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Using viruses to fight viruses: New approach eliminates 'dormant' HIV-infected cells

While Ottawa researchers are known for their work on cancer-fighting viruses, one team is applying these viruses to a new target: HIV.

Researchers at The Ottawa Hospital and the University of Ottawa have discovered that the Maraba virus, or MG1, can target and destroy the kind of HIV-infected cells that standard antiretroviral therapies can't reach. This laboratory discovery was published in the Journal of Infectious Diseases. If this technique works in humans, it might possibly contribute to a cure for HIV.

While daily medications keep the level of HIV virus in the blood low, there is currently no way to totally eliminate dormant HIV-infected cells from the body. If a person living with HIV stops taking antiretroviral medications, these hidden viruses rapidly rebound.

These latently HIV-infected cells are hard to target because they are not distinguishable from normal cells. Dr. Jonathan Angel and his team tried a new approach of identifying these dormant cells by using the MG1 virus. This virus attacks cancer cells that have defects in their interferon pathway, which makes the cells more vulnerable to viruses. Dr. Angel and his team previously found that latently HIV-infected cells also have defects in this pathway.

"We thought that because latently HIV-infected cells had similar characteristics to cancer cells, that the virus would enter and destroy them," said Dr. Angel, senior scientist and infectious disease physician at The Ottawa Hospital, and professor at the University of Ottawa. "It turns out we were right."

Using a number of laboratory models of latently HIV-infected cells, the researchers found that the MG1 virus targeted and eliminated the infected cells, and left healthy cells unharmed.

While most of these cells in patients are in the lymph nodes and other organs, a tiny number are found in the blood. When the researchers added MG1 to relevant blood cells taken from HIV-positive individuals, the levels of HIV DNA in the sample dropped. This indicated that the HIV-infected cells had been eliminated.

"We know that the Maraba virus is targeting and killing the latently HIV-infected cells, but we don't know exactly how it's doing this," said Dr. Angel, who is also Head of the Division of Infectious Disease. "We think the virus is able to target the cells because of an impaired interferon pathway, but we need to do more research to know for sure."

The research team's next step is to try the virus in animal models of HIV or move directly to clinical trials pending funding and approvals.

All research at The Ottawa Hospital is supported by generous donors who contribute to hospital priorities, including research to improve patient care and a research chair in gay men's health. The study was also funded by the Department of Medicine, University of Ottawa, Canadian Institutes of Health Research, Canadian Foundation for AIDS Research,

Full reference: "The oncolytic virus, MG1, targets and eliminates latently HIV-1-infected cells: implications for an HIV cure." Nischal Ranganath, Teslin S. Sandstrom, Stephanie C. Burke Schinkel, Sandra C. Côté, Jonathan B. Angel. Journal of Infectious Disease. December 8, 2017.

http://bit.ly/2l6ZwbN

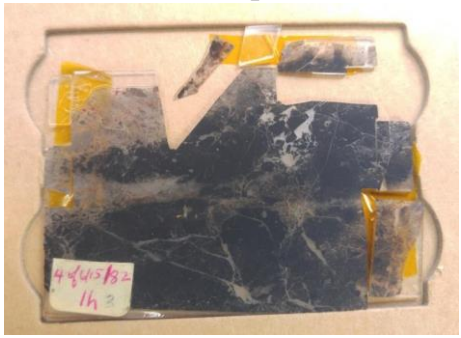
Oldest fossils ever found show life on Earth began before 3.5 billion years ago

Researchers at UCLA and the University of Wisconsin-Madison have confirmed that microscopic fossils discovered in a nearly 3.5 billion-year-old piece of rock in Western Australia are the oldest fossils ever found and indeed the earliest direct evidence of life on Earth.

MADISON, Wis. -- The study, published today [Dec. 18, 2017] in the Proceedings of the National Academy of Sciences, was led by J. William Schopf, professor of paleobiology at UCLA, and John W. Valley, professor of geoscience at the University of Wisconsin-Madison.

The research relied on new technology and scientific expertise developed by researchers in the UW-Madison WiscSIMS Laboratory.

The study describes 11 microbial specimens from five separate taxa, linking their morphologies to chemical signatures that are characteristic of life. Some represent now-extinct bacteria and microbes from a domain of life called Archaea, while others are similar to microbial species still found today. The findings also suggest how each may have survived on an oxygen-free planet.



This sample of rock was taken from the Apex Chert, a rock formation in western Australia that is among the oldest and best-preserved rock deposits in the world, in 1982 and was soon found to contain evidence of early life on Earth. A study published by UCLA and UW-Madison scientists in 2017 used sophisticated chemical analysis to confirm the microscopic structures found in the rock are indeed biological, rendering them -- at 3.5 billion years -- the oldest fossils yet found. This is the rock after analysis in the WiscSIMS Laboratory. **Courtesy of John Valley, UW-Madison**

The microfossils -- so called because they are not evident to the naked eye -- were first described in the journal Science in 1993 by Schopf and his team, which identified them based largely on the fossils' unique, cylindrical and filamentous shapes.

Schopf, director of UCLA's Center for the Study of Evolution and the Origin of Life, published further supporting evidence of their biological identities in 2002.

He collected the rock in which the fossils were found in 1982 from the Apex chert deposit of Western Australia, one of the few places on the planet where geological evidence of early Earth has been preserved, largely because it has not been subjected to geological processes that would have altered it, like burial and extreme heating due to plate-tectonic activity.

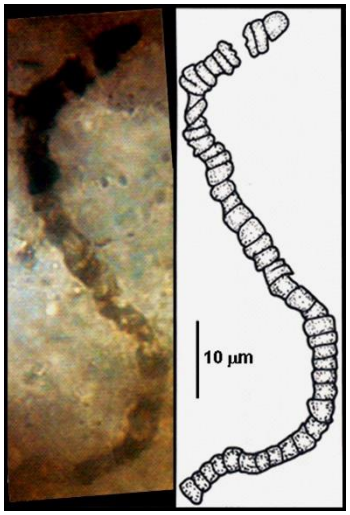
But Schopf's earlier interpretations have been disputed. Critics argued they are just odd minerals that only look like biological specimens. However, Valley says, the new findings put these doubts to rest; the microfossils are indeed biological.

"I think it's settled," he says.

Using a secondary ion mass spectrometer (SIMS) at UW-Madison called IMS 1280 - one of just a handful of such instruments in the world - Valley and his team, including department geoscientists Kouki Kitajima and Michael Spicuzza, were able to separate the carbon composing each fossil into its constituent isotopes and measure their ratios.

Isotopes are different versions of the same chemical element that vary in their masses. Different organic substances - whether in rock, microbe or animal - contain characteristic ratios of their stable carbon isotopes.

Using SIMS, Valley's team was able to tease apart the carbon-12 from the carbon-13 within each fossil and measure the ratio of the two compared to a known carbon isotope standard and a fossil-less section of the rock in which they were found.



An example of one of the microfossils discovered in a sample of rock recovered from the Apex Chert, a rock formation in western Australia that is among the oldest and best-preserved rock deposits in the world. The fossils were first described in 1993 but a 2017 study published by UCLA and UW-Madison scientists used sophisticated chemical analysis to confirm the microscopic structures found in the rock are indeed biological, rendering them -- at 3.5 billion years -- the oldest fossils yet found. **Courtesy of J. William Schopf, UCLA**

"The differences in carbon isotope ratios correlate with their shapes," Valley says. "If they're not biological there is no reason for such a correlation. Their C-13-to-C-12 ratios are characteristic of biology and metabolic function."

Based on this information, the researchers were also able to assign identities and likely physiological behaviors to the fossils locked inside

the rock, Valley says. The results show that "these are a primitive, but diverse group of organisms," says Schopf.

The team identified a complex group of microbes: phototrophic bacteria that would have relied on the sun to produce energy, Archaea that produced methane, and gammaproteobacteria that consumed methane, a gas believed to be an important constituent of Earth's early atmosphere before oxygen was present.

It took Valley's team nearly 10 years to develop the processes to accurately analyze the microfossils -- fossils this old and rare have never been subjected to SIMS analysis before.

The study builds on earlier achievements at WiscSIMS to modify the SIMS instrument, to develop protocols for sample preparation and analysis, and to calibrate necessary standards to match as closely as possible the hydrocarbon content to the samples of interest.

In preparation for SIMS analysis, the team needed to painstakingly grind the original sample down as slowly as possible to expose the delicate fossils themselves -- all suspended at different levels within the rock and encased in a hard layer of quartz -- without actually destroying them.

Spicuzza describes making countless trips up and down the stairs in the department as geoscience technician Brian Hess ground and polished each microfossil in the sample, one micrometer at a time.

Each microfossil is about 10 micrometers wide; eight of them could fit along the width of a human hair.

Valley and Schopf are part of the Wisconsin Astrobiology Research Consortium, funded by the NASA Astrobiology Institute, which exists to study and understand the origins, the future and the nature of life on Earth and throughout the universe.

Studies such as this one, Schopf says, indicate life could be common throughout the universe. But importantly, here on Earth, because several different types of microbes were shown to be already present by 3.5 billion years ago, it tells us that "life had to have begun substantially earlier -- nobody knows how much earlier -- and confirms it is not difficult for primitive life to form and to evolve into more advanced microorganisms," says Schopf.

Earlier studies by Valley and his team, dating to 2001, have shown that liquid water oceans existed on Earth as early as 4.3 billion years ago, more than 800 million years before the fossils of the present study would have been alive, and just 250 million years after the Earth formed.

"We have no direct evidence that life existed 4.3 billion years ago but there is no reason why it couldn't have," says Valley. "This is something we all would like to find out."

