, daily hospitalizations are up 15 percent over the last two weeks, to an average of 35,651. Admission to intensive care units is also up 16 percent. Deaths remain plateaued at around 320 per day.

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Building blocks for RNA-based life abound at center of our galaxy

Nitriles, a class of organic molecules with a cyano group, are typically toxic, but they are also a key precursor for molecules essential for life

Nitriles, a class of organic molecules with a cyano group—that is, a carbon atom bound with a triple unsaturated bond to a nitrogen atom—are typically toxic. But paradoxically, they are also a key precursor for molecules essential for life, such as ribonucleotides, composed of the nucleobases or "letters" A, U, C, and G joined to a ribose and phosphate group, which together make up RNA. Now, a team of researchers from Spain, Japan, Chile, Italy, and the US show that a wide range of nitriles occurs in interstellar space within the molecular cloud G+0.693-0.027, near the center of the Milky Way.

Dr. Víctor M. Rivilla, a researcher at the Center for Astrobiology of the Spanish National Research Council (CSIC) and the National Institute of Aerospace Technology (INTA) in Madrid, Spain, and first author of the new study published in *Frontiers in Astronomy and Space Sciences*, said, "Here we show that the chemistry that takes place in the interstellar medium is able to efficiently form multiple nitriles, which are key molecular precursors of the 'RNA World' scenario."

Possible 'RNA-only' world

According to this scenario, life on Earth was originally based on RNA only, and DNA and protein enzymes evolved later. RNA can fulfill both their functions: storing and copying information like DNA, and catalyzing reactions like enzymes. According to the "RNA World" theory, nitriles and other building blocks for life needn't necessarily all have arisen on Earth itself: They might also have originated in space and "hitchhiked" to the young Earth inside meteorites and comets during the "Late Heavy Bombardment" period, between 4.1 and 3.8 billion years ago. In support, nitriles and other precursor molecules for nucleotides, lipids, and amino acids have been found inside contemporary comets and meteors.

But from where in space could these molecules have come? Prime candidates are molecular clouds, which are dense and cold regions of the interstellar medium, and are suitable for the formation of complex molecules. For example, the molecular cloud G+0.693-0.027 has a temperature of around 100 K and is approximately three light years across, with a mass approximately one thousand times that of our sun. There's no evidence that stars are currently forming inside G+0.693-0.027, although scientists suspect that it might evolve to become a stellar nursery in the future.

"The chemical content of G+0.693-0.027 is similar to those of other star-forming regions in our galaxy, and also to that of solar system objects like comets. This means that its study can give us important insights about the chemical ingredients that were available in the

nebula that give rise to our planetary system," explained Rivilla.

Electromagnetic spectra studied

Rivilla and colleagues used two telescopes in Spain to study the electromagnetic spectra emitted by G+0.693-0.027: the 30-meter-wide IRAM telescope Granada, and the 40-meter-wide Yebes telescope in Guadalajara. They detected the nitriles cyanoallene (CH_2CCHCN), propargyl cyanide ($HCCCH_2CN$), and cyanopropyne, which hadn't yet been found in G+0.693-0.027, although they had been reported in 2019 in the TMC-1 dark cloud in the constellations Taurus and Auriga, a molecular cloud with very different conditions than G+0.693-0.027.

Rivilla and the team also found possible evidence for the occurrence in G+0.693-0.027 of cyanoformaldehyde (HCOCN) and glycolonitrile ($HOCH_2CN$). Cyanoformaldehyde was detected for the first time in the molecular clouds TMC-1 and Sgr B2 in the constellation Sagittarius, and glycolonitrile in the Sun-like protostar IRAS16293-2422 B in the constellation Ophiuchus.

Other recent studies have also reported other RNA precursors inside G+0.693-0.027 such as glycolaldehyde ($HCOCH_2OH$), urea (NH_2CONH_2), hydroxylamine (NH_2OH), and 1,2-ethenediol ($C_2H_4O_2$), confirming that the interstellar chemistry is able to provide the most basic ingredients for the "RNA World."

Nitriles among most abundant chemical families in space

Final author Dr. Miguel A Requena-Torres, a lecturer at Towson University in Maryland, U.S., said, "Thanks to our observations over the past few years, including the present results, we now know that nitriles are among the most abundant chemical families in the universe. We have found them in molecular clouds in the center of our galaxy, protostars of different masses, meteorites and comets, and also in the atmosphere of Titan, the largest moon of Saturn."

