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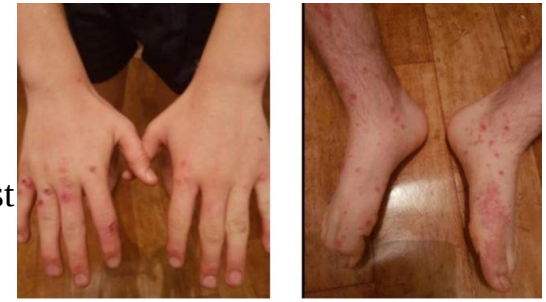
Teenager's cowpox diagnosis surprises doctors

A 15-year-old boy has surprised doctors by contracting cowpox, a historical disease now so rare it has not been seen in Wales for more than a decade.

By Gemma Ryall BBC News 16 June 2018

The teenager, who lives on the Wrexham-Cheshire border, developed lesions on his hands after feeding calves.

Public Health Wales said the last reported human case in Wales was some 10 to 15 years ago.



Distinctive cowpox lesions appeared on the boy's hands, arms and feet
Countess of Chester Hospital NHS Foundations Trust

Cowpox was more common in the 18th Century when milking maids often caught it. The virus, which is not contagious from person to person, has all but disappeared because industrial farming methods mean fewer people milk cows by hand.

Now it is very rare in both humans and animals, according to Public Health Wales, with feral cats most likely to catch it from rodents.

The boy's mother, who does not want to be identified because her son is embarrassed, said the calves he had been feeding had nibbled on his hands, causing them to become grazed.

He then developed pus-filled lesions on his hands, arms and feet.

"We were really unsure what it was," she said. "The one on his ankle was worrying - it was weeping a clear liquid down his ankle."

After seeing their GP, they got sent straight to the Countess of Chester Hospital, where he was diagnosed with cowpox. "I didn't really know what it was, so I was quite concerned. The first thing you do is look on the internet and that's when I found out it was quite rare," she said.

"My son was quite embarrassed - it looked quite a mess, they (the lesions) weren't nice and it wasn't pleasant for him. "It took weeks and weeks to go, a long time. He still has some marks on his hands."

Dr Aysha Javed, who diagnosed the teenager after seeing the distinctive pus-filled lesions on his hands, arms and feet, said it was the first case of cowpox she had seen.

"I think the boy and his family were quite bemused when we told them - I don't think they expected that to be the diagnosis," she said. "I think it was very itchy for him but it wasn't particularly painful."

How cowpox helped eradicate smallpox

In the 1790s Dr Edward Jenner observed that milking maids seemed less susceptible to smallpox. Smallpox was at the time an extremely common childhood infection, which killed about one in five of those who caught it, mostly children under five.

Cowpox was used to create the smallpox vaccine in 1796 **Getty Images**

Jenner hypothesised protection was due to contact with cowpox lesions and went on to test his theory on an eight-year-old boy called James Phipps. In 1796 he immunised James with fluid from a cowpox lesion on the arm of a milking maid called Sarah Nelmes and then, after exposing the boy to smallpox, confirmed he was protected against it.

Immunisation programmes using cowpox fluid quickly gained popularity across Europe. Later vaccines were made using a purified form of the vaccinia virus. The word vaccination is derived from "vacca", Latin for cow. As a result of global immunisation programmes, the World Health Organisation declared smallpox had been eradicated worldwide in 1980.

Dr Robert Smith, clinical scientist lead for zoonoses at Public Health Wales, said cowpox had not been reported in Wales for some 10 to 15 years. "A total of 29 laboratory reports of cowpox were received by the public health laboratories (PHLS) communicable disease surveillance centre between 1975 and 1992 (with a range of 0 to four reports annually)," he added.

The boy was diagnosed about three months ago, but his case came to light when Dr Javed and her colleagues alerted other medics to it during a recent European Society for Pediatric Dermatology annual meeting. "We have to inform other colleagues about rare cases and, if it's something that's going to be re-emerging, public health professionals need to be alerted," she added. "We don't really see cowpox anymore - it's one of those diseases that went away."

The British Association of Dermatologists said it was very useful for doctors and members of the public to be aware of "what we might consider historical diseases making a resurgence".

"Cowpox is quite unusual and, as the doctors note, when you look at a pox-like rash on a child these days the first thing that tends to spring to mind is chicken pox," a spokesman said. "Although this resurgence is interesting, it's not something that is particularly worrying as cowpox tends to be benign in nature to otherwise healthy people."

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HPV vaccine cuts cancer-causing infection

There has been a significant fall in the number of cases of HPV, the virus that causes cervical cancer, following the introduction of a vaccine for young women, a new study says.

The Human Papilloma Virus vaccine fights high-risk infections which cause the majority of cervical cancer cases.

HPV infections decreased in women aged 16 to 21 by 86% between 2010 and 2016 data from Public Health England show. It comes as newspapers say the vaccine may soon be offered to boys too.

HPV

Cervical cancer remains the most common cancer in women under 35. Experts say these results suggest that the vaccine, introduced just 10 years ago, could eventually lead to a virtual eradication of the disease, which kills around 850 women a year.

Mary Ramsay, head of immunisation at Public Health England, said: "These results are very promising and mean that in years to come we can expect to see significant decreases in cervical cancer. "The study also reminds us how important it is to keep vaccination rates high to reduce the spread of this preventable infection. "I encourage all parents of girls aged 12 to 13 to make sure they take up the offer for this potentially life-saving vaccine."

The HPV vaccine, first introduced in 2008, is delivered through schools in two doses to girls from the age of 12 to their 18th birthday. It is not offered to women over the age of 18. More than 80% of people aged 15-24 have now been vaccinated in the UK.

The Joint Committee on Vaccination and Immunisation (JCVI), an expert advisory group, has reportedly told health ministers vaccinating boys will be cost-effective. A Department of Health and Social Care spokeswoman would not confirm the reports, but said any advice from the JCVI would be "carefully considered" once received.

What is the Human Papilloma Virus (HPV)?

- ***HPV is the name given to a common group of viruses; there are more than 100 types of HPV***
- ***Many women will be with infected with HPV over the course of their lifetime without any ill-effect***
- ***In the vast majority of cases, there will be no symptoms and the infection will clear on its own, but in some cases persistent infection can lead to cervical disease***
- ***Some types of HPV are high risk because they are linked to the development of some cancers***
- ***Other lower risk HPV types can lead to genital warts***

•Nearly all cervical cancers (99.7%) are caused by infection from a high risk HPV

•The HPV vaccine protects against four types of HPV which cause around 80% of cervical cancer and the vast majority of genital warts

Source: NHS Choices

In addition, the HPV vaccine is leading to a decline in genital warts, caused by low risk strains of HPV.

The number of genital wart diagnoses in sexual health clinics between 2009 and 2017 fell in girls aged 15-17 by 89%, and in boys of the same age by 70% as a result of girls not infecting them.

However, the HPV virus is also implicated in cancers in men, such as anal and throat, head and neck. Last year, the vaccine was extended to gay men aged 16-45, but is not currently offered to boys.

Extending the vaccine is currently under review by the Joint Committee on Vaccination and Immunisation, but some researchers believe this is not happening fast enough.

Prof Mark Lawler, of the Centre for Cancer Research and Cell Biology at Queens's University Belfast, is calling for the vaccine to be extended to boys. "Head and neck cancer is one of the fastest growing cancers in the UK, so why can't we have a vaccine that protects boys as well as girls? Yes some boys are protected if there is a high rate of girls getting vaccinated, but in areas where there is a low take-up rate, then that immunity is not going to happen.

"Many countries now vaccinate both girls and boys, including Canada which has a similar health system to the UK," he added.

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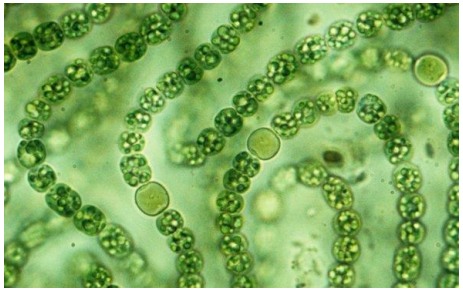
Weird Low-Light Bacteria Could Potentially Thrive on Mars

The photosynthetic organisms subsist on redder, lower-energy light than other species, and could be a new source of fuel and air for interplanetary outposts

By Sarah Lewin, SPACE.com on June 18, 2018

An international team of scientists has found that a strange type of bacteria can turn light into fuel in incredibly dim environments. Similar bacteria could someday help humans colonize Mars and expand our search for life on other planets, researchers said in a statement released with the new work.