UW-Madison has a legacy of pushing back the accepted dates of early life on Earth. In 1953, the late Stanley Tyler, a geologist at the university who passed away in 1963 at the age of 57, was the first person to discover microfossils in Precambrian rocks. This pushed the origins of life back more than a billion years, from 540 million to 1.8 billion years ago.

"People are really interested in when life on Earth first emerged," Valley says.

"This study was 10 times more time-consuming and more difficult than I first imagined, but it came to fruition because of many dedicated people who have been excited about this since day one ... I think a lot more microfossil analyses will be made on samples of Earth and possibly from other planetary bodies."

The research was supported by the NASA Astrobiology Institute at the University of Wisconsin-Madison and the Center for the Study of Evolution and the Origin of Life at UCLA. WiscSIMS is supported by the National Science Foundation (EAR-1355590) and UW-Madison.

In an excerpt from a book J. William Schopf published in 1999, "Cradle of Life," he describes the microfossils he recovered in 1982 as such:

"The Apex fossils are scrappy. Hard to find. Difficult to study. They are abundant but charred, shredded, overly cooked. Tiny bits and pieces are common but generally nondescript; short two-or-three-celled fragments are rare and easy to overlook; many-celled specimens are few and far between; and fossils that could be called "well-preserved" -- like those of the Gunflint and Bitter Springs deposit -- are nonexistent. Were these remnants not so remarkably ancient they would not merit much attention."

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Viruses can transfer genes across the superkingdoms of life

New research shows that viruses can transfer genes to organisms they are not known to infect, and may cast light on the ancient origins of viruses

New research shows that viruses can transfer genes to organisms that they aren't known to infect - including organisms in different superkingdoms, or domains. The study, published in open-access journal Frontiers in Microbiology, also finds that viruses and cellular organisms share a large group of genes that help cells to function, suggesting that viruses may have an ancient cell-like origin.

Viruses can sometimes infect very different organisms during their lifecycle, such as mosquitoes and humans in the case of Zika virus. Viruses can also jump between different species, such as from birds to humans in the case of avian flu. However, no virus has been discovered that can infect organisms from different superkingdoms - the highest-level divisions of life, also known as domains.

"Normally, we associate viruses with very specific host organisms, and we do not know of any virus that, for example, can infect both bacteria and humans," explains Arshan Nasir from COMSATS Institute of Information Technology, Pakistan, and University of Illinois, USA, and one of the study's authors. "Virus-host boundaries make sense since organisms that are separated by large evolutionary distances differ starkly in their cellular biology. This makes it hard for a virus to successfully replicate inside two very diverse environments."

Nevertheless, Nasir and his colleagues suspected leaps between such distant species could occur, not necessarily involving virus infection. "In addition to infecting and killing cells, viruses can also insert their genes into a cell's DNA," says Nasir. "We therefore hypothesized that viruses might interact in non-harmful ways to exchange genes between distantly related organisms."

To investigate such viral gene exchange, Nasir and colleagues looked at protein structures found in all known viruses and cellular organisms. By looking for protein structures that are specifically associated with viruses or cells, the researchers could detect virus-derived genes in cellular organisms and cell-derived genes in viruses.

Strikingly, viral hallmark genes weren't just found in the expected host organisms, but in all sorts of species - including those from different superkingdoms. For example, the research team found examples where viruses thought to only infect bacteria had likely transferred genes to complex organisms, such as plants and animals. This suggests that viruses can transfer genes to organisms that are dramatically different from their usual host, and that they can influence and interact with a much wider range of organisms than previously thought.

The team also found evidence that viruses and cellular organisms share a large group of protein structures that help cells to function. This is a little surprising in the case of viruses, as they aren't cells and have no obvious need for these proteins. One intriguing possibility is that viruses may have originally evolved from primitive cells, and these proteins were once useful during their ancient origins.

Nasir believes the results could change the way we think about virus-host relationships. "The study shows that the concept of a 'virus host' is rather blurry, since viruses do not necessarily need to kill a cell in order to interact with it," he says. "We should consider viruses to be a source of new genes that cellular organisms can acquire, and not necessarily just as a source of disease."

http://bbc.in/2C0V8TL

Herbal remedy ginkgo biloba 'can help stroke recovery'

A study claims that the popular herbal extract ginkgo biloba may help the brain recover after a stroke.

The herbal remedy, available in health food shops and some pharmacies in the UK, is used in China to aid memory and fight depression.

In a trial of 330 stroke patients over six months in China, the supplement was linked with better cognitive skill scores on tests.

Experts say the evidence for ginkgo is too weak to recommend it.

Those behind the small study - published in the online journal Stroke & Vascular Neurology - admit that larger, longer and more robust trials are needed.

It was carried out by Nanjing University Medical School, with patients from five Chinese hospitals.

All 330 participants began the trial within a week of having an ischaemic stroke. The average age of the patients was 64.

Roughly half of them were given 450mg of ginkgo biloba daily, in addition to 100mg of aspirin, while the remainder were given only the aspirin.

During a stroke, the blood supplying vital parts of the brain is interrupted, often leading to impaired memory and a decline in organisational and reasoning skills among stroke survivors.

Researchers wanted to see if combining ginkgo biloba with aspirin might help lessen or halt the cognitive decline.

Previous experimental studies in animals have suggested that ginkgo biloba protects against the nerve cell death associated with blood clots in the brain, possibly by increasing blood flow in the cerebral arteries.

Strokes - the definitions

Transient ischaemic attacks (also known as mini-strokes) *- symptoms resolve within 24 hours but the majority resolve within 10-60 minutes.*

Minor stroke *- symptoms last more than 24 hours but often resolve within a few days - and are usually relatively mild*

Major stroke *- usually taken to mean some permanent symptoms remain*

Source: Peter Rothwell, University of Oxford

All the participants took a neuropsychological test (Montreal Cognitive Assessment) at the start of the trial, and then 12, 30, 90 and 180 days later, to check for any cognitive impairment.

The results showed that those taking the combination of aspirin and ginkgo biloba had higher scores for cognitive skills, including memory and reasoning, than those who weren't.

Speech problems and muscle strength also improved more rapidly, with indications of improved functional capacity 12 and 30 days after the start of treatment. However, both the clinicians and the patients knew which treatment they had been assigned to, which may have skewed the results, and the monitoring period was not very long.

Ginkgo

Ginkgo biloba is one of the oldest living tree species.

Researchers say the extract used in the study contained more protective, and fewer harmful, chemicals than the extract typically used in previous studies. Few side-effects were reported during the trial.

The participants were subsequently monitored for nearly two years, with little difference in the vascular health of the two groups: 16 people in the combined treatment group, and 20 in the aspirin group had further problems, including recurrent stroke and aneurysm.

However, longer term studies looking at stroke severity are necessary, before any more definitive conclusions can be reached.

Dr David Reynolds, Chief Scientific Officer of Alzheimer's Research UK, criticised the methodology used in the trial: "The researchers were able to tell which participants received the ginkgo biloba extract and which didn't - a set up that can strongly influence results.

"There have been extensive trials investigating the effects of this herbal extract in people with dementia and they have not shown convincing evidence of a benefit."

How to recognise a stroke

- ***F****ace - has their face fallen on one side? Can they smile?*
- ***A****rms - can they raise both their arms and keep them there?*
- ***S****peech - is their speech slurred? If you notice any of these symptoms it is...*
- ***T****ime - time to call 999 if you see any single one of these signs*

Additional symptoms of stroke and mini-stroke can include:

- *Sudden loss of vision or blurred vision in one or both eyes*
- *Sudden weakness or numbness on one side of the body*
- *Sudden memory loss or confusion*
- *Sudden dizziness, unsteadiness or a sudden fall, especially with any of the other symptoms*

Source: Stroke Association

http://bit.ly/2kTVzIc

Should uninfected patients accept hepatitis C-infected livers to reduce waiting time?

Study suggests that antiviral drugs may allow safe transplantation of HCV-positive livers into uninfected recipients

A modeling study by Massachusetts General Hospital (MGH) investigators finds that the availability of directly-acting antiviral (DAA) drugs to treat hepatitis C virus (HCV) infection could allow the transplantation of livers from HCV-positive donors into HCV-negative recipients without posing undue risk. The team's report will appear in the journal Hepatology and has been released online.

"The availability of donor livers continues to be the limiting factor in increasing the number of liver transplant surgeries," says Jagpreet Chhatwal, PhD, of the MGH Institute for Technology Assessment, lead and corresponding author of the report. "Our study shows that transplanting HCV-positive livers into HCV-negative patients and treating with new antivirals can reduce waiting time to transplant and improve overall life expectancy."

It is not uncommon for HCV-positive organs to be discarded and not utilized for transplant because of the risks associated with HCV infection after transplantation. The recent availability of DAA drugs to treat HCV-positive recipients has led to post-transplant cure rates greater than 90 percent, significantly improving overall transplant success. DAA drugs have also reduced the number of HCV-infected patients who progress to the point of requiring a transplant, increasing the proportion of patients needing a transplant for reasons other than HCV infection. At the same time, the persistent opioid epidemic has led to a greater number of potential donors infected with HCV, who are often young and otherwise healthy. All of these factors have led to increased interest in exploring the possibility of utilizing HCV-positive livers in HCV-negative patients on the transplant waiting list.

Since a randomized clinical trial of the use of HCV-infected donor livers in HCV-negative recipients would need to be large and conducted over several years, the MGH team decided to conduct a virtual trial by simulating the life courses of HCV-negative patients on the waiting list, and comparing probable outcomes under two scenarios - waiting for an HCV-negative liver or being open to accepting any appropriate liver, with the initiation of antiviral treatment if an HCV-positive liver was used. Based on the profiles of multiple patients on the liver transplant waiting list, the model included factors such as each patient's probable waiting time, based on disease severity and geographic region; the supply of donor livers in each region, the risk of complications from an HCV-positive liver, and the efficacy of post-transplant antiviral treatment.