Second author Dr. Izaskun Jiménez-Serra, likewise a researcher at CSIC and INTA, looked ahead: "We have detected so far several simple precursors of ribonucleotides, the building blocks of RNA. But there are still key missing molecules that are hard to detect. For example, we know that the origin of life on Earth probably also required other molecules such as lipids, responsible for the formation of the first cells. Therefore, we should also focus on understanding how lipids could be formed from simpler precursors available in the interstellar medium."

More information: *Molecular precursors of the RNA-world in space: new nitriles in the G+0.693-0.027 molecular cloud, Frontiers in Astronomy and Space Sciences (2022). DOI: 10.3389/fspas.2022.876870, www.frontiersin.org/articles/1 ... pas.2022.876870/full*

https://wb.md/3uBK8Jd

Study Finds Possible Causes of, and Treatments for, Long COVID

New study reveals possible causes of long COVID, and how best it can be treated

Kara Grant

Long COVID continues to plague millions of people who have contracted and recovered from their initial COVID infections.

Despite the high number of people who get the condition, there are still many unknowns when it comes to long COVID. But a new study examining mice has revealed the possible causes of long COVID, and how best it can be treated.

Researchers found that the surviving mice had pulmonary fibrosis – or a scarring of lung tissue – as well as chronic inflammation in the lungs a few weeks after they were cleared of the virus. The mice that were given an early dose of molnupiravir – one of the three FDA-approved antivirals for the treatment of COVID-19 – saw that their disease and its lingering symptoms were less severe.

While results from mouse studies don't apply directly to humans, "COVID-19 in mice and humans represent key findings that may prove translatable to other future emerging coronavirus disease pathologies," the authors wrote.

The most recent data from the CDC found that nearly 1 in 5 American adults who previously had COVID-19 get symptoms of what has come to be known as long COVID, which include fatigue, shortness of breath, brain fog, mental health issues, and more.

Sources

Science Translational Medicine: "SARS-CoV-2 infection produces chronic pulmonary epithelial and immune cell dysfunction with fibrosis in mice."

CDC: "Nearly One in Five American Adults Who Have Had COVID-19 Still Have 'Long COVID.'"

https://bit.ly/3It0eue

A Common ADHD Drug Shows Promise in Treating Some Symptoms of Alzheimer's

Drugs normally used to treat ADHD may actually show promise in managing symptoms of Alzheimer's disease.

Eleftheria Kodosaki & Katie Sedgwick

The search for a way to treat Alzheimer's disease has puzzled scientists for decades. This may be why some researchers are shifting their focus slightly, investigating whether treating the systems affected by Alzheimer's (as opposed to the causes) may better help them find a treatment.

This is exactly what researchers of a new study have shown – finding that drugs normally used to treat ADHD may actually show promise in managing symptoms of Alzheimer's disease.

The researchers conducted a systematic review which looked at how noradrenergic drugs (commonly used for ADHD) work for managing Alzheimer's disease symptoms. The review found that taking these drugs improved certain brain functions and other symptoms, such as apathy, in patients with Alzheimer's disease.

Noradrenergic drugs target the noradrenergic system, which comprises a small part of the brainstem called the locus coeruleus. This area is involved in a broad array of brain functions, such as memory, attention and learning. This system is primarily controlled by a neurotransmitter (a special type of brain cell that sends and receives messages in the brain) called noradrenaline – which also plays an important role in our body's "fight or flight" response.

The locus coeruleus is also the first recorded brain area to show pathological signs of Alzheimer's disease. These signs occur in the form of tau tangles. Tau is an important protein that is essential for good brain function. But in people with Alzheimer's disease, tau proteins accumulate together.

As these tangles build up, they interfere with the noradrenergic system's ability to keep neurons healthy. Since the noradrenergic system also helps regulate the brain's immune system, loss of function can lead to neuroinflammation, which is another telltale sign of Alzheimer's disease.

Problems with the way the noradrenergic system functions have also been seen in other mental health conditions, such as depression, ADHD, and anxiety. This is why noradrenergic treatments may also be prescribed for these disorders. Interestingly, patients with these disorders have higher risk of developing Alzheimer's.

Symptoms such as depression and anxiety often also appear prior to memory issues in people with Alzheimer's disease. The presence of depression, anxiety and other mental health issues is also associated with higher risk of premature death in patients with Alzheimer's.