Getty Images

Organisms called cyanobacteria absorb sunlight to create energy, releasing oxygen in the process. But until now, researchers thought these bacteria could absorb only specific, higher-energy wavelengths of light. The new work reveals that at least one species of cyanobacteria, called *Chroococcidiopsis thermalis*—which lives in some of the world's most extreme environments—can absorb redder (less energetic) wavelengths of light, thus allowing it to thrive in dark conditions, such as deep underwater in hot springs.

"This work redefines the minimum energy needed in light to drive photosynthesis," Jennifer Morton, a researcher at Australian National University (ANU) and a co-author of the new work, said in the statement. "This type of photosynthesis may well be happening in your garden, under a rock." (In fact, a related species has even been found living inside rocks in the desert.)

By studying the physical mechanism behind these organisms' absorption abilities, researchers are learning more about how photosynthesis works—and raising the possibility of using similar low-light organisms to generate oxygen in places like Mars.

"This might sound like science fiction, but space agencies and private companies around the world are actively trying to turn this aspiration into reality in the not-too-distant future," Elmars Krausz, study co-author and a professor emeritus at ANU, said in the statement.

"Photosynthesis could theoretically be harnessed with these types of organisms to create air for humans to breathe on Mars.

"Low-light-adapted organisms, such as the cyanobacteria we've been studying, can grow under rocks and potentially survive the harsh conditions on the Red Planet," Krausz added.

Researchers originally thought that a particular chlorophyll pigment, called chlorophyll f, helped capture light but couldn't directly participate in converting it into energy, according to the new work, which was released yesterday (June 14) in the journal Science. But this research shows that, in fact, the pigment does participate in energy conversion, and lets the organism pull energy from longer wavelengths than ever observed.

"Chlorophyll adapted to absorb visible light is very important in photosynthesis for most plants, but our research identifies the so-called 'red' chlorophylls as critical components in photosynthesis in low-light conditions," Morton said.

Not to mention, it could play a key role in the search for life beyond Earth: "Searching for the signature fluorescence from these pigments could help identify extra-terrestrial life," she said. Knowing such organisms exist on Earth not only broadens where we look for alien organisms but also suggests what to search for when we look.

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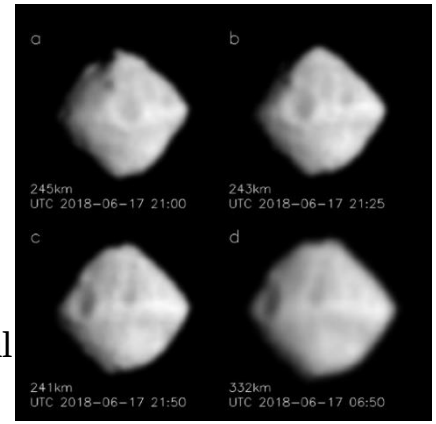
'Dumpling-shaped' space rock comes into view

A Japanese spacecraft is sending back images as it approaches an irregularly shaped asteroid that some on the mission have compared to a dumpling.

By Paul Rincon Science editor, BBC News website

The Hayabusa 2 spacecraft was launched in 2014 on a quest to study the asteroid Ryugu and deliver rocks and soil from its surface to Earth. The craft is now about 215km away from Ryugu and should arrive on 27 June.

Hayabusa's camera is starting to resolve its shape, which has been likened to a Japanese dango dumpling. But closer inspection shows that the object is pitted with dents or craters. In addition, the asteroid's orbit is retrograde, meaning that it spins in the opposite direction to the Sun and the Earth. The video shown above was compiled from 52 images captured by the spacecraft's ONC-T camera (Optical Navigation Camera - Telescopic) between 14 and 15 June.



Images of Ryugu taken with the Hayabusa 2 probe. These photographs were taken on June 17, 2018, at around 3:00 p.m. and June 18 at around 6:00 a.m. JST. **(Photo courtesy of JAXA)**

Around 27 June, the spacecraft will arrive at a distance of 20km from the asteroid, which goes by the formal name of 162173 Ryugu.

The Japanese Aerospace Exploration Agency (Jaxa) spacecraft will then survey the object for a year-and-a-half, during which it will aim to deploy several landing craft on the surface and use an explosive device to dig out a "fresh" rocky sample from within Ryugu.

Some of the landing craft could be deployed as early as September; they include a German-made instrument package called Mascot (Mobile Asteroid Surface Scout). The mission will depart Ryugu in December 2019 with the intention of returning to Earth with the asteroid samples in 2020.

The first Hayabusa spacecraft was launched in 2003 and reached the asteroid Itokawa in 2005. It was also designed to deliver asteroid samples to Earth but was hit by a series of mishaps. For example, the attempt to recover soil from Itokawa suffered from communication problems, leading to initial confusion over whether the probe had actually touched down. But the spacecraft eventually returned to

Earth in 2010 with a small amount of material from the asteroid. An American asteroid sample return mission, Osiris-Rex, will rendezvous with the asteroid 101955 Bennu in August.

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A molecular signature for social isolation identified in the brain

Extended social isolation causes debilitating effects in social mammals such as humans. A study in mice shows that the gene Tac2 is upregulated throughout the brains of socially isolated animals, driving massive behavioural changes.

Noga Zilkha & Tali Kimchi

Even the toughest prisoners fear solitary confinement. There is a growing awareness across the globe that we are facing an epidemic of loneliness. Prolonged social isolation and loneliness can lead to many profound physiological and neuropsychiatric conditions, including depression and heart disease, and to increased mortality rates[1]. In the United States, more than 50% of people over the age of 60 experience loneliness[2], and the United Kingdom has appointed a government minister to tackle the issue of loneliness. But the biological mechanisms underlying the effects of social isolation are poorly understood. Writing in *Cell*, Zelikowsky *et al*.[3] reveal a signalling mechanism that acts in several brain regions in mice to drive some of the harmful effects of the stress caused by chronic social isolation.

The authors examined the effects of two weeks of social isolation on the brains and behaviour of male mice (equivalent to more than a year in these conditions for humans[4]). First, the researchers used an array of behavioural tests to compare mice kept in isolation with control mice that had been housed in groups. These assays revealed widespread effects. Compared to control animals, isolated mice showed enhanced aggression and hypersensitivity to diverse stressful stimuli. For example, the socially isolated mice responded more aggressively to an unfamiliar mouse placed in their cage. In another assay, the researchers presented mice with a dark circle that loomed overhead, simulating an approaching predator. Control animals froze in response to the threat, but moved normally after the stressful stimulus was removed, whereas isolated mice remained frozen long after the apparent threat was removed.

Next, Zelikowsky *et al*. investigated the brain mechanisms underlying this behaviour. In a previous study of fruit flies, the same group had identified the gene *Tac* as essential for the regulation of aggression induced by social isolation[5]. Rodents have two versions of *Tac*, which are expressed in various brain regions, including regions associated with social behaviour, anxiety and emotions. Using several independent methods, Zelikowsky and colleagues now found a massive increase in the expression of *Tac2* throughout the brain following social isolation.

The gene *Tac2* encodes a protein called neurokinin B (NkB), which binds specifically to the receptor Nk3R. The researchers performed a series of experiments to alter NkB signalling in the brain. First, they systemically inhibited NkB signalling in isolated male mice using a drug called osanetant, which inhibits the activity of Nk3R. Administration of osanetant, either throughout the social-isolation period or 20 minutes before behavioural testing, substantially reduced the effects of social isolation on behaviour. Next, the authors genetically upregulated *Tac2* expression and simultaneously activated *Tac2*-expressing neurons in group-housed animals, using specially designed viruses that were injected intravenously but could cross the blood–brain barrier to reach the brain. They found that this genetic manipulation led to group-housed mice behaving in a similar way to those that had been isolated.

Finally, Zelikowsky *et al*. locally manipulated *Tac2* expression and NkB signalling, by injecting either osanetant or viruses to downregulate *Tac2* expression or inhibit the activity of *Tac2*-

expressing neurons, into particular locations in the brain. These experiments enabled the authors to attribute specific behaviours to regulation of *Tac2* in specific brain regions. The main social effect of isolation — enhanced aggression towards an intruder — was controlled by *Tac2* in the dorsomedial hypothalamus. By contrast, acute and persistent stress responses were regulated primarily by *Tac2* in the central amygdala (Fig. 1).