Their analysis revealed that the benefit of accepting an HCV-positive liver outweighs the risks in the majority of patients on the transplant waiting list. The magnitude of the benefits depended on the severity of a patient's liver disease, which is measured by what is called a MELD score. Determined by a number of laboratory values, the MELD score ranges from 6 to 40, with a higher score indicating more severe illness. Patients can be referred for transplant evaluation with a score as low as 12, but the average MELD score for undergoing transplant is 28.

The MGH team found that HCV-negative patients with MELD scores of 20 or higher could benefit from receiving an HCV-positive liver, followed by antiviral treatment. The benefits were greatest for patients with scores of 28 and in regions hard hit by the opioid epidemic, such as the Northeast, that have greater numbers of HCV-positive donors.

"Prior to the availability of DAA drugs, the risks of transplanting HCV-positive livers into HCV-uninfected recipients were felt to be prohibitively high and not justifiable," says Raymond Chung, MD, director of Hepatology, medical director of the MGH Liver Transplant Program and a co-author of the paper. "Every patient has extensive discussions with their care providers during the transplant listing process, part of which includes discussing the potential of accepting a 'high-risk' donor organ, such as one that tests positive for HCV. More clinical studies evaluating the use of HCV-positive donor livers and the

efficacy and optimal treatment duration for antiviral drugs will be needed before this approach can be widely applied."

Co-lead author Sumeyye Samur, PhD, of the MGH Institute for Technology Assessment says, "By simulating a virtual trial, we could assess the benefits and risks of transplanting HCV-positive organs into HCV-negative patients without putting patients at risk. Our study can thus inform efficient design of future trials and clinical practice in liver transplantation."

Co-author Emily Bethea, MD, of MGH Gastroenterology and the Institute for Technology Assessment adds, "DAA treatment is expensive and is only covered by insurers for patients with documented HCV infection. If we hope to expand future coverage to HCV-negative patients on the transplant waiting list, we will need data on the cost-effectiveness of preemptive antiviral therapy to help payers recognize the importance and long-term success of this approach."

Chhatwal stresses that, while the opioid epidemic has led to the increased availability of HCV-positive organs of all types, the trend should not be seen as beneficial. "The opioid epidemic is a major health crisis affecting communities across the country, and we want to reiterate our support for efforts to address the growing epidemic."

Chhatwal is an assistant professor, Samur and Bethea are fellows, and Chung is an associate professor at Harvard Medical School. Additional co-authors of the Hepatology paper are Chin Hur, MD, MPH, MGH Institute for Technology Assessment; Turgay Ayer, PhD, Georgia Institute of Technology; Fasiha Kanwal, MD, MSHS, Baylor College of Medicine; Mark S. Roberts, MD, MPP, University of Pittsburgh School of Medicine; and Norah Terrault, MD, University of California San Francisco Medical Center. Support for the study includes American Cancer Society Research Scholar Grant RSG-17-022-01-CPPB, Health Resources and Services Administration contract 234-2005-37011C, National Institutes of Health grant DK078772, National Science Foundation award 1722665, and the MGH Research Scholars Program.

Massachusetts General Hospital, founded in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH Research Institute conducts the largest hospital-based research program in the nation, with an annual research budget of more than $900 million and major research centers in HIV/AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, genomic medicine, medical imaging, neurodegenerative disorders, regenerative medicine, reproductive biology, systems biology, photomedicine and transplantation biology. The MGH topped the 2015 Nature Index list of health care organizations publishing in leading scientific journals and earned the prestigious 2015 Foster G. McGaw Prize for Excellence in Community Service. In August 2017 the MGH was once again named to the Honor Roll in the U.S. News & World Report list of "America's Best Hospitals."

http://bit.ly/2l7LnLO

Beauty is in the eye of the beer holder

New research into the influence of alcohol on how men objectify women could inform sexual violence prevention programs

Men under the influence of alcohol are more likely to see women as sexual objects. This is according to a study which moves beyond the mere anecdotal to investigate some of the circumstances and factors that influence why men objectify women. The research is published in Springer's journal Sex Roles and is led by Abigail Riemer of the University of Nebraska-Lincoln in the US.

The study involved 49 men in their twenties and was conducted in the safe space of a college laboratory. Of the 49 subjects, 29 received two alcoholic drinks to mildly intoxicate them, and the rest received placebo drinks. All were shown photographs of 80 undergraduate women dressed to go out, and were asked to rate the women's appearances and personality. The women's photos were previously rated by an independent panel on how much warmth, good-naturedness, friendliness, competence, intelligence, confidence, and attractiveness they exuded. Eye-tracking technology noted which part of the women's bodies men were looking at when they were shown the images.

When the men assessed a photographed woman based on her appearance, the instruction most often triggered objectifying gazes from them. They spent less time looking at faces and focused far longer on chests and waists. This was particularly true when viewing women who had been rated high in attractiveness. It happened to a lesser degree when viewing women who exuded warmth and competence, especially when men were slightly drunk. The findings suggest that whether a man will sexually objectify a woman depends on the alcohol intoxication of the man, as well as how attractive, warm and competent a woman is perceived to be.

"The sum of these results supports the notion that being perceived as high in humanizing attributes, such as warmth and competence, or being average in attractiveness provides a buffer that protects women from sexual objectification," says Riemer.

"Environments in which alcohol is present are ripe with opportunities for objectifying gazes," adds Riemer, who says that the only other study previously done on the link between alcohol and objectification by men relied on self-reports from women. "Adopting objectifying gazes toward women leads perceivers to dehumanize women, potentially laying the foundation for many negative consequences such as sexual violence and workplace gender discrimination."

She hopes findings from the study will help to challenge specific maladaptive beliefs held by some men that it is OK and acceptable to direct objectifying gazes toward women, especially those who are not typically considered to be attractive or who are not perceived as being competent or to have a warm personality.

"Understanding why the objectifying gaze occurs in the first place is an initial step toward stopping its incidence and its damaging effects," says Riemer, who believes that there might be value in mindfulness-based interventions to help men reflect on how they perceive women. "This may inform primary prevention programs to reduce the continuum of sexual violence that women disproportionately experience."

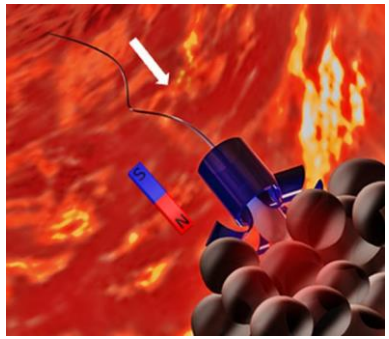
Reference: Riemer, A.R. et al (2017). Beauty is in the Eye of the Beer Holder: An Initial Investigation of the Effects of Alcohol, Attractiveness, Warmth, and Competence on the Objectifying Gaze in Men, Sex Roles DOI: 10.1007/s11199-017-0876-2

http://bit.ly/2ps6M7A

Harnessing sperm to treat gynecological diseases

A new potential drug carrier to treat gynecological conditions has joined the fleet of drug carriers: sperm

Delivering drugs specifically to cancer cells is one approach researchers are taking to minimize treatment side effects. Stem cells, bacteria and other carriers have been tested as tiny delivery vehicles. Now a new potential drug carrier to treat gynecological conditions has joined the fleet: sperm. Scientists report in the journal *ACS Nano* that they have exploited the swimming power of sperm to ferry a cancer drug directly to a cervical tumor in lab tests.



The swimming power of sperm could deliver cancer drugs directly to cervical tumors. **American Chemical Society**

Creating an effective way to target cancer cells with drugs is challenging on multiple fronts. For example, the drugs don't always travel deeply enough through tissues, and they can get diluted in body fluids or sidetracked and taken up by healthy organs.

To get around these issues, scientists have turned in some cases to loading pharmaceuticals into bacteria, which can effectively contain drug compounds and propel themselves. The microbes can also be guided by a magnetic field or other mechanism to reach a specific target. However, the body's immune system can attack the microbes and destroy them before they reach their target. Looking for another self-propelled cell as an alternative drug carrier to bacteria, Mariana Medina-Sánchez and colleagues at the Leibniz Institute for Solid State and Materials Research--Dresden (IFW Dresden) turned to sperm.

The researchers packaged a common cancer drug, doxorubicin, into bovine sperm cells and outfitted them with tiny magnetic harnesses. Using a magnetic field, a sperm-hybrid motor was guided to a lab-grown tumor of cervical cancer cells. When the harness arms pressed against the tumor, the arms opened up, releasing the sperm. The sperm then swam into the tumor, fused its membrane with that of a cancer cell, and released the drug. When unleashed by the thousands, drug-loaded sperm killed more than 80 percent of a cancerous ball while leaking very little of their payload en route. Further work is needed to ensure the system could work in animals and eventually humans, but researchers say the sperm motors have the potential to one day treat cancer and other diseases in the female reproductive tract.

The authors acknowledge funding from the Chinese Scholarship Council and the German Research Foundation. The abstract that accompanies this study is available here.

http://bit.ly/2DbhhhR

Putting a fork in cognitive decline

One serving of leafy greens a day may slow brain aging by 11 years

While cognitive abilities naturally decline with age, eating one serving of leafy green vegetables a day may aid in preserving memory and thinking skills as a person grows older, according to a study by researchers at Rush University Medical Center in Chicago.

The study results were published in the December 20, issue of Neurology, the medical journal of the American Academy of Neurology.

"Adding a daily serving of green leafy vegetables to your diet may be a simple way to help promote brain health," said study author Martha Clare Morris, ScD, a nutritional epidemiologist at Rush. "There continues to be sharp increases in the percentage of people with dementia as the oldest age groups continue to grow in number. Effective strategies to prevent dementia are critically needed."