Treating Alzheimer's

To conduct their study, the researchers pooled together 19 studies, looking at data from a total of over 1,800 patients. They also looked at a number of different noradrenergic drugs, including those used to treat ADHD and depression.

They found that in the majority of studies, these drugs improved the overall thinking and understanding of people with Alzheimer's disease. However, they weren't shown to improve the performance of specific memory functions (such as verbal and episodic memory), executive functions (being able to focus and remember instructions), visuospatial abilities (such as drawing or buttoning a shirt), or

agitation.

These drugs were also shown to improve apathy, which is a common symptom of Alzheimer's. Apathy can greatly reduce quality of life and can advance loss of brain function. Interestingly, a drug used predominantly in treating ADHD, named methylphenidate – better known as Ritalin – was the drug most commonly shown to improve apathy in Alzheimer's patients.

Overall, this study suggests that noradrenergic drugs can be beneficial for some people with Alzheimer's disease, so long as the right dosage is used. However, caution should be taken when drawing conclusions, as this is not an experimental study – such as a randomized controlled trial, which would compare the effect of an intervention (such as drug). There was also a lot of variation between the studies included in the review in how they were conducted and their results.

It's also worth noting that although these drugs were shown to have some benefit for brain function, they can come with a range of side effects. These include heart problems, addiction and, especially when misused, may result in brain changes or psychiatric symptoms, including psychosis-like symptoms such as hallucinations and paranoia. So it will be important for future studies to be conducted further proving the benefits of these drugs – and that the benefits far outweigh any potential risks.

When it comes to the noradrenergic drugs investigated in this study, methylphenidate (Ritalin) has recently been used short term (six months) in a clinical trial and has shown positive results when it comes to apathy. But other drugs investigated in the study, such as the antidepressant mirtazapine, not only showed zero improvement in apathy, but were associated with increased risk of premature death.

While the study didn't show any improvement in memory issues for people with Alzheimer's, it has shown us that it may be time to move in a new direction when it comes to treating this disease. Instead of focusing only on potential causes (such as the amyloid and tau hypotheses), research could now benefit from including treatments that target the systems which are involved in different Alzheimer's symptoms.

Eleftheria Kodosaki, Research Associate in Neuroimmunology, Cardiff University and Katie Sedgwick, Neuroscience PhD student, Cardiff University.

https://bit.ly/3NW54Bt

Dogs Could Be Lowering Crime Levels in Your Neighborhood. Seriously

According to new research, a higher concentration of dog ownership in a neighborhood is linked with lower crime levels.

Peter Dockrill

Dogs are beyond great. These wonderful animals are so clever, and so connected with us. For people lucky enough to be dog owners, they're truly our best friends.

Now researchers have discovered another reason to love dogs, and it's something that's not so obvious. According to new research, a higher concentration of dog ownership in a neighborhood is linked with lower crime levels. In their own way, dogs are actually helping us to fight crime. Seriously.

Not that dogs can take all the credit, mind you. Researchers from Ohio State University think the reason this link exists is because owning a dog means you need to walk it, and dog walking involves getting out and about in your community.

That increased level of civilian activity on streets – and the extra interactions with your neighbors that result – provide a heightened level of surveillance over the local neighborhood, which in turn helps to keep things safer, so the thinking goes.

"People walking their dogs are essentially patrolling their neighborhoods," says sociologist Nicolo Pinchak, lead author of the new study.

"They see when things are not right, and when there are suspect outsiders in the area. It can be a crime deterrent."

The researchers' hypothesis – inspired by the work of urban theorist Jane Jacobs – takes cues from Jacobs' "eyes on the street" concept: the idea that people in public places help to maintain order and safety simply through their presence, as it gives them an opportunity for surveillance of their surroundings.

A continuous stream of "eyes on the street" and communal interactions by people in public places helps to create a web of public respect and trust within a neighborhood, which together can help deter crimes from occurring, Jacobs argued.

While the idea has been influential in sociology, urban planning, and academic circles, Pinchak and his team say there have been few attempts to quantify whether the hypothesis demonstrably works to lower neighborhood-level crime rates.

To test this, the researchers focused on dog ownership, reasoning that the daily routines of dog-walkers fit with the theories of Jacobs (and others) on being an activity that could contribute to neighborhood surveillance and safety while building trust within a community by facilitating interactions among strangers.

The researchers used data from multiple sources, including crime statistics for neighborhoods in Columbus, Ohio; a marketing survey showing the concentration of dog-owning neighborhoods in the city; and data from a separate sociological project led by study co-author Christopher Browning, measuring levels of trust and social climates of neighborhoods in the area.