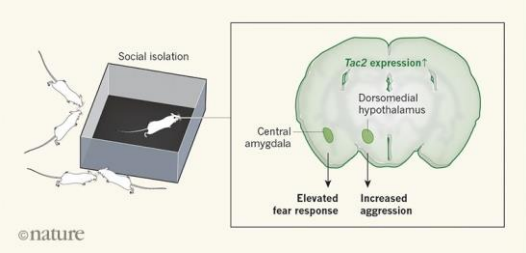


Figure 1 | The gene *Tac2* mediates various effects of social isolation in mice. Zelikowsky *et al.*[3] investigated how two weeks of isolation affected the brains and behaviour of male mice. They found that *Tac2* expression is upregulated throughout the brain, and that the gene's upregulation in particular areas — including the central amygdala and dorsomedial hypothalamus — led to specific changes in the animals' social behaviour and in their response to various stressful stimuli.

This work opens a gateway to much future research. First and foremost, it will be interesting to determine whether *TAC3*, the human equivalent of *Tac2*, is involved in mediating the effects of loneliness and social isolation in people. To our knowledge, *TAC3* has not yet been directly associated with sociality or social behaviour of any kind in humans. However, it is expressed in the human brain and has shown abnormal gene-expression levels in children with autism-spectrum disorder[6], which profoundly affects social interaction. The systemic manipulations presented in Zelikowsky and colleagues' paper could be rapidly applied to humans, because osanetant and other NkB inhibitors have already been tested in clinical trials. These drugs could potentially treat anti-social disorders induced by isolation, as well as mood and anxiety disorders.

Although most of their experiments focused on male mice, Zelikowsky *et al.* found upregulation of *Tac2* in response to social isolation in both males and females. Sex differences in response to stress and isolation are well documented, and are usually conserved across species[7]. It will therefore be interesting to test whether the roles of *Tac2* in mediating the effects of social isolation in females are similar to or different from those in males.

The need for social interactions and the response to social isolation can differ enormously between and within species. Mice and humans, for example, are typically considered to be highly social creatures[8]. When their social needs are not filled, they can experience debilitating outcomes[1,9]. Some species (and individuals within a species), however, are more solitary, or even avoid social inter-actions[10]. Such species or individuals might harbour neuronal mechanisms that are adapted to the lack of social inter-action. Whether or not members of the *Tac* gene family act differently in solitary individuals or species compared to how they do in more-social individuals or species remains to be determined.

Finally, one has to wonder: to what extent can we rely on a mouse model of social isolation to truly examine the underlying mechanisms of human loneliness? After all, loneliness and mental isolation are subjective, and a person might feel alone even when surrounded by other people. The traits exhibited by mice under prolonged social isolation greatly resemble those found in humans experiencing solitary confinement, so these animals do provide a good model for studying this process. What we currently lack are relevant animal models for other forms of human loneliness, such as social withdrawal or antisocial personality disorder. Expanding our research toolbox — for example, by studying various species, including non-social and community-living animals, as well as humans — might bring us closer to understanding the biology of human loneliness. *doi: 10.1038/d41586-018-05447-9*

http://bit.ly/2KaYKcp

New material for splitting water

A promising new material has the right properties to capture solar energy and split water into hydrogen and oxygen.

WASHINGTON, D.C Solar energy is clean and abundant. But when the sun isn't shining, you must store the energy in batteries or through a process called photocatalysis -- in which solar energy is used to make fuels. In photocatalytic water splitting, sunlight separates water into hydrogen and oxygen. The hydrogen and oxygen can then be recombined in a fuel cell to release energy.

Now, a new class of materials -- halide double perovskites -- may have just the right properties to split water, according to a newly published paper in *Applied Physics Letters*, from AIP Publishing.

"If we can come up with a material that can be useful as a water-splitting photocatalyst, then it would be an enormous breakthrough," said Feliciano Giustino, a co-author on the paper.

Researchers have experimented with many photocatalytic materials before, such as titanium dioxide (TiO2). While TiO2 can harness sunlight to split water, it's inefficient because it doesn't absorb visible light well. So far, no photocatalytic material for general water splitting has become commercially available.

Using supercomputers to calculate the quantum energy states of four halide double perovskites, George Volonakis and Giustino, both of the University of Oxford, found that Cs2BiAgCl6 and Cs2BiAgBr6 are promising photocatalytic materials because they absorb visible light much better than TiO2. They also generate electrons and holes (the positively charges absence of electrons) that have sufficient energy (or nearly ideal energies) to split water into hydrogen and oxygen.

Very few other materials have all these features at once, Giustino said. "We can't say this will work for sure, but these compounds seem to have all the right properties."

Giustino and his team originally discovered this type of perovskite while looking for materials to make solar cells. Over the last several years, perovskites have garnered interest as materials to boost the efficiency of silicon-based solar cells through tandem designs that integrate a perovskite cell directly onto a high-efficiency silicon cell, but they contain a small amount of lead. If they were used for energy harvesting in a solar farm, the lead could pose a potential environmental hazard.

In 2016, using computer simulations to identify alternative materials, the researchers found a new type of lead-free perovskite with potential for high-efficiency solar cells. The present paper shows these new materials may also split water. "These new double perovskites are not only promising as a complementary material for tandem solar cells, but they can also be promising in areas like photocatalysis," Volonakis said.

Still, the new analysis is theoretical, assuming the compounds form perfect crystals. The next step, the authors said, is for experimentalists to see if the material works in the real world as well as predicted. In the meantime, the researchers are using their computational techniques to explore whether these double perovskites have properties useful for other applications like light detectors.

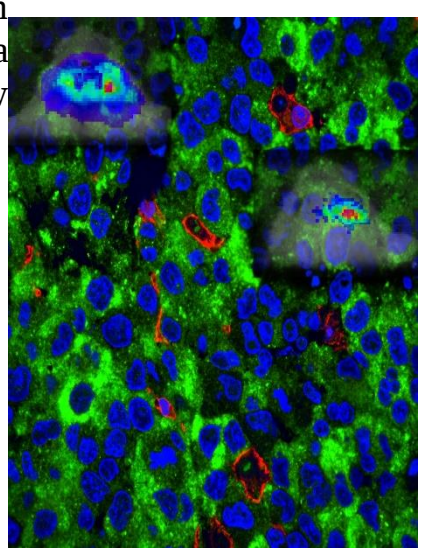
The article, "Surface properties of lead-free halide double perovskites: Possible visible-light photo-catalysts for water splitting," is authored by George Volonakis and Feliciano Giustino. The article appeared in Applied Physics Letters *June 12, 2018, (DOI: 10.1063/1.5035274) and can be accessed at https://aip.scitation.org/doi/full/10.1063/1.5035274.*

http://bit.ly/2tlUuqB

Study suggests well-known growth suppressor actually fuels lethal brain cancers

Research points to potential treatment target that lacks a workable drug

CINCINNATI - Scientists report finding a potentially promising treatment target for aggressive and deadly high-grade brain cancers like glioblastoma. But they also say the current lack of a drug that hits the molecular target keeps it from being advanced for testing as a therapeutic strategy for patients with few treatment options.



Publishing their data online June 18 in *Nature Cell Biology*, researchers at the Cincinnati Children's Cancer and Blood Diseases Institute point to a protein that helps regulate cell metabolism called AMPK (AMP-activated protein kinase). Their data suggest AMPK is a key driver of the mostly untreatable brain cancers, and blocking it may produce therapeutic benefit for very ill patients.

***This image of molecularly stained brain cells shows the AMPK target protein (green) in a large glioblastoma brain tumor that grew from transplanted human cancer cells in a mouse brain. Scientists report in Nature Cell Biology that tumor growth was reduced when the researchers genetically inhibited AMPK, suggesting it may be a potential treatment strategy for lethal and mostly untreatable brain cancers like high-grade glioblastoma.* Cincinnati Children's**

But the finding also challenges the scientific status quo regarding AMPK. This is because current research literature characterizes it as a cancer suppressor, according to the study's senior investigators, Biplab Dasgupta, PhD, and first author Rishi Raj Chhipa, PhD--both scientists in the Division of Oncology at Cincinnati Children's.

"AMPK is considered to play a suppressive role in cancer because it inhibits cancer-promoting enzymes like mammalian target of rapamycin (mTOR) and acetyl Co-A carboxylase (ACC)," Dasgupta said. "Our study uses analysis of The Cancer Genome Atlas to show that AMPK proteins are highly expressed in lethal human glioblastoma, that inhibiting AMPK by genetic means shrinks brain tumors and prolongs survival in mice. It also shows that deleting AMPK from the whole body of adult mice is safe for the animals."

The Cancer Genome Atlas is a collaboration between the National Cancer Institute (NCI) and the National Human Genome Research Institute that has generated comprehensive, multi-dimensional maps of the key genomic changes in 33 types of cancer. According to the NCI, the database is publicly available, making it helpful to the cancer research community to improve the prevention, diagnosis, and treatment of cancer.