The study results suggest that people who ate one serving of green, leafy vegetables had a slower rate of decline on tests of memory and thinking skills than people who rarely or never ate them.

The study results also suggest that older adults who ate at least one serving of leafy green vegetables showed an equivalent of being 11 years younger cognitively.

960 older adults completed food questionnaires and received annual cognitive assessments

The study enlisted volunteers already participating in the ongoing Rush Memory and Aging Project, which began in 1997 among residents of Chicago-area retirement communities and senior public housing complexes. A "food frequency questionnaire" was added from 2004 to February 2013, which 1,068 participants completed. Of them, 960 also received at least two cognitive assessments for the analyses of cognitive change.

This study involved these 960 people, who at the study start were an average age of 81 years old and did not have dementia. They had their thinking and memory skills tested every year and were followed for an average of 4.7 years.

The participants also completed the food frequency questionnaire, which assessed how often and how many half-cup servings they ate of either spinach; kale/collards/greens; or a one-cup serving of lettuce/salad.

The study divided the participants into five groups based on how often they ate green leafy vegetables, and compared the cognitive assessments of those who ate the most (an average of about 1.3 servings per day) and those who ate the least (0.1 servings per day).

Overall, the participants' scores on the thinking and memory tests declined at a rate of 0.08 standardized units per year.

Over 10 years of follow-up, the rate of decline for those who ate the most leafy greens was slower by 0.05 standardized units per year than the rate for those who ate the least leafy greens. This difference was equivalent to being 11 years younger in age, according to Morris.

More research needed in younger and minority populations

The results remained valid after accounting for other factors that could affect brain health, such as seafood and alcohol consumption, smoking, high blood pressure, obesity, education level and amount of physical and cognitive activities.

"The study results do not prove that eating green, leafy vegetables slows brain aging, but it does show an association," Morris said. "The study cannot rule out other possible reasons for the link."

Because the study focused on older adults with the majority of participants being white, the results may not apply to younger adults and to people of color.

The results need to be confirmed by other investigators in different populations and through randomized trials to establish a cause-and-effect relationship between the eating leafy greens and reductions in the incidence of cognitive decline, Morris said.

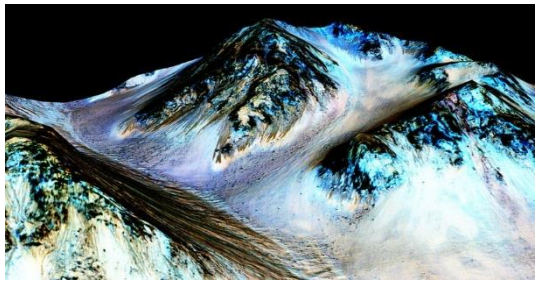
The study was supported by the National Institutes of Health and the USDA Agricultural Research Service.

http://bit.ly/2DbD6hf

Wet Mars "doomed from the start"

Basalts on the Red Planet sucked away much of the planet's early ocean, according to new research. Richard A Lovett reports.

Scientists have long known that Mars once had water, probably filling an ocean in its northern hemisphere. But today, other than its polar ice caps and possible traces in enigmatic gullies, the surface of Mars is dry. So where did that water go?



Hale Crater, seen here in an image taken by NASA's Mars Reconnaissance Orbiter, shows clear signs of the ancient presence of large amounts of water. **NASA**

One theory is that it was lost to space early in the Red Planet's history, when changes in the deep interior of Mars caused its magnetic field to collapse. This allowed high-energy particles and magnetic fields from the solar wind to hit the planet's upper atmosphere, knocking molecules, including all-important water vapour, into space.

But the early Mars probably had a lot of water — between 20 million and 200 million cubic kilometres of it, according to recent estimates. By contrast, Earth's oceans hold about 1.3 billion cubic kilometres.

And data from NASA's orbiting Mars Atmosphere and Volatile Evolution (MAVEN) mission — sent in part to measure exactly this atmosphere-eroding process — have not found it to be occurring fast enough to account for the geologically rapid disappearance of that much water from the early Martian surface.

Apparently, something else also happened. And while there are theories that much of the missing water is locked up in permafrost beneath the Martian soil, a new suggestion, published in the journal *Nature*, is that the water was trapped in hydrated minerals that were then sucked into the Martian interior.

This would have happened, says Jon Wade, an experimental petrologist at the University of Oxford, UK, when iron-rich lava flows encountered surface water and chemically reacted with it. A similar process occurs on Earth, but measurements by Mars rovers have found that Martian basalts contain nearly twice as much iron as their earthly counterparts.

That would have allowed them able to sponge up more water into a variety of iron-rich hydrous minerals, says Wade, who is the lead author of the new study. "Assuming these water-rock reactions were efficient, it is possible that the process could have consumed in excess of a three-kilometre-thick ocean covering the entire Martian surface," he says.

As these rocks got buried by successive flows of lava, they would have heated up with depth, just as occurs on Earth. But instead of producing new water-rich magma that returns the water to the surface, as happens on Earth, the different chemistry of the Martian rocks would have caused much of the water to be drawn into the Martian mantle, never to return.

What this means, he says, is that the young, wet Mars was "doomed from the start" due to the high iron content of its lavas. "It was likely inevitable that its surface water would have been sucked back into the mantle," he says.

It's an important find not just for understanding the early Mars, but in the search for exoplanets that might be suitable for life. That's because it may not be enough simply to find a planet that is the right size, right overall composition, and right distance from its sun.

"What we suggest is that the rock chemistry may also play a significant role in setting a planet's future fate," Wade says. "Small subtleties such as the amount of iron may have a disproportionate role in deciding a planet's fate. [They] may play a significant role on whether the planet's surface can 'hang on' to water for lengths of time relevant to the evolution of complex life."

Other scientists are impressed. Tomohiro Usui, a geologist and geochemist at Tokyo Institute of Technology, calls it a "possible and reasonable" explanation of the fate of the missing Martian water. The

reason for the high levels of iron in the Martian basalts, he adds, it that during Mars's formation, less iron went to its core than did on Earth, leaving more to be included in its upper layers.

Another scientist not involved in Wade's research is David Brain, a co-investigator on the MAVEN mission from the Laboratory for Atmospheric and Space Physics, in Boulder, Colorado. He calls the new study "an interesting stride forward".

Whatever the details might have been, there are only two directions in which the Martian water could have gone, he says: "'up' to space, or 'down' to the subsurface."

MAVEN, he adds, has been measuring the 'up's - showing that the loss of atmosphere to space has been substantial over the course of Martian history.

"The Wade paper," he says, "suggests that the 'down's are important too — substantial water could have been 'hidden' in the Martian subsurface. I think the history of Martian climate is best understood by taking the ups and downs together."

http://bit.ly/2prX45q

Physicists negate century-old assumption regarding neurons and brain activity

New types of experiments call activity of hundreds of labs and thousands of scientific studies in neuroscience into question, and could impact research into the origin of degenerative diseases

Neurons are the basic computational building blocks that compose our brain. Their number is approximately one Tera (trillion), similar to Tera-bits in midsize hard discs. According to the neuronal computational scheme, which has been used for over a century, each neuron functions as a centralized excitable element. The neuron accumulates its incoming electrical signals from connecting neurons through several terminals, and generates a short electrical pulse, known as a spike, when its threshold is reached.

Using new types of experiments on neuronal cultures, a group of scientists, led by Prof. Ido Kanter, of the Department of Physics at Bar-Ilan University, has demonstrated that this century-old assumption regarding brain activity is mistaken.

In an article published today in the journal Scientific Reports, the researchers go against conventional wisdom to show that each neuron functions as a collection of excitable elements, where each excitable element is sensitive to the directionality of the origin of the input signal. Two weak inputs from different directions (e.g., "left" and "right") will not sum up to generate a spike, while a strong input from "left" will generate a different spike waveform than that from the "right".

"We reached this conclusion using a new experimental setup, but in principle these results could have been discovered using technology that has existed since the 1980s. The belief that has been rooted in the scientific world for 100 years resulted in this delay of several decades," said Prof. Kanter and his team of researchers, including Shira Sardi, Roni Vardi, Anton Sheinin, and Amir Goldental.

The new results call for a re-examination of neuronal functionalities beyond the traditional framework and, in particular, for an examination into the origin of degenerative diseases. Neurons which are incapable of differentiating between "left" and "right" -- similar to distortions in the entire human body -- might be a starting point for discovering the origin of these diseases.

The new realization for the computational scheme of a neuron calls into question the spike sorting technique which is at the center of activity of hundreds of laboratories and thousands of scientific studies in neuroscience. This method was mainly invented to overcome the technological barrier to measure the activity from many neurons simultaneously, using the assumption that each neuron tends to fire spikes of a particular waveform which serves as its own electrical signature. However, this assumption, which resulted from enormous scientific efforts and resources, is now questioned by the work of Kanter's lab.

This research is supported in part by the TELEM grant of the Council for Higher Education in Israel.

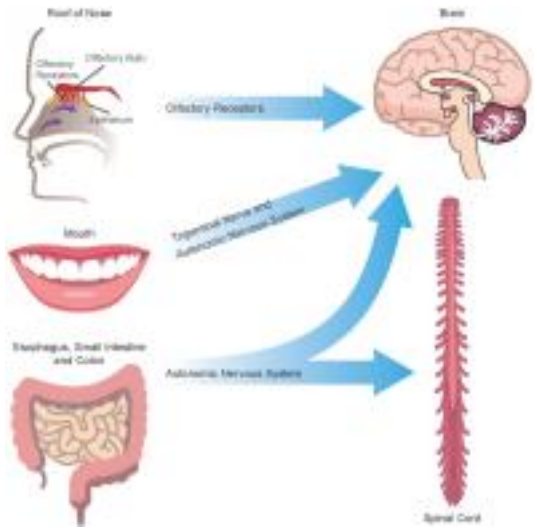
http://bit.ly/2BOplJe

UofL researcher proposes new term for the role of microbiota in neurodegeneration

Research in the past two decades has revealed that microbial organisms in the gut influence health and disease in many ways, particularly related to immune function, metabolism and resistance to infection.