While the results don't offer evidence of any kind of causative effect, the researchers did find an association between the presence of dogs and reduced crime rates. "Consistent with Jacobs' crime control model, we found that neighborhood dog concentration is inversely associated with rates of robbery, homicide, and, to a less consistent degree, aggravated assault rates among neighborhoods higher in local trust," the team writes in their paper, noting that property crime also showed an inverse association with dog concentration, independent of levels of neighborhood trust.

The results so far have only been seen in one city. Plus, the researchers acknowledge that they can't rule out the influence of various biases in the data, so future studies are needed to explore the issue in more detail.

Nonetheless, the study does offer new data to support the idea that dog ownership and dog walking contribute to lower crimes in the community, perhaps by equipping residents with increased familiarity to identify suspect outsiders, or putting would-be offenders off, given that dog-walkers may appear more likely to intervene in the event of a crime.

More research is needed to unpack this further, the researchers say, but for now, it certainly looks like dogs could be having a beneficial effect on these neighborhoods – simply by bringing people together, and maybe the other effects flow from there.

"Trust doesn't help neighborhoods as much if you don't have people out there on the streets noticing what is going on. That's what dog walking does," Pinchak says.

"When people are out walking their dogs, they have conversations, they pet each other's dogs. Sometimes they know the dog's name and not even the owners. They learn what's going on and can spot potential problems." The findings are reported in *Social Forces*.

https://bit.ly/3nR55vN

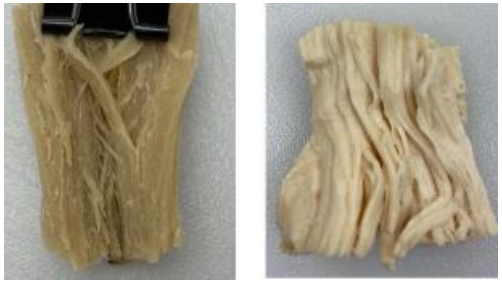
Humans Absorb Less Protein From Plant-Based Meat Than Normal Meat

Plant-based meat supplies less protein to human cells than chicken meat

The push for plant-based meat has already gained a lot of support. However, it’s not understood how much of the protein makes it into human cells, despite the fact that protein-rich plants like soybeans

are often used as components.

Researchers report that proteins in a model plant-based alternative were not as easily absorbed by cells as those from meat in a recent study published in the American Chemical Society's *Journal of Agricultural and Food Chemistry*.



A meat substitute (left) resembles chicken meat (right), but its proteins are not absorbed as well by human cells. **Credit: Adapted from Journal of Agricultural and Food Chemistry 2022, DOI: 10.1021/acs.jafc.2c01711**

Almost every kind of replacement meat, from ground beef to fish sticks, is now available for purchase by consumers. Plants are dried into a powder and combined with spices to simulate the appearance and texture of the real thing. Typically, the combinations are then heated, moistened, and put through an extruder.

Because the plants used to manufacture them are rich in protein and low in unhealthy fats, these products are often considered to be healthier than animal meats. However, laboratory tests have shown that the breakdown of replacement proteins into peptides is inferior to that of proteins from meat.

Osvaldo Campanella, Da Chen, and colleagues wanted to go a step further and see if human cells can absorb similar amounts of peptides from a model meat alternative as they can from a piece of chicken.

The researchers created a model meat alternative made of soy and wheat gluten with the extrusion process. When cut open, the material had long fibrous pieces inside, just like chicken. Cooked pieces of the substitute and chicken meat were then ground up and broken down with an enzyme that humans use to digest food.

In vitro tests showed that meat-substitute peptides were less water-soluble than those from chicken, and they also were not absorbed as well by human cells. With this new understanding, the researchers say the next step is to identify other ingredients that could help boost the peptide uptake of plant-based meat substitutes.

The study was funded by the College of Food, Agricultural, and Environmental Sciences at The Ohio State University.

Reference: "Characterization and Cellular Uptake of Peptides Derived from In Vitro Digestion of Meat Analogues Produced by a Sustainable Extrusion Process" by Da Chen, Diana Rocha-Mendoza, Shengyue Shan, Zachary Smith, Israel García-Cano, Julie Prost, Rafael Jimenez-Flores and Osvaldo Campanella, 22 June 2022, Journal of Agricultural and Food Chemistry. DOI: 10.1021/acs.jafc.2c01711