Although data in the current study support the feasibility of using pharmacological inhibitors of AMPK to treat glioblastoma, years of additional research are needed before it will be known if the findings are clinically relevant. "We are hopeful our studies will encourage pharmaceutical companies to screen for AMPK inhibitors," Dasgupta said.

Investigators are planning the next research phases that will be needed to translate the findings to patient care. Dasgupta explained that fostering research collaborations with companies or other institutions with expertise in developing pharmaceutical compounds would help advance the potential therapeutic strategy.

Molecular Hijacking

Cancer cells--high-grade brain cancer cells in particular--manage to survive in a highly stressful tumor environment. But the tumor cells maintain their ability to aggressively expand.

Although medical science has been able to leverage this stress in part to find effective treatments for a large number of cancers, high-grade brain cancers like glioblastoma remain especially stubborn survivors, defying every treatment strategy thrown at them.

But the current study's authors found that cancer-associated stress chronically activates AMPK, which normally works as a

bioenergetic sensor that helps regulate cell metabolism and stress. They also learned that brain tumor cells hijack a molecular stress- and metabolism-management process regulated by AMPK to help cancer cells maintain their survival abilities.

After discovering this, Dasgupta and colleagues genetically deleted AMPK in human glioblastoma cells and transplanted them into mouse brains. Tumors grew, but very slowly and this prolonged the animals' survival.

"It remains to be seen if inhibiting AMPK in combination with standard of care therapy prolongs survival even further."

Cancer Evolution

In the course of their research, Chhipa and Dasgupta observed something critical they said could change the way scientists interpret data from cell culture models. The observation also underscores how high-grade brain gliomas are able to evolve genetically to evade targeted molecular treatments, according to the scientists.

They noticed that while AMPK was necessary for the survival of patient-derived stem-like cancer cells recently derived from fresh cancer tissue, the protein was not required for the survival of traditional glioblastoma cell lines cultured for decades.

"Decades of culture could have altered genetic, epigenetic and metabolic characteristics of the lines, which adapted AMPK-independent survival pathways," said Dasgupta.

Because the large majority of cancer research still relies on cell culture models, Dasgupta said that the study's findings could become important for the research community, particularly when metabolic pathways of cancer cells are investigated.

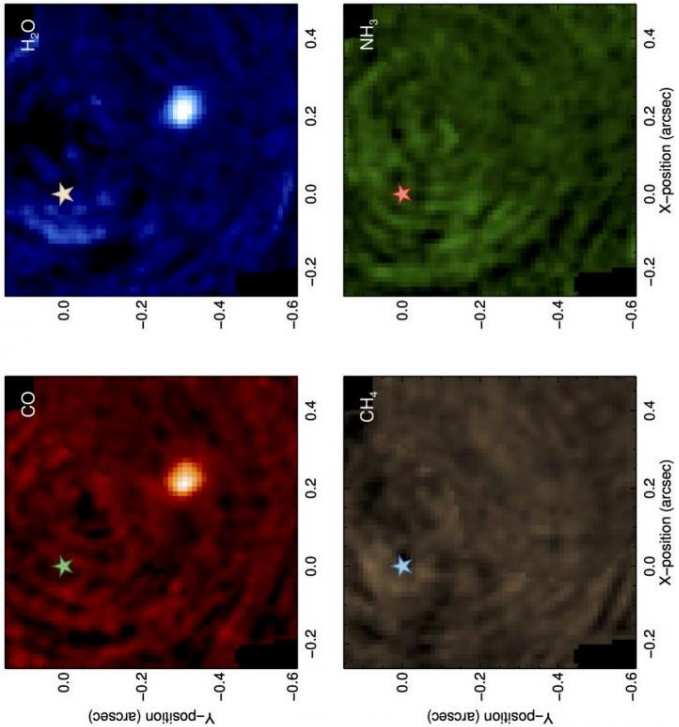
Funding support for the study came from: a Center for Clinical and Translational Science and Training Translational Grant Award; a Pilot Innovation award from Cincinnati Children's; a University of Cincinnati Cancer Center Affinity Grant Award; CancerFreeKids; and the National Institutes of Health (1R01NS075291-01A and 1R01NS099161-01).

http://bit.ly/2KeSqAU

Hunting molecules to find new planets

An international team of astronomers led by UNIGE makes planets visible by detecting molecules on their surface.

Each exoplanet revolves around a star, like the Earth around the Sun. This is why it is generally impossible to obtain images of an exoplanet, so dazzling is the light of its star. However, a team of astronomers, led by a researcher from the University of Geneva (UNIGE) and member of NCCR PlanetS, had the idea of detecting certain molecules that are present in the planet's atmosphere in order to make it visible, provided that these same molecules are absent from its star. Thanks to this innovative technique, the device is only sensitive to the selected molecules, making the star invisible and allowing the astronomers to observe the planet directly. The results appear in the journal *Astronomy & Astrophysics*.



The planet becomes visible when looking for H2O or CO molecules. However, as there is no CH4 nor NH3 in its atmosphere, it remains invisble when looking for these molecules, just as its host star which contains none of those four elements. **© UNIGE**

Until now, astronomers could only very rarely directly observe the exoplanets they discovered, as they are masked by the enormous luminous intensity of their stars. Only a few planets located very far from their host stars could be distinguished on a picture, in particular thanks to the SPHERE instrument installed on the Very Large Telescope (VLT) in Chile, and similar instruments elsewhere. Jens Hoeijmakers, researcher at the Astronomy Department of the Observatory of the Faculty of Science of the UNIGE and member of NCCR PlanetS, wondered if it would be possible to trace the molecular composition of the planets. "By focusing on molecules present only on the studied exoplanet that are absent from its host star, our technique would effectively "erase" the star, leaving only the exoplanet," he explains.

Erasing the star thanks to molecular spectra

To test this new technique, Jens Hoeijmakers and an international team of astronomers used archival images taken by the SINFONI instrument of the star beta pictoris, which is known to be orbited by a giant planet, beta pictoris b. Each pixel in these images contains the spectrum of light received by that pixel. The astronomers then compared the spectrum contained in the pixel with a spectrum corresponding to a given molecule, for example water vapour, to see if there is a correlation. If there is a correlation, it means that the molecule is present in the atmosphere of the planet.

By applying this technique to beta pictoris b, Jens Hoeijmakers notices that the planet becomes perfectly visible when he looks for water (H2O) or carbon monoxide (CO). However, when he applies his technique to methane (CH4) and ammonia (NH3), the planet remains invisible, suggesting the absence of these molecules in the atmosphere of beta pictoris b.

Molecules, new planetary thermometer

The host star beta pictoris remains invisible in all four situations. Indeed, this star is extremely hot and at this high temperature, these four molecules are destroyed. "This is why this technique allows us not only to detect elements on the surface of the planet, but also to sense the temperature which reigns there", explains the astronomer of the UNIGE. The fact that astronomers cannot find beta pictoris b using the spectra of methane and ammonia is therefore consistent with a temperature estimated at 1700 degrees for this planet, which is too high for these molecules to exist.

"This technique is only in its infancy", enthuses Jens Hoeijmakers. "It should change the way planets and their atmospheres are characterized. We are very excited to see what it will give on future spectrographs like ERIS on the Very Large Telescope in Chile or HARMONI on the Extremely Large Telescope which will be inaugurated in 2025, also in Chile," he concludes.

http://bit.ly/2yydOMT

Why being left-handed matters for mental health treatment

Treatment for the most common mental health problems could be ineffective or even detrimental to about 50 percent of the population, according to a radical new model of emotion in the brain.

ITHACA, N.Y. - Since the 1970s, hundreds of studies have suggested that each hemisphere of the brain is home to a specific type of emotion. Emotions linked to approaching and engaging with the world - like happiness, pride and anger - lives in the left side of the brain, while emotions associated with avoidance - like disgust and fear - are housed in the right.

But those studies were done almost exclusively on right-handed people. That simple fact has given us a skewed understanding of how emotion works in the brain, according to Daniel Casasanto, associate professor of human development and psychology at Cornell University.

That longstanding model is, in fact, reversed in left-handed people, whose emotions like alertness and determination are housed in the right side of their brains, Casasanto suggests in a new study. Even more radical: The location of a person's neural systems for emotion depends on whether they are left-handed, right-handed or somewhere in between, the research shows.

The study, "Approach motivation in human cerebral cortex," is published in *Philosophical Transactions of the Royal Society B: Biological Sciences*.

According to the new theory, called the "sword and shield hypothesis," the way we perform actions with our hands determines how emotions are organized in our brains. Sword fighters of old would wield their swords in their dominant hand to attack the enemy -- an approach action -- and raise their shields with their non-dominant hand to fend off attack -- an avoidance action. Consistent with these action habits, results show that approach emotions depend on the hemisphere of the brain that controls the dominant "sword" hand, and avoidance emotions on the hemisphere that controls the non-dominant "shield" hand.