LOUISVILLE, Ky. - Recent studies have shown that gut microbes also may cause or worsen Parkinson's disease, Alzheimer's disease and other neurodegenerative conditions.

University of Louisville neurology professor Robert P. Friedland, M.D., and Matthew R. Chapman, Ph.D., professor at the University of Michigan, have proposed a new term to describe an interaction between gut microbiota and the brain in an article released today in PLOS Pathogens.



Amyloid produced by commensal bacteria may cause changes in protein folding and neuroinflammation in the central nervous system through the autonomic nervous system (particularly the vagus nerve), the trigeminal nerve in the mouth and nasopharynx, and the gut (including mouth, esophagus, stomach and intestines), as well as via the olfactory receptors in the roof of the nose.
University of Louisville

Friedland and Chapman propose the term "mapranosis" for the process by which amyloid proteins produced by microbes (bacteria, fungi and others) alter the structure of proteins (proteopathy) and enhance inflammation in the nervous system, thereby initiating or augmenting brain disease. The term is derived from Microbiota Associated Protepathy And Neuroinflammation + osis (a process).

Friedland hopes that giving the process a name will facilitate awareness of the process, as well as research leading to therapeutic opportunities.

"It is critical to define the ways in which gut bacteria and other organisms interact with the host to create disease, as there are many ways in which the microbiota may be altered to influence health," Friedland said.

Research into the multitude of microbes that inhabit the human body has expanded considerably in recent years. Genomic analysis has begun to reveal the full diversity of bacteria, viruses, fungi, archaea and parasites living in and on the body, the majority of them in the gut. Even more recently, researchers have begun to explore how the proteins and other metabolites produced by microbes inhabiting the gut influence functions in other parts of the body, including the brain. However, we do not yet have a full understanding of how these systems work. The relationship between the microbiota and the brain has been called the "gut-brain axis."

It is understood that the clumping of misfolded amyloid proteins, structures produced by neurons in the brain, are associated with neurodegeneration and conditions such as Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS).

"It is well known that patterns of amyloid misfolding of neuronal proteins are involved in age-related brain diseases. Recent studies suggest that similar protein structures produced by gut bacteria, referred to as bacterial amyloid, may be involved in the initiation of neurodegenerative processes in the brain," Friedland said. "Bacterial amyloids are produced by a wide range of microbes that inhabit the GI tract, including the mouth."

In research published in 2016 in Scientific Reports, Friedland and colleagues showed that when E. coli microbes in the gut of rats and worms (nematodes) produced misfolded amyloids, the amyloids produced in the animals' brains and intestines also misfolded, a process called cross-seeding.

"Our work suggests that our commensal microbial partners make functional extracellular amyloid proteins, which interact with host proteins through cross-seeding of amyloid misfolding and trigger neuroinflammation in the brain," Friedland said.

In today's article, Friedland and Chapman also address other factors related to the microbiota and its products and how they influence neurodegenerative disorders.

1. The microbiota modulates (enhances) immune processes throughout the body, including the central nervous system.

2. The microbiota may induce oxidative toxicity (free radicals) and related inflammation that contributes to neurodegeneration.

3. Metabolites produced by the microbiota may be either beneficial (health sustaining) or damaging (pathogenic).

4. Host genetics influence microbiota populations, illustrating that the gut-brain axis is bidirectional.

Friedland believes further research in this area may lead to therapies for these neurodegenerative diseases, which are increasing in frequency and for which there are few effective treatments.

Chapman's research is supported by the National Institutes of Health. Friedland's work has been supported by The Michael J. Fox Foundation.

http://bit.ly/2DLAcRn

Brain inflammation sows the seeds of Alzheimer's

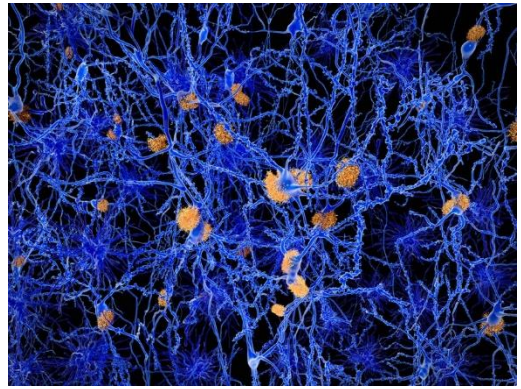
Scientists have found out how the body's own immune response can trigger Alzheimer's disease. Elizabeth Finkel reports.

When it comes to the perpetrator of Alzheimer's disease (AD), the finger of blame has long pointed to hard deposits of protein in the brain known as amyloid plaques. But smouldering signs of inflammation are also clearly evident in the background.

Now a paper in *Nature* reveals how the two processes connive. During inflammation, specks of a protein called ASC are released. Like the grit inside a pearl, they seed the deposition of amyloid. The authors – Carmen Venegas at the University of Bonn, Germany and colleagues – showed that in mice, removing the specks prevented the formation of amyloid and slowed progression of the disease.

"The paper bridges different camps and puts inflammation front and centre as a potential cause of AD," says Bryce Vissel, an AD researcher at the University of Technology, Sydney.

The finding also suggests that anti-inflammatory drugs, particularly those that target the formation of the ASC specks, offer a new therapeutic way forward.



Amyloid plaques can be seen gumming up the spaces between neurons in this illustration. **Juan Gaertner / Science Photo Library**

"This is an extremely important paper for the Alzheimer's field and is likely to greatly influence the way researchers think about potential Alzheimer's treatment strategies going forward," adds Vissel.

The AD-afflicted brain is like a crime scene. The victims are masses of dead neurons that leave many parts of the brain shrunken. The suspects are many: alongside amyloid plaques, tangles of tau proteins inside the neurons have also been interrogated, and investigators find signs of riled-up immune cells called microglia everywhere they look.

But amyloid plaques have been at the top of the list. That's because people who inherit rare genetic forms of the disease also inherit abnormal genes that cause excessive production of sticky forms of amyloid protein that are more likely to aggregate into plaques. Assuming that the plaques were also the cause of neuron death in more common forms of AD, researchers have for the last three decades been developing plaque-busting drugs. But while some, like the promising antibody aducanumab, have scrubbed away plaque, so far they do not appear to have halted the disease.

Given the dead end, many researchers have turned their interest to other suspects. An irritable brain has become a hot favourite. Those agitated microglia and the mobilizing chemicals factors they secrete are found

all over the brains of AD sufferers. General signs of body inflammation in middle age also appear to correlate with an increased risk of AD in later life.

The Venegas team decided to piece together the chain of events that occurs after microglia become irritated. A key occurrence is the formation of a protein complex inside them called an inflammasome. Like a smouldering fire, it continues to release inflammatory signals which mobilize other microglia.

One of the other things the inflammasome does is to release tiny specks of aggregated ASC protein. The researchers had a hunch that ASC specks might be affecting the course of the disease. Not only are they visible in the brain tissue of people with AD, but mice studies had shown that when the formation of the inflammasome was impaired, the mice were protected from their version of the disease.

To test if the specks played some role, the researchers carried out experiments in mice that are genetically engineered to overproduce amyloid plaque. Some of the mice were also engineered not to produce the ASC protein.

For starters, the researchers found that mice lacking ASC produced less amyloid plaque and their disease appeared less severe: they performed better at memorizing mazes, for instance. When brain extracts from plaque-ridden mice were injected into young mice, they seeded the development of new amyloid plaques.

But strikingly, if antibodies to ASC were injected at the same time, it interfered with the seeding.

If the recipient animals lacked ASC altogether, no spreading was seen. ASC did indeed appear to be acting as the grit that seeded the plaque deposits.

The findings show how inflammation and amyloid may collude in a vicious cycle to cause the disease. Amyloid deposits cause inflammation; inflammation releases ASC; ASC seeds the deposition of more amyloid plaque.

What this means, explains senior author Michael Heneka, is that minor insults to the brain – perhaps a virus or mild injury – could snowball into a major inflammatory cascade that kills off neurons.

So what's to be done?

Heneka points out that population studies already show the use of anti-inflammatory drugs like ibuprofen allay the onset of AD. But he says these drugs are too non-specific. Many drug companies are now focussed on finding drugs that inhibit the function of the inflammasome in a particular tissue. "This is all under way," he says.

http://bit.ly/2BN3PVc

Acid reflux associated with head and neck cancers in older adults

Bottom Line: ***Acid reflux was associated with cancer of the respiratory and upper digestive tracts in older adults.***

Why the Research is Interesting: Cancers of the respiratory and upper digestive tracts account for more than 360,000 deaths worldwide each year. These cancers are thought to be caused by various factors, including chronic inflammation. Studies examining a link between the inflammatory condition gastroesophageal reflux disease (GERD or acid reflux) and the development of cancer in the respiratory and upper digestive tracts have had conflicting results.

Who and When: 13,805 patients (66 or older) with cancer of the respiratory and upper digestive tracts and 13,805 patients without cancer; patient information came from the Surveillance, Epidemiology, and End Results (SEER)-Medicare database, a registry of cancer patients and their treatments and outcomes, between 2003-2011.

What (Study Measures): Cancer of the respiratory and upper digestive tracts

How (Study Design): This was a case-control observational study. Patients with cancer of the respiratory and upper digestive tracts (outcome) were compared to those without cancer to examine whether GERD (exposure) was associated with cancer. Researchers were not

intervening for purposes of the study and cannot control natural differences that could explain the study findings.

Authors: Edward D. McCoul, M.D., M.P.H., Tulane University School of Medicine, New Orleans, and coauthors

Results: GERD was associated with cancer of the throat, tonsils and parts of the sinuses.

Study Limitations: Data about patient tobacco and alcohol use, which are the most well-established risk factors for cancer of the respiratory and upper digestive tracts, were not reported in the database. Diagnoses were based on ICD-9 codes which are used for billing rather than clinical purposes.

Study Conclusions: GERD was associated with cancer in older adults in the respiratory and upper digestive tracts. This association requires further study to determine causality and to possibly identify an at-risk population so surveillance can be improved and treatment initiated earlier.

For more details and to read the full study, please visit the For The Media website. (doi:10.1001/jamaoto.2017.2561)

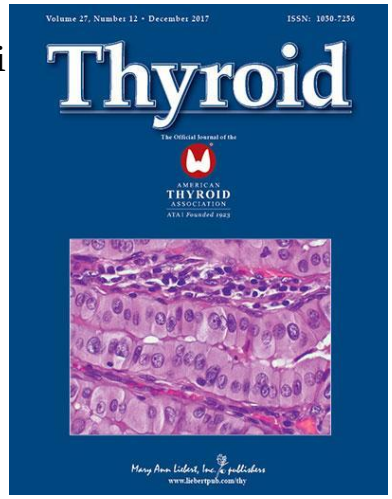
http://bit.ly/2DN98Be

How did the Fukushima nuclear power plant accident impact thyroid cancer risk?

New lessons are being learned about risk assessment and predicting the extent of thyroid cancer occurrence following radiation exposure due to a nuclear power plant accident such as the one in March 2011 in Fukushima Prefecture of Japan.

New Rochelle, NY - The article entitled "Lessons from Fukushima: Latest Findings of Thyroid Cancer after the Fukushima Nuclear Power Plant Accident," is part of a special section on Japanese Research led by Guest Editor Yoshiharu Murata, Nagoya University, Japan, in the January 2018 issue of *Thyroid*, a peer-reviewed journal from Mary Ann Liebert, Inc., publishers and the official journal of the American Thyroid Association (ATA). The article is available free on the *Thyroid* website.

Coauthors Shunichi Yamashita, Shinichi Suzuki, Satoru Suzuki, Hiroki Shimura, and Vladimir Saenko, from Fukushima Medical University and Nagasaki University, Japan discuss the implications of the results of two rounds of large-scale ultrasound screening, which detected a relatively high rate of thyroid cancer in young individuals from the Fukushima area. The researchers examine the challenges in distinguishing radiation-induced thyroid cancer from thyroid cancer that develops spontaneously and thus the difficulty in establishing a causal relationship.



Thyroid, *the official journal of the American Thyroid Association, publishes original articles and timely reviews that reflect the rapidly advancing changes in our understanding of thyroid physiology and pathology, from the molecular biology of the cell to clinical management of thyroid disorders.* Mary Ann Liebert, Inc., publishers

They explore in detail numerous topics, including studies of the link between radiation exposure, thyroid cancer, and related genetic alterations; the occurrence of thyroid cancer after the Chernobyl nuclear power plant accident, hereditary factors that may increase a person's susceptibility to radiation-induced thyroid cancer, and the findings from children, adolescents, and young adults in Fukushima with thyroid cancer treated with surgery.

"The careful study of the nuclear accidents in Chernobyl and Fukushima on health and societal issues continues to be highly informative. At this point, there is no clear evidence that the Fukushima accident has resulted in an increased incidence of thyroid carcinomas, a finding that contrasts with the observations after the Chernobyl accident," says Peter A. Kopp, MD, Editor-in-Chief of *Thyroid* and Professor of Medicine, Division of Endocrinology, Metabolism, and Molecular Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL. "The relatively high incidence of thyroid

malignancies detected through the screening of the Fukushima population highlights the challenges associated with screening programs. However, any definite conclusion would be premature, and continuing observation of the Fukushima population, as well as detailed characterization of the genetic and pathological alterations in the detected thyroid carcinomas, remain important. Our Japanese colleagues are to be commended on the rigorous approach to this highly important public health problem."

http://bit.ly/2l8zGV1

How a Pioneering Botanist Broke Down Japan's Gender Barriers

Kono Yasui was the first Japanese woman to publish in an academic journal, forging a new path for women in her country

By Leila McNeill

When Kono Yasui received her doctoral degree in 1927 from the Tokyo Imperial University, she said: "Blessed by the understanding of those around me and with nothing to encumber me, I have simply plodded along a path of my own choosing."

Kono Yasui at Tokyo University. **Ochanomizu University archive**

That last part was accurate, if an understatement: At 47, Yasui had just become the first Japanese woman ever to earn a PhD in a science. But her path was not entirely unencumbered. She spent much of her life navigating an education system and culture that worked to cultivate women as wives and mothers—rather than leaders of scientific inquiry.

From an early age, Yasui showed an interest in learning. She found an encouraging atmosphere for her studiousness in her parents, who owned a shipping business in the port town of Kagawa Prefecture, writes Miwae Yamazaki in the 2001 compilation *Blazing a Path: Japanese Women's Contributions to Modern Science*. In elementary school, Yasui's father gave her a copy of *Encouragement of Learning* by Fukuzawa Yukichi, a prominent intellectual and founder of Keio University. Yukichi advocated for education reform based on his philosophical principles of independence and equality and argued for women's equality with men.

Yasui must have been bright, indeed, to read such a philosophical text as a young girl. It is also clear that she was raised with the belief that she was not inferior to men.

Yasui was first encouraged to pursue learning at home to supplement an education system that failed to do so. She grew up during the Meji period (1868-1912), in which Japan underwent rapid changes in attempts to modernize the country's industry and economy. A core aspect of the modernization project was education reform. "In order to build new industries, science and engineering were (naturally) seen as essential, so the key was to establish education institutions, modelled upon Western Universities/colleges," write authors Naonori Kodate and Kashiko Kodate in *Japanese Women in Science and Engineering: History of Policy Change*.

Modelling an education system based on that of the West, however, was not necessarily promising for women. At this point, American girls' primary education did not typically include science and mathematics and many universities in Europe and the United States still excluded women.

Education for girls and women in Japan was equally deficient: girls attended separate schools from boys, and their education was predominantly meant to produce *ryōsai kenbo:* 'good wives and wise mothers.' Designating women as wives and mothers meant that, according to the Kodates, "[t]here was no incentive for parents to give [educational] aspirations to their daughters ... and, indeed, social institutions did not provide women with equal opportunities."

Prefectures were not required to offer secondary education for girls until 1899. Women were not allowed in Imperial Universities—similar to the American Ivy Leagues—until 1913 (even then there were only

three). If girls did receive occupational training, it was to become teachers, a career that safely stayed within society's gendered expectations for women.

Despite this unequal education system, Yasui made the most of the opportunities she was given. In 1898, she graduated from Kagawa Prefecture Normal School (the Japanese equivalent of American high school) and went on to study science and mathematics at Tokyo Women's Higher Normal School (TWHNS), which had been upgraded to college status in 1890. Before she had even completed her college degree, she published her first paper "Weber's Organ of Carp Fish" in *Zoological Science*, becoming the first woman to publish in a Japanese science journal.

Kono Yasui (left) at Tokyo University. **Ochanomizu University archive**

In 1907, she took an assistant professorship at TWHNS. In addition to her teaching duties, and despite not having the support of a research university, Yasui also embarked on her own research in plant cytology, the study of plant cells. In 1911, after years of independent research, Yasui set another record by publishing her study "On the Life History of *Salvinia Natans*" in the British journal *Annals of Botany*, which included 119 drawings of microtome cut sections. It was the first time a Japanese woman published in any foreign journal.

In light of Yasui's accomplishments, TWHNS petitioned the Ministry of Education to support Yasui in studying overseas since she could not do so at an Imperial University. At first, the ministry did not approve. This was likely due to deeply embedded assumptions that women could not be successful in scientific fields; In the book chapter "Women Scientists and Gender Ideology," anthropologist Sumiko Otsubo found that between 1875 and 1940, the Ministry of Education funded a total of 3,209 people for study in Europe and the U.S., and only 39 of those were women, most of whom studied English or physical education.

With the help of Kenjiro Fuji, a cytologist (a scientist who studies the structure and function of living cells) at University of Tokyo, the Ministry approved Yasui's request for overseas funding, but with the curious agreement that she add "research in home economics" along with science as her area of study. She also made another, even more unusual agreement with the Ministry: that she not marry but dedicate her life to her research instead.

Both of these compromises were highly gendered; she at once had to efface her conferred cultural role as a 'good wife and wise mother' and obscure her actual scientific work through a veil of domesticity.

Kono Yasui's passport photograph. **Ochanomizu University archive**

In 1914, Yasui arrived at the University of Chicago. For one year, she studied the morphology of the aquatic fern species *azolla* in the Department of Botany. She intended to study in Germany next, but derailed by World War I, she instead landed in Radcliffe College in Cambridge, Massachusetts in 1915 where she studied under botanist Edward C. Jeffrey of Harvard. Under Jeffrey's mentorship, Yasui focused her studies on coal and adopted Jeffery's method for slicing hard materials for microscopic study.

When Yasui returned to Japan in 1916, she continued her studies of Japanese coal and once again took up her teaching post at her alma mater TWHNS. In 1919, she received a grant from the Ministry of Education to continue her research in cytology—yet another unprecedented achievement for a woman. Over the course of her research, she discovered six ancient plant species, including a species of Sequoia that she uncovered in a coal field.