The work has implications for a current treatment for recalcitrant anxiety and depression called neural therapy. Similar to the technique used in the study and approved by the Food and Drug Administration, it involves a mild electrical stimulation or a magnetic stimulation to the left side of the brain, to encourage approach-related emotions.

But Casasanto's work suggests the treatment could be damaging for left-handed patients. Stimulation on the left would decrease life-affirming approach emotions. "If you give left-handers the standard treatment, you're probably going to make them worse," Casasanto said.

"And because many people are neither strongly right- nor left-handed, the stimulation won't make any difference for them, because their approach emotions are distributed across both hemispheres," he said. "This suggests strong righties should get the normal treatment, but they make up only 50 percent of the population. Strong lefties should get the opposite treatment, and people in the middle shouldn't get the treatment at all." However, Casasanto cautions that this research studied only healthy participants and more work is needed to extend these findings to a clinical setting.

The research was funded by a James S. McDonnell Foundation Scholar Award and the National Science Foundation.

http://bit.ly/2tvUidV

Combining different malaria vaccines could reduce cases by 91 percent

Using two experimental anti-malarial vaccines, which work in different ways, can greatly reduce the number of malaria infections in animal studies.

Experimental vaccines, which independently achieve 48% and 68% reductions in malaria cases, can achieve 91% reduction when combined.

Presently, each vaccine is at a different stage of human trials, and there have not been efforts to combine them. However, a team led by Imperial College London have now tested the effectiveness when using the two types of vaccine together.

The study, published today in the journal *eLife*, used genetically altered mouse parasites that express proteins expressed on the human version of the malaria parasite. The research was funded by the PATH Malaria Vaccine Initiative and the Medical Research Council (MRC), including researchers at Imperial's MRC Centre for Outbreak Analysis and Modelling.

Lead researcher Dr Andrew Blagborough, from the Department of Life Sciences at Imperial, said: "This is the first direct evidence than

combining vaccines of different types significantly improves their efficacy in terms of reducing malarial burden.

"Reaching a potential 91% reduction in cases would have a huge impact on public health because the vaccines could be effective in areas where malaria is more prevalent."

Malaria is caused by a group of parasites that have a complex life cycle, spending time in the mosquito midgut and salivary glands, in the human liver, and circulating in human blood, where they cause the disease.

The team tested two types of vaccines: those that prevent mosquitoes from transferring the parasites, called transmission-blocking vaccines (TBVs), and those that prevent the parasite from infecting the liver, termed pre-erythrocytic vaccines (PEVs).

RTS,S is the world's first PEV malaria vaccine that has been shown to provide partial protection against malaria in young children by blocking infection of the liver. However, its maximum efficacy is under 50% (i.e. it reduces cases by around 50%).

There are currently several types of transmission-blocking vaccines in early trials, which are thought to reduce the number of parasites in the mosquito salivary glands. Their efficacy typically ranges from around 50-95%.

It has been assumed that combining these vaccines would increase their efficacy, but it has never been tested until now. The team found that when a partially effective PEV was combined with the most effective transmission-blocking vaccine, the efficacy was around 91%.

The team also found that combining any of the two types of vaccines improved efficacy of the mixture more than might be expected from the single efficacy of each vaccine separately.

Dr Morven Roberts, Programme Manager for parasites and neglected tropical diseases at the MRC, said: "While these findings are in the preliminary stages, they're valuable as they shed light on optimising strategies for preventing malaria. Learning that combining vaccines can dramatically boost efficacy in mice provides another potential tactic for controlling this disease. This is timely research as global health officials work towards WHO targets to eliminate malaria by 2030."

The team will next study how combined vaccines could work in more complex situations. Dr Blagborough said: "In the real world, the vaccine coverage we can achieve- how many people we can give it to - is important, as are the local levels of transmission, and how prevalent malaria currently is in that area.

"We plan to use a combination of rodent experiments and computer modelling to help us estimate effectiveness requirements for future vaccines."

The efficacy of current lead malaria vaccines is known to reduce over time after vaccines are administered, so the team will also investigate how combined vaccines perform in the long term.

http://bit.ly/2lv5fJp

D for danger! Speech sounds convey emotions

An analysis of 37,000 words in five languages, conducted by Bocconi's Zachary Estes and colleagues, shows that single sounds, especially at the beginning of the word (e.g. the d sound in dog), can signal emotions beyond the word's meaning alone

Individual speech sounds - phonemes - are statistically associated with negative or positive emotions in several languages, new research published in the journal Cognition by Bocconi Professor Zachary Estes, his Warwick colleague James Adelman and Bocconi student Martina Cossu shows. These associations help us quickly avoid dangers, because the phoneme-emotion associations are strongest at the beginning of the word and the phonemes that are spoken fastest tend to have a negative association.

It has long been known that phonemes systematically convey a range of physical properties such as size and shape. For example, the 'e'

sound in Beetle sounds small, whereas the 'u' sound in Hummer sounds big. This is known as sound symbolism.

Given the evolutionary importance of avoiding dangers and approaching rewards, Estes and colleagues hypothesized that, like size and shape, emotion should also have sound symbolic associations. They tested this prediction in five languages - English, Spanish, Dutch, German and Polish - and in all five languages particular phonemes did indeed occur more often in positive or negative words.

Estes and colleagues also tested whether this emotional sound symbolism could be an adaptation for survival. To aid survival, communication about opportunities and especially dangers needs to be fast. The researchers tested this assumption in two ways.

First, they showed that in all five languages the phoneme-emotion associations are stronger at the beginnings of words than at the middle or ends of words. This allows emotion to be understood fast, even before the whole word is spoken.

Second, they examined the speed with which specific phonemes can be spoken. Estes and colleagues discovered that phonemes that can be spoken faster are more common in negative words. This allows dangers to be understood faster than opportunities, and this aids survival because avoiding dangers is more urgent than winning rewards. For instance, being too slow to avoid a snake can be fatal, but if you're too slow to catch a bird, you will probably have other chances.

Estes and his colleagues argue that emotional sound symbolism evolved due to its adaptive value to humans: it made communication about dangers and opportunities more efficient, allowing a quicker reaction to vital objects and thereby supporting the fitness and survival of the human species.

First author James Adelman said "In debates about whether human language abilities evolved from more general cognitive skills or more specific communicative adaptations, these findings reveal one specific adaptation. Our findings suggest that the ability to appreciate very short speech sounds could have helped humans to efficiently warn kin and peers, aiding survival."

Zachary Estes added "We have also begun testing applications in business, because emotional phonemes provide an opportunity for companies to inform consumers about their products. For example, a pharmaceutical company might want to use positive sounds for a drug that promotes health benefits like a vitamin, but they might want to use negative sounds for a drug the prevents health detriments like an anti-malarial drug."

James Adelman, Zachary Estes, Martina Cossu, Emotional sound symbolism: Languages rapidly signal valence via phonemes, Cognition 175 (2018) 122-130, DOI: 10.1016/j.cognition.2018.02.007

http://bit.ly/2tylaKe

Stop looking for ET: modelling suggests we're alone in the universe

Oxford University researchers run the numbers and conclude intelligent life beyond Earth is highly unlikely.

Andrew Masterson reports.

Despite the small matter of lack of evidence, most astrophysicists and cosmologists today are persuaded that extra-terrestrial intelligent life must exist. The logic behind the assumption seems compelling. There are billions of galaxies in the universe, each containing billions of stars, around a proportion of which orbit billions of planets. Given the vastness of those numbers, it would be statistically perverse to suggest that intelligent life evolved only once in the entire system.

But what, however, if the startlingly improbable is nevertheless the truth? What if Homo sapiens is, in fact, the only species ever in the entire history of the universe to invent radio, build an X-ray observatory, and send a ship into space?

What if – the existence of exoplanets coated in blue-green slime notwithstanding – we are utterly on our own?

That's the contention of physicists Anders Sandberg, Eric Drexler and Toby Ord, all of the Future of Humanity Institute at Oxford University in the UK. In a paper lodged on the pre-print server *Arxiv*, and thus still awaiting peer review, the trio model what happens when two touchstones of astrobiology – the Fermi Paradox and the Drake Equation – are combined and subjected to mathematical rigour.

The results, it must be said, aren't good, at least for people hopeful that somewhere, out there, at least one alien civilisation is bubbling along.

Existing calculations for the probability of extra-terrestrial intelligent life, they report, rest on uncertainties and assumptions that lead to outcomes containing margins for error spanning "multiple orders of magnitude". Constraining these, as much as possible, by factoring in models of plausible chemical and genetic mechanisms, results, they conclude, in the finding "that there is a substantial probability that we are alone".