The main crux of her research, however, was the changes that plant tissue underwent during the carbonization process in which plant matter becomes coal. In her profile, Yamazaki writes that Yasui collected many of her specimens herself, descending into coal mines to choose her own samples for study.

In 1927, she published her decade-long botanical study of coal, a collection of nine papers that ultimately showed that it was the work of geological upheavals, not microbes, in which plants turned to sediment for gradual carbonization through interaction with its surrounding matter. In recognition of her pioneering research, Tokyo Imperial University awarded Yasui a doctoral degree in science even though she was not an official student.

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Over the course of her career, Yasui broke ground in both research and teaching. She published a total of 99 papers and received multiple honors for her work. Meanwhile, she campaigned for women's higher education, ultimately helping to establish TWHNS as a national research university for women in 1949, renamed Ochanomizu University. There she became a professor of science and eventually professor emeritus upon her retirement in 1952.

Yet when it came to advocating for women in science, Yasui's efforts can seem ambivalent. While she was actively campaigning for a women-centered research university, she rejected the efforts to establish women only scientific societies. Sumiko Otsubo writes that Yasui believed that women only groups exacerbated inequality between men and women and further implied that women's work was inferior; when asked to join the Society for Women Scientists, she declined.

Yamazaki and Otsubo both report that Yasui strictly avoided seemingly special treatment of her female students and refused to treat them like girls. At the same time, she and fellow scientist Chika Kuroda, the second Japanese woman to earn a PhD in science, established the Yasui-Kuroda Scholarship, a fund to support women's work in the natural sciences. Yasui's ambivalence about how to achieve equality was undoubtedly informed by her own professional experiences, in which equality and respect came by rejecting Japanese cultural standards for womanhood.

Despite her prolific research publications, Yasui was taciturn when it came to writing about herself, meaning that most of what was written about her life was written by others. Yet the few words we have of hers are telling. "I do not seek fame, nor do I desire high status," she said, as quoted by Yamazaki, "but will be content to know that my work lives on after me."

This rings true for both her scientific work and her efforts to raise the status of women's education. Despite her conflicting ideas on how best to achieve gender equality, Yasui worked in many ways to helped open the field a little wider—so that if a woman wanted to make the compromises Yasui did, it would be of her own choosing.

http://bbc.in/2DOj65t

Shingles vaccine 'has cut cases by a third' in England

Cases of shingles have reduced by 35% in England since a vaccine was offered to 70-year-olds, Public Health England says.

By Philippa Roxby Health reporter, BBC News

But it is urging more people in their 70s to get their free injection against the painful condition.

They are most at risk of shingles and more likely to develop complications, such as severe nerve pain.

Shingles is caused by the reactivation of the chicken pox virus and results in a nasty skin rash and fever.

The vaccine programme started in England in 2013 and 5.5m people were eligible for the free single injection over the first three years.

A report in the Lancet Journal of Public Health on how much difference the jab has made between 2013 and 2016 found that roughly 17,000 GP visits for shingles had been avoided.

And another 3,300 consultations were avoided for one of the main complications of shingles - post-herpetic neuralgia (PHN) or long-term pain.

'Nasty disease'

From the data collected, PHE estimate that the vaccine is 62% effective against shingles and between 70-88% effective against PHN.

Despite the reduction in shingles cases, however, the numbers taking up the offer of the vaccine have gone down slightly since 2013.

Dr Mary Ramsay, head of immunisations at Public Health England, encouraged all those eligible to make an appointment at their GP practice to get the shingles vaccine.

"It's the best way to avoid this very nasty disease and the long-term complications that can develop from having it," she said.

"Our population is aging and the risk from getting shingles and complications is higher as you get older.

"Immunisation is the best way to protect yourself from this painful, sometimes debilitating condition."

More than 50,000 cases of shingles occur in people aged 70 years and over each year in England and Wales - and around 50 cases are fatal.

Who can have the shingles vaccination?

- ***All those aged 70, or at 78 as part of a catch-up option***
- ***Also, anyone who missed out up until their 80th birthday***
- ***The shingles vaccine is not available on the NHS if you are aged 80 or over***

See if you are eligible for the shingles vaccine here

What is shingles?

- ***It is a form of the chicken pox virus which has been hiding in the body and been reactivated***
- ***Symptoms are a skin rash on one side of the body, sharp stabbing pain and burning of the skin, headache and fever***
- ***It can last for two to four weeks and be very debilitating***
- ***Shingles can sometimes lead to complications, including severe nerve pain lasting for several months or more***
- ***It is not contagious, but it is possible to catch chickenpox from someone with shingles if you haven't had chickenpox before***

http://bit.ly/2C4wsfU

Folic acid late in pregnancy may increase childhood allergy risk

Research from the University of Adelaide suggests that taking folic acid in late pregnancy may increase the risk of allergies in children affected by growth restriction during pregnancy.

Folic acid, a type of B vitamin, is widely used to prevent neural tube defects in the fetus, and to aid in the development of the central nervous system. The neural tube develops in the first month of pregnancy, and Australian guidelines recommend that women take a daily folic acid supplement at least one month before, and three months after conception.

"Taking a folic acid supplement during the first trimester of pregnancy is important to reduce the risk of neural tube defects," says Dr Kathy Gatford from the University of Adelaide's Robinson Research Institute. "However, continued supplementation with folic acid into the later stage of pregnancy doesn't reduce that risk, and there's growing evidence that this may increase the risk of allergies in offspring," Dr Gatford says.

Allergies are one of the main causes of non-communicable diseases in the world and are estimated to affect 30-40% of the world's population. Susceptibility to these diseases after birth is partly determined by an individual's early life environment.

Previous research has also shown that a complication of pregnancy known as intrauterine growth restriction (IUGR) - a form of growth restriction in the womb often resulting in lower birth weight - may in fact have a protective effect against childhood allergies.

In studies of sheep born from normal or growth-restricted pregnancies, Dr Gatford and colleagues measured skin reactions to two common allergens: dust mites and egg whites.

"Sheep from growth-restricted pregnancies were less likely to have allergic reactions to egg white protein than those born to normal pregnancies. Importantly, if the sheep with growth restricted

pregnancies were fed supplements containing folic acid in late pregnancy, their offspring had similar rates of allergic reactions as control progeny," Dr Gatford says. "Our findings suggest that folic acid supplementation partially reduced the protection that has previously been seen in pregnancies with restricted growth.

"Studies in animal models like this allow us to directly investigate these effects of the environment before birth on later allergy. While the results help us to better understand the potential allergy risk in humans, more research is needed before any recommendations about the right timing of supplementation should or could be made in humans," she says.

"We are now in the process of analyzing how a growth-restricted pregnancy and the dietary supplement affect the nutrient status of offspring at birth, and how this might switch on or off genes that regulate the immune system."

This research has been funded by the National Health and Medical Research Council (NHMRC). It is published online ahead of print in the American Journal of Physiology--Regulatory, Integrative and Comparative Physiology.

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Stromatolites Defy Odds by A) Living B) on Land

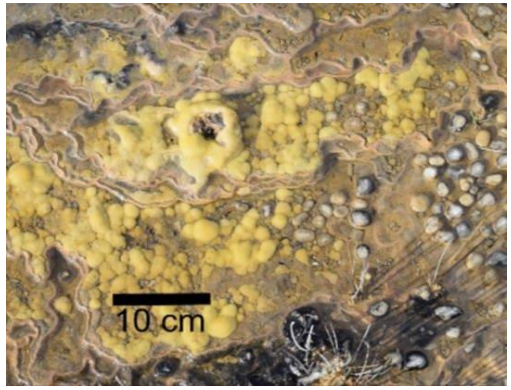
A life form that once ruled the planet has turned up unexpectedly in Tasmania

By Jennifer Frazer on December 21, 2017

One of the first things life did after it evolved -- after making lots more of itself and taking over the planet, of course -- was to invent the high rise. Fossils from 3.7 billion years ago, just under a billion years after Earth formed, tell us films of bacteria started trapping tiny particles of rock and welding them into finely layered stone pillows that plumped into microbial skyscrapers.

The resulting geological confections, today called stromatolites, are the first evidence we have for life on Earth. Once, they covered the seafloor of all the shallow seas on the planet and their fossils are abundant. But they were long thought to be extinct, because no one could find a living example. Where had they gone?

The prime suspects, unfortunately, were thugs like us: newfangled grazing animals, which rapidly decimated the defenseless neighborhoods of placid bacterial towers. But given the hordes of ravenous animal crawling all over Earth at present, how could they possibly survive now?



Giblin River stromatolites. Proemse et al. 2017

Scientists were thus probably delighted in 1956 by the discovery of the Hamelin Pool at Shark Bay, halfway up Australia's western coast. In this special place where the salinity is twice that of normal seawater, stromatolites built of blue-green algae called cyanobacteria persist, like a dream of a planet half-remembered by its former self. This is only possible, of course, because the hypersaline water acts as a natural defense system, forbidding hungry, destructive animals from entering.

Although a few other environments on Earth have been found to host stromatolites since then, they remain indisputably rare, and presumably only possible where "exotic" chemistry prevents animals from wreaking havoc. Such places include super salty environments in the Hamelin Pool, at Storr's Lake in the Bahamas, in a lake on the Kiritimati Atoll in the Central Pacific, and in a few freshwater environments with their own peculiar chemistry like British Columbia's Pavilion Lake or the Ruidera Pools Natural Park in Spain.

So it was with great surprise that I read the other day that stromatolites have been discovered in Australia again, but this time *on land*. Touché, cyanobacteria. I did not expect that one.

In a paper published in November in the journal *Scientific Reports*, scientists from Tasmania report on yellow-green globular growths in the sand and gravel beds of alkaline spring mounds scattered among the wetland in the Giblin River Catchment of the Tasmanian Wilderness World Heritage Area.

There, cold springs releasing mildly alkaline water filled with calcium and bicarbonate permeate the soil for a short distance before dissipating in the acidic water of the surrounding bogs. The stromatolites are growing on wetted ground, but the top several centimeters of the towers where the bacteria grow are bathed in air.

Giblin River stromatolites. Proemse et al. 2017

That is a highly unusual configuration, but the region does get 11 feet of rain a year. The largest stromatolites are around four inches across, but most are much smaller, and they have fine internal calcite layers.

The scientists examined the DNA of the bacteria in these mas and discovered they seem to be a unique team, unlike those seen in stromatolites anywhere else on Earth, including those in other freshwater and lake environments. This discovery, the scientists say, means that stromatolites may be more common than realized, because people have not been looking for them in freshwater springs. Perhaps if we do, we will discover that they are not so rare after all.

This particular geologic setup seems to permit stromatolites to form, they add, because of an Achilles heel in the construction of the major grazers' mobile homes. Snails, of course, have calcium carbonate shells. And snails sure like to eat stromatolites. But in the alkaline waters of these springs, the carbonate in the water will anneal to the shell of a snail, causing snail shells to grow increasingly heavy and unwieldy. The snail's mobile defense system rapidly becomes a fortress of death, as it slowly taxes its builder's resources to the breaking point.

Snails both young and old seem to be affected. Few live snails of any age were seen, while dense piles of empty shells testify to the lethal effectiveness of the water, but probably still fail to warn even especially bright snails away. Some of the discarded shells were so encrusted that they were no longer recognizable as a snail's.

Although an assortment of other small mostly shell-less predators are around – a flatworm, some roundworms and various other worms, some juvenile stoneflies, and miscellaneous small crustaceans – their feeding does not seem to be an impediment to the stromatolites.

Cast-away snail shells showing various stages of calcite encrustation in the Giblin River catchment. Proemse et al. 2017

These spring mounds remind me of the Greco-Roman idea that there are nymphs who tend every spring and pool, protecting the creatures that dwell there. The waters of these Tasmanian springs are the spirits that protect their odd, land-lubbing stromatolites, allowing them to exist in seemingly the most improbable of places.

Reference *Proemse, Bernadette C., Rolan S. Eberhard, Chris Sharples, John P. Bowman, Karen Richards, Michael Comfort, and Leon A. Barmuta. "Stromatolites on the rise in peat-bound karstic wetlands." Scientific Reports 7, no. 1 (2017): 15384.*

http://s.nikkei.com/2zsPUh1

Otsuka invests in startup making iPS-derived blood platelets

Japanese drugmaker gains access to Megakaryon's game-changing tech

TOKYO -- Japanese drugmaker Otsuka Holdings is making inroads into blood products with an investment in compatriot Megakaryon, a venture that creates platelets out of induced pluripotent stem cells, in hopes of commercializing the technology by 2020.

Otsuka Pharmaceutical and Otsuka Pharmaceutical Factory have together shelled out 1 billion yen ($8.82 million) to acquire shares newly issued by Megakaryon, taking a roughly 10% stake.

The Otsuka group is now Megakaryon's second-largest shareholder, after the public-private Innovation Network Corp. of Japan, which

holds a 50%-plus interest. Megakaryon has raised 3.7 billion yen in total, with Sysmex, CMIC Holdings, Kyoto Seisakusho and Satake Chemical Equipment Manufacturing also purchasing shares.

Otsuka has been seeking a new avenue for growth in the years since the Abilify schizophrenia drug, which brought in more than 600 billion yen a year at its peak, lost patent protection. It aims to diversify by turning cancer drugs into a business pillar while actively investing in new cutting-edge technology.

Megakaryon intends to use the funds raised to begin clinical trials in Japan in 2019 and build production lines capable of producing about 5,000 packs a year of iPS-derived platelets. It aims to commercialize the technology in 2020 and is also looking to expand abroad.

The production of platelet products, which are used as clotting agents, still depends entirely on donations. But with the Japanese population shrinking, donations are seen falling 15% under necessary levels in 2027. iPS-derived products could fill this gap in Japan's 73 billion yen market for platelet products.

Platelet products made the conventional way keep for just four days, but those derived from iPS cells are good for two weeks.

http://bit.ly/2BQ8IfW

Research shows Clean Air Act is likely responsible for dramatic decline in atmospheric organic aerosol

New research proposes that the EPA's legislation may have saved even more lives than initially reported.

The air we breathe contains particulate matter from a range of natural and human-related sources. Particulate matter is responsible for thousands of premature deaths in the United States each year, but legislation from the U.S. Environmental Protection Agency (EPA) is credited with significantly decreasing this number, as well as the amount of particulate matter in the atmosphere. However, the EPA may not be getting the full credit they deserve: new research from MIT's Department of Civil and Environmental Engineering (CEE) proposes that the EPA's legislation may have saved even more lives than initially reported.

"In the United States, the number of premature deaths associated with exposure to outdoor particulate matter exceeds the number of car accident fatalities every year. This highlights the vital role that the EPA plays in reducing the exposure of people living in the United States to harmful pollutants," says Colette Heald, associate professor of CEE and Earth, Atmospheric and Planetary Sciences.

The EPA's 1970 Clean Air Act and additional amendments enacted in 1990 address the health effects of particulate matter, specifically by regulating emissions of air pollutants and promoting research into cleaner alternatives. In 2011 the EPA announced that the legislation was responsible for a considerable decrease in particulate matter in the atmosphere, estimating over 100,000 lives saved every year from 2000 to 2010. However, the report did not consider organic aerosol, a major component of atmospheric particulate matter, to be a large contributor to the decline in particulate matter during this period. Organic aerosol is emitted directly from fossil fuel combustion (e.g. vehicles), residential burning, and wildfires but is also chemically produced in the atmosphere from the oxidation of both natural and anthropogenically-emitted hydrocarbons.

The CEE research team, including Heald; Jesse Kroll, an associate professor of CEE and of chemical engineering; David Ridley, a research scientist in CEE; and Kelsey Ridley SM '15, looked at surface measurements of organic aerosol from across the United States from 1990 to 2012, creating a comprehensive picture of organic aerosol in the United States.

"Widespread monitoring of air pollutant concentrations across the United States enables us to verify changes in air quality over time in response to regulations. Previous work has focused on the decline in particulate matter associated with efforts to reduce acid rain in the United States. But to date, no one had really explored the long term trend in organic aerosol," Heald says.

The MIT researchers found a more dramatic decline in organic aerosol across the U.S. than previously reported, which may account for more lives saved than the EPA anticipated. Their work showed that these changes are likely due to anthropogenic, or human, behaviors. The researchers' findings were published in a paper, "Causes and Consequences of decreasing atmospheric organic aerosol in the U.S." in the Proceedings of the National Academy of Sciences the week of December 25.

"The EPA report showed a very large impact from the decline in particulate matter, but we were surprised to see a very little change in the organic aerosol concentration in their estimates," explains David Ridley. "The observations suggest that the decrease in organic aerosol had been six times larger than estimated between 2000 and 2010 in the EPA report."

Using data from the Interagency Monitoring of Protected Visual Environments (IMPROVE) network, the researchers found that organic aerosol decreased across the entire country in the winter and summer seasons. This decline in organic aerosol is surprising, especially when considering the increase in wildfires. But the researchers found that despite the wildfires, organic aerosols continue to decline.

The researchers also used information from the NASA Modern-Era Retrospective Analysis for Research and Applications to analyze the impact of other natural influences on organic aerosol, such as precipitation and temperature, and found that the decline would be occurring despite cloud cover, rain, and temperature changes.

The absence of a clear natural cause for the decline in organic aerosol suggests the decline was the result of anthropogenic causes. Further, the decline in organic aerosol was similar to the decrease in other measured atmospheric pollutants, such as nitrogen dioxide and carbon monoxide, which are likewise thought to be due to EPA regulations. Also, similarities in trends across both urban and rural areas suggest that the declines may also be the result of behavioral changes stemming from EPA regulations.

By leveraging the emissions data of organic aerosol and its precursors from both natural and anthropogenic sources, the researchers simulated organic aerosol concentrations from 1990 to 2012 in a model. The researchers found that more than half of the decline in organic aerosol is accounted for by changes in human emissions behaviors, including vehicle emissions and residential and commercial fuel burning.

"We see that the model captures much of the observed trend of organic aerosol across the U.S., and we can explain a lot of that purely through changes in anthropogenic emissions. The changes in organic aerosol emissions are likely to be indirectly driven by controls by the EPA on different species, like black carbon from fuel burning and nitrogen dioxide from vehicles," says Ridley. "This wasn't really something that the EPA was anticipating, so it's an added benefit of the Clean Air Act."

In considering mortality rates and the impact of organic aerosol over time, the researchers used a previously established method that relates exposure to particulate matter to increased risk of mortality through different diseases like cardiovascular disease or respiratory disease. The researchers could thus figure out the change in mortality rate based on the change in particulate matter. Since the researchers knew how much organic aerosol is in the particulate matter samples, they were able to determine how much changes in organic aerosol levels decreased mortality.

"There are costs and benefits to implementing regulations such as those in the Clean Air Act, but it seems that we are reaping even greater benefits from the reduced mortality associated with particulate matter because of the change in organic aerosol," Ridley says. "There are health benefits to reducing organic aerosol further, especially in urban locations. As we do, natural sources will contribute a larger fraction, so we need to understand how they will vary into the future too."

Explore further: Researchers find new vehicle emissions to be deceptively clean

More information: D. A. Ridley el al., "Causes and consequences of decreasing atmospheric organic aerosol in the United States," PNAS (2017).

www.pnas.org/cgi/doi/10.1073/pnas.1700387115