The Fermi Paradox is named after physicist Enrico Fermi, who noted in 1950 that there are so many stars, just in the Milky Way, that given the age of the universe even a small probability that intelligent life has evolved would mean that their existence should be plain to humanity by now.

Yet, he continued, in terms of evidence, we have squat, which, given the probability of intelligent life emerging, is odd. Hence the paradox. "Where are they?" he asked.

The Drake Equation, formulated by American astronomer Frank Drake in 1961, attempts to place an analytical framework around Fermi's contention, by estimating the number of intelligent civilisations that exist in the universe, regardless of the fact that we can't see them.

Drake's work can be expressed thus: $N = R * f_p * n_e * f_l * f_i * f_c * L$

In the equation, *N* represents the number of civilisations within the Milky Way capable of emitting detectable electromagnetic signals. The number is determined by the other factors in the model, which express the rate of suitable star formation, the fraction of those stars with exoplanets, the number of those planets suitable for life and the number on which life actually appears.

That total is then further reduced by adding in other refinements – the number of life-bearing planets on which intelligence emerges, the number of those that produce technology capable of emitting signals into space, and the number of those that actually go ahead and do so.

It's all very impressive, but "sciencey" rather than scientific. Sandberg, Drexler and Ord gleefully quote US astronomer Jill Tarter, who described the Drake Equation as "a wonderful way to organise our ignorance".

The problem with the way the equation is usually wielded, the researchers argue, is that the parameters assigned to most of the various elements represent simply best guesses – and those guesses, furthermore, are heavily influenced by whether the person making them is optimistic or pessimistic about the chances of intelligent life existing. The result, they note, often involves well-estimated astronomical numbers multiplied by *ad hoc* figures.

They quote another US astronomer, Steven J. Dick: "Perhaps never in the history of science has an equation been devised yielding values differing by eight orders of magnitude ... each scientist seems to bring his own prejudices and assumptions to the problem."

Dick, they note, was being nice. Many outcomes from Drake Equation calculations yield probabilities that range over hundreds of orders of magnitude.

In a not altogether unrelated sidebar, the researchers acknowledge a recent calculation by Swedish-American cosmologist Max Tegmark, estimating the chances of intelligent civilisations arising in the universe.

Tegmark assumes there is no reason two intelligent civilisations should be any particular distance from each other, and then argues that – given the Milky Way is a minuscule fraction of the observable universe, which is itself only a tiny part of the universe beyond what we can see – it is unlikely that two intelligent civilisations would arise in the same observable universe. Thus, to all intents and purposes, we are very probably alone.

Sandberg, Drexler and Ord use a different approach in their modelling, incorporating current scientific uncertainties that produce values for different parts of the equation ranging over tens and hundreds of orders of magnitude. Some of these concern critical questions regarding the emergence of life from non-living material – a process known as abiogenesis – and the subsequent likelihoods of early RNA-like life evolving into more adaptive DNA-like life.

Then there is the essential matter of that primitive DNA-like life undergoing the sort of evolutionary symbiotic development that occurred on Earth, when a relationship between two different types of simple organisms resulted in the complex "eukaryotic" cells that constitute every species on the planet more complicated than bacteria.

The results are depressing enough to send a thousand science-fiction writers into catatonic shock. The Fermi Paradox, they find, dissolves.

"When we take account of realistic uncertainty, replacing point estimates by probability distributions that reflect current scientific understanding, we find no reason to be highly confident that the galaxy (or observable universe) contains other civilizations," they conclude.

"When we update this prior in light of the Fermi observation, we find a substantial probability that we are alone in our galaxy, and perhaps even in our observable universe.

"'Where are they?' — probably extremely far away, and quite possibly beyond the cosmological horizon and forever unreachable."

http://bit.ly/2lv17ZT

Dogs understand what's written all over your face

New research shows that dogs use different parts of their brains to process negative and positive emotions cued by human facial expressions

Dogs are capable of understanding the emotions behind an expression on a human face. For example, if a dog turns its head to the left, it could be picking up that someone is angry, fearful or happy. If there is a look of surprise on a person's face, dogs tend to turn their head to the right. The heart rates of dogs also go up when they see someone who is having a bad day, say Marcello Siniscalchi, Serenella d'Ingeo and Angelo Quaranta of the University of Bari Aldo Moro in Italy. The study in Springer's journal *Learning & Behavior* is the latest to reveal just how connected dogs are with people. The research also provides evidence that dogs use different parts of their brains to process human emotions.

By living in close contact with humans, dogs have developed specific skills that enable them to interact and communicate efficiently with people. Recent studies have shown that the canine brain can pick up on emotional cues contained in a person's voice, body odour and posture, and read their faces.

In this study, the authors watched what happened when they presented photographs of the same two adults' faces (a man and a woman) to 26 feeding dogs. The images were placed strategically to the sides of the animals' line of sight and the photos showed a human face expressing one of the six basic human emotions: anger, fear, happiness, sadness, surprise, disgust or being neutral.

The dogs showed greater response and cardiac activity when shown photographs that expressed arousing emotional states such as anger, fear and happiness. They also took longer to resume feeding after seeing these images. The dogs' increased heart rate indicated that in these cases they experienced higher levels of stress.

In addition, dogs tended to turn their heads to the left when they saw human faces expressing anger, fear or happiness. The reverse happened when the faces looked surprised, possibly because dogs view it as a non-threatening, relaxed expression. These findings therefore support the existence of an asymmetrical emotional modulation of dogs' brains to process basic human emotions.

"Clearly arousing, negative emotions seem to be processed by the right hemisphere of a dog's brain, and more positive emotions by the left side," says Siniscalchi.

The results support that of other studies done on dogs and other mammals. These show that the right side of the brain plays a more important part in regulating the sympathetic outflow to the heart. This is a fundamental organ for the control of the 'fight or flight' behavioural response necessary for survival.

Reference: Siniscalchi, M. d'Ingeo, S. Quaranta, A. (2018). Orienting asymmetries and physiological reactivity in dogs' response to human emotional faces, Learning & Behavior DOI: 10.3758/s13420-018-0325-2

http://bit.ly/2Kq7z1z

Asylum seekers are not a 'burden' for European economies

Does the arrival of asylum seekers lead to a deterioration in the economic performance and public finances of the European countries that host them?

The answer is no, according to economists from the CNRS, Clermont-Auvergne University, and Paris-Nanterre University [(1)], who have estimated a dynamic statistical model based on thirty years of data from fifteen countries in Western Europe. On the contrary, the economic impact tends to be positive as a proportion of the asylum seekers become permanent residents. This study is published in *Science Advances* on June 20, 2018.

Over a million people claimed asylum in one of the European Union countries in 2015, making it a record year. What is the economic and fiscal impact of these migration flows? This study is not the first to consider this question [(2)], but the method it uses is new. Traditional approaches mainly adopt an accountancy approach: they compare the taxes paid by the immigrants with the public transfers paid to them, but do not take into account the economic interactions [(3)].

The researchers used a statistical model introduced by Christopher Sims, who in 2011 was awarded the Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel. Widely used to evaluate the effects of economic policies, this model lets the statistical data speak for themselves by imposing very few assumptions. The macroeconomic data and data on migration flows come from Eurostat and the OECD and concern 15 countries in Western Europe: Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Ireland, Italy, Norway, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom.

The researchers distinguished the flows of asylum seekers from flows of other migrants. They evaluated the latter flows on the basis of net migration, which does not take into account asylum seekers. The flows of asylum seekers are made up of people who have a legal right to reside in the host country while their application is processed; the host country will consider them to be residents only if their asylum application is granted.

During the period studied (1985-2015), Western Europe experienced a significant increase in the flows of asylum seekers following the wars in the Balkans between 1991 and 1999 and, after 2011, in the wake of the Arab Springs and the conflict in Syria. At the same time, flows of migrants, particularly EU nationals, have increased after the EU's expansion eastwards in 2004. These events provide numerous opportunities to test the consequences of an unforeseen increase in migration flows on GDP per capita, the unemployment rate, and public finances.

The researchers show that an increase in the flow of permanent migrants (i.e., not asylum seekers) at a given date produces positive effects up to four years after that date: GDP per capita increases, the unemployment rate falls, and additional public expenditure is more than compensated by the increase in tax revenues. In the case of asylum seekers, no negative effect is observed and the effect becomes positive after three to five years, when a proportion of asylum seekers obtain asylum and join the category of permanent migrants.

According to these results, it is unlikely that the ongoing migration crisis is a burden for European countries; on the contrary, it could be an economic opportunity.

Notes:

(1) Hippolyte d'Albis, CNRS researcher at the Paris Jourdan Sciences Economiques laboratory (CNRS/EHESS/ENS Paris/École des Ponts ParisTech/Inra/Paris 1 Panthéon-Sorbonne University), Ekrame Boubtane, lecturer at Clermont-Auvergne University, at the Centre d'études et de recherches sur le développement international (CNRS/Clermont-Auvergne University), and Dramane Coulibaly, lecturer at Paris-Nanterre University, at the EconomiX laboratory (CNRS/Paris-Nanterre University).

(2) The previous studies focused on permanent immigration (i.e., not asylum seekers). Some of these studies have shown positive economic consequences of immigration, and others negative effects.

(3) To take an example, the increase in public expenditure may revive economic activity, and, as a consequence, increase tax revenues.

http://bit.ly/2KaVYAK

Forgetting may help improve memory and learning

Research suggests that forgetting plays a positive role in learning

Madison, WI - Forgetting names, skills or information learned in class is often thought of as purely negative. However unintuitive it may seem, research suggests that forgetting plays a positive role in learning: It can actually increase long-term retention, information retrieval and performance. The findings will be presented today at the American Physiological Society (APS) Institute on Teaching and Learning in Madison, Wis.

Contextual clues play a role in what people are able to store and retrieve from their memory, says Robert A. Bjork, PhD, distinguished research professor in the department of psychology at the University of California, Los Angeles. A change in context can cause forgetting, but it can also change--and enrich--how information is encoded and retrieved, which can enhance learning. Bjork defines forgetting as "a decrease in how readily accessible some information or procedure is at a given point in time." For example, some items may be strongly imprinted in our memories (referred to as "strong storage strength")--such as a childhood phone number--but may be difficult to retrieve quickly due to the length of time since that information has been accessed ("weak retrieval strength").

Bjork will discuss the differences in storage and retrieval and how "forgetting enables, rather than undoes, learning" in the plenary session "Forgetting as a friend of learning" on Wednesday, June 20, at the Madison Concourse Hotel.

http://bit.ly/2lx33Rw

Selfies show worm slithered through woman's face for 2 weeks

After doctors yanked the worm out, she made a full recovery.

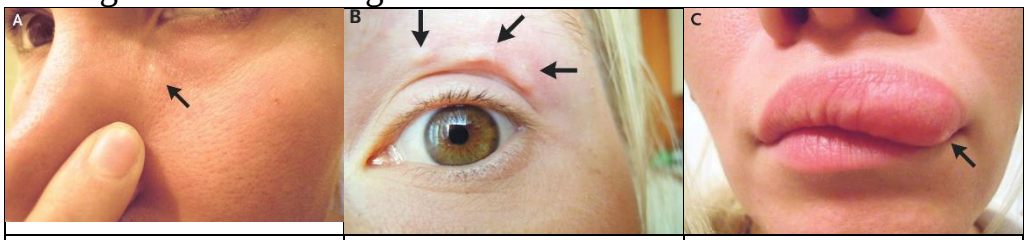
Beth Mole - 6/23/2018, 6:19 AM

Doctors were able to extract the worm, a D. repens. Kartashev and Simon

A 32-year-old woman who visited a rural area outside of Moscow returned home with a surprising stowaway—in her face. And it was a restless one at that, according to a short report published this week in the *New England Journal of Medicine* (*NEJM*).

fter her trip, she noticed an unusual lump on her cheek, below her left eye. Five days later it was gone, but another had formed just above

her left eye. Ten days after that, a lump resurfaced on her upper lip, causing massive swelling.



The first nodule, under the left eye.	***The nodule moved above the left eye.***	***The nodule later reappeared on the upper lip.***

To track the progress of her roving blemish, she took selfies. In reports to doctors, she said that the nodules caused some burning and itchiness but no other symptoms or problems. She also noted her recent trip and recalled being frequently bitten by mosquitoes.

Doctors determined that the wandering wart was actually a marauding parasite, likely transmitted by a mosquito bite on her trip. Using forceps, they pinned it down and surgically removed the long, thin, yellowish stowaway. Subsequent genetic tests identified the worm as a *Dirofilaria repens.*

D. repens are parasitic worms that primarily prey on dogs and other carnivores and move around via mosquitoes—they only infect humans by accident. They tend to be found in parts of Europe, Asia, and Africa, where they've been known to grow up to 170 millimeters long and live up to 10 years. The Centers for Disease Control and Prevention reports that *D. repens* are not found in the US, but the country does harbor relatives *D. immitis*, which cause heartworm disease in dogs, and *D. tenuis*, which affect raccoons.

In their preferred canine host, *D. repens* dwell in tissue under the skin, and the females release larvae into the blood stream. Those larvae then get picked up by biting mosquitoes, which incubate the mini mooches before transferring them to new hosts at their next blood meal. In humans, *D. repens* are caught crawling under the skin by victims noticing shifting subcutaneous nodules, as did the woman in the case report. Doctors sometimes call this "creeping eruption." In rare cases, the worms can squirm into organs, such as lungs, breasts, male genitalia, and eyes.

The lead author of the report in *NEJM*, Vladimir Kartashev, an infectious disease expert at Rostov State Medical University in Rostov-na-Donu, Russia, told *The Washington Post* in an email that *D. repens* is an "emerging disease" in the western part of the former Soviet Union and certain parts of Europe. Since 1997, he said that there have been more than 4,000 cases in the region, particularly in Russia and Ukraine.

Luckily, the worms are easy to remove and, once yanked out, cause no lasting problems. The woman in the case in *NEJM* reportedly made a full recovery.

NEJM, 2018. DOI: 10.1056/NEJMicm1716138 (About DOIs).

http://bit.ly/2Ki5pyi

Key molecule of aging discovered

Discovery of a protein that represents a central switching point in the aging process

Every cell and every organism ages sooner or later. But why is this so? Scientists at the German Cancer Research Center in Heidelberg have now discovered for the first time a protein that represents a central switching point in the aging process. It controls the life span of an individual - from the fly to the human being. This opens up new possibilities for developing therapies against age-related diseases.

Oxidative stress causes cells and entire organisms to age. If reactive oxygen species accumulate, this causes damage to the DNA as well as changes in the protein molecules and lipids in the cell. The cell ultimately loses its functionality and dies. Over time, the tissue suffers and the body ages. "The theory of oxidative stress or the accumulation of reactive oxygen species as the cause of aging has existed since the 1950s," says Peter Krammer of the German Cancer

Research Center (DKFZ). "So far, however, the details of this process were unclear."

In fact, reactive oxygen species do more than just damage the body. For example, they are essential for the T-cells of the immune system to become active. DKFZ researchers led by Krammer and Karsten Gülow* have now discovered the key regulator that is responsible for shifting the sensitive balance from vital to harmful amounts of reactive oxygen molecules and thus accelerating the aging process: A protein molecule called TXNIP (thioredoxin-interacting protein).

One way in which the body disposes of harmful reactive oxygen species is their conversion by the enzyme thioredoxin-1 (TRX-1). TRX-1 has been proven to play a role in protecting DNA from oxidative stress and slowing down aging processes. Its antagonist TXNIP inhibits thioredoxin-1 and thus ensures that the reactive oxygen molecules are retained.

The DKFZ researchers led by Krammer and Gülow now wanted to know whether more TXNIP is formed in the body with increasing age, thereby undermining the protective mechanism against oxidative stress. To this end, they first compared T cells from the blood of a group of over 55-year-old volunteers with the T cells of younger blood donors, who were between 20 and 25 years old. In fact, it turned out that the cells of older subjects produce significantly more TXNIP. The DKFZ scientists have also observed similar findings in other human cell and tissue types.

The researchers also found out that more TXNIP is produced in the fly Drosophila with increasing age. In order to test whether TXNIP is actually responsible for aging, they bred flies that produce significantly more TXNIP than their relatives as well as flies in which TXNIP synthesis is greatly reduced. "Flies that produced more TXNIP lived on average much shorter, while flies with less TXNIP had a longer average life," sums up Tina Oberacker, who was responsible for the fly experiments.

"TRX-1 and its opponent TXNIP are highly conserved in the course of evolution; they hardly differ between flies and humans," explains Krammer. It can therefore be assumed that the two proteins perform similar functions in flies and humans. If more TXNIP is produced with increasing age, this means that TRX is gradually switched off with its protection function. This leads to more oxidative stress, which damages cells and tissue and eventually causes them to die.

Krammer is convinced that TXNIP is a key regulator for aging. "Scientists have found hundreds of genes that are somehow related to the aging process," says the DKFZ researcher summarizing the results. "But it is enough to switch off TXNIP to delay aging. Similarly, aging can be accelerated if we get the cells to produce TXNIP. "And that makes it an interesting candidate to intervene in the aging process in the future."

The research was funded by the European Union and the Wilhelm Sander Foundation.

Tina Oberacker, Jörg Bajorat, Sabine Ziola, Anne Schroeder, Daniel Röth, Lena Kastl, Bruce A. Edgar, Wolfgang Wagner, Karsten Gülow, Peter H. Krammer: Enhanced expression of thioredoxin interacting protein regulates oxidative DNA damage and aging. FEBS Letters, 2018, doi: 10.1002/1873-3468.13156

http://bit.ly/2KfSyA2

Around the world, people have surprisingly modest notions of the 'ideal' life

People's sense of perfection is surprisingly modest

It seems reasonable that people would want to maximize various aspects of life if they were given the opportunity to do so, whether it's the pleasure they feel, how intelligent they are, or how much personal freedom they have. In actuality, people around the world seem to aspire for more moderate levels of these and other traits, according to findings published in *Psychological Science*, a journal of the Association for Psychological Science.

"Our research shows that people's sense of perfection is surprisingly modest," says psychological scientist Matthew J. Hornsey of the University of Queensland, first author on the research. "People

wanted to have positive qualities, such as health and happiness, but not to the exclusion of other darker experiences - they wanted about 75% of a good thing."

Furthermore, people said, on average, that they ideally wanted to live until they were 90 years old, which is only slightly higher than the current average life expectancy. Even when participants imagined that they could take a magic pill guaranteeing eternal youth, their ideal life expectancy increased by only a few decades, to a median of 120 years old. And when people were invited to choose their ideal IQ, the median score was about 130 - a score that would classify someone as smart, but not a genius.

The data also revealed that participants from holistic cultures - those that value notions of contradiction, change, and context - chose ideal levels of traits that were consistently lower than those reported by participants from nonholistic cultures.

"Interestingly, the ratings of perfection were more modest in countries that had traditions of Buddhism and Confucianism," says Hornsey. "This makes sense -- these Eastern philosophies and religions tend to place more emphasis on the notion that seemingly contradictory forces coexist in a complementary, interrelated state, such that one cannot exist without the other."

In one study, Hornsey and colleagues analyzed data from a total of 2,392 participants in Australia, Chile, China, Hong Kong, India, Japan, Peru, Russia, and the United States. The researchers classified China, Hong Kong, India, and Japan as holistic cultures, predominantly influenced by religions or philosophies (such as Buddhism, Hinduism, or Taoism) that emphasize a more holistic worldview. They classified the other five regions - Australia, Chile, Peru, Russia, and the United States - as nonholistic cultures.

Participants in each region received a questionnaire translated into their native language. In response to a series of questions, participants reported their ideal level of intelligence; they also reported how long they would choose to live under normal circumstance and how long they would choose to live if they could take a magic pill ensuring eternal youth.

Using a scale that ranged from 0 (none) to 100 (maximum), participants indicated their ideal levels of health, individual freedom, happiness, pleasure, and self-esteem. They used the same scale to rate ideal levels of societal characteristics, such as morality, equality of opportunity, technological advancement, and national security.

In general, participants tended to rate their ideal levels of individual characteristics to be about 70-80%, although there was some variation across the traits. For example, many more participants chose to maximize health than chose to maximize happiness. Participants' ideals were also relatively modest for both intelligence and longevity, even when there were no limits on the levels they could choose.

The researchers found that participants in holistic cultures reported lower ideal levels for each individual trait than did participants who lived in nonholistic cultures.

A second study with 5,650 participants in 27 countries produced a similar pattern of results. Importantly, this study showed that participants from the Philippines and Indonesia - regions that are collectivist but not holistic - reported ideal levels of individual traits that were similar to those of participants from other nonholistic countries. This finding suggests that the difference between holistic and nonholistic cultures is unlikely to be explained by differences in collectivism.

In both studies, the researchers found no crosscultural differences in ideal levels of societal characteristics.

"This principle of maximization is threaded through many prominent philosophical and economic theories," Hornsey notes. "But our data suggest that people have much more complex, blended notions of perfection, ones that embrace both light and dark."

Co-authors on the research include Paul G. Bain (University of Bath), Emily *Ann Harris (University of Queensland), Nadezhda Lebedeva (National research University), Emiko S. Kashima (LaTrobe University), Yanjun Guan (Durham University Business School), Roberto González (Pontificia Universidad Católica de Chile), Sylvia X. Chen (Hong Kong Polytechnic University), and Sheyla Blumen (Pontificia Universidad Católica del Perú).*
Chilean data collection was supported by the Centre for Social Conflict and Cohesion Studies (FONDAP15130009) and the Center for Intercultural and Indigenous Research (FONDAP15110006). Russian data collection was supported by a subsidy granted by the government of the Russian Federation for implementation of the Global Competitiveness Program.

https://wb.md/2K2YVYa

Praying With Patients: Clinicians Debate

Should physicians pray with their patients? A recent article on Medscape posed this question to healthcare professionals. The responses ranged from the spiritual to the practical and the satirical.

Brandon Cohen June 20, 2018

Many wholeheartedly supported sharing a prayer with patients. A primary care physician was typical of this camp:

I pray with my patients all the time! I usually say "Ms Jones, do you believe in prayer?" If she says yes, then I'll pray with her. If they say no, I'll say, "No worries. Just thought I'd ask." Not once has a patient said no.

An emergency department physician was also eager to call on a higher power:

I...have asked patients if it was all right with them to give a prayer. Not once during this time have I been refused, and I feel that the patient, their family, and I benefit greatly from doing this. I cannot fathom for me not to ask the Almighty for His help when it is needed.

But colleagues pushed back, specifically against the idea of a doctor initiating the prayer. An infectious disease specialist posed a difficult question:

Do you think they would say something if they did object [to a physician praying]? We are in a position of authority, and patients have enough trouble telling us that they didn't understand our instructions or explanations or that they cannot afford...their medications.

A colleague agreed and added:

I think that it's very selfish and inappropriate when a believer forces me into a situation when refusing to pray seems rude or somehow harmful.

Some made a distinction between initiating the prayer and simply complying with a request from a patient. An orthopedic surgeon was broad-minded:

I would gladly pray with any of my patients regardless of their religion. I take it as an honor that they would ask me to be a part of that and gladly comply.

An anesthesiologist reported much the same experience:

Many patients ask me to pray with them before they undergo anesthesia/surgery. Regardless of the patient's religious beliefs, I participate wholeheartedly and find it mutually beneficial.

But others found it counterproductive to participate in rites they did not believe in.

An emergency department physician wrote, "I would never intentionally lie to a patient. Pretending to believe as they do is a lie."

A surgeon added:

If the doctor's very demeanor does not instill trust throughout, then the doctor is the one who is in urgent need of prayer! We are healers, but definitely not faith healers!

But a radiologist quickly shot back, "A patient asked for help. Give it. Just because you're a healer with faith doesn't make you a faith healer."

One optometrist offered satire: "I usually get out my cup of phalanges bones or my Magic 8-Ball, depending on the age of the person requesting the use of mysticism."

Another doctor was similarly acerbic:

Should physicians do rain dances with patients? Should physicians help perform exorcisms of the evil spirits patients think are causing their afflictions? Prayer...is really no different than any other form of magical thinking and is, ultimately, irrational.

But an excitable emergency medicine specialist found these objections unconvincing: "To be angry about it? Feel forced? That is self-righteous ego. Come on! Chill!"

And an anesthesiologist even questioned the quality of care from atheist practitioners:

Maybe physicians should disclose to their patients whether or not they have any spiritual belief. I, for one, would not care to receive medical care from someone who did not believe in a higher spiritual being.

Some healthcare professionals carefully sorted through the possibilities. One registered nurse considered a number of scenarios:

Assuming [the prayer] is of the generic variety, involving the expression of a desire for respite and so forth, and not...a plea for divine intervention, [such as a] miracle, then it may be feasible. However, you can only accommodate a patient so far. I wouldn't be comfortable invoking the power of Jesus to drive the forces of Satan out of the patient.

And an emergency department physician fretted through the complex calculus of physician prayer with great rigor:

If the patient asks and you feel comfortable: absolutely. If the patient asks and you do not feel comfortable: no. Should the doctor ask: depends. If we [feel] the patient will be receptive: yes. If we read wrong, I don't think any irreparable harm [is] done. If you're a believer who doesn't ask and the patient needed it, you missed an opportunity.

The final word goes to a neurologist who drew a stark line right down the middle of the debate:

I believe that praying with a patient can be a psychologically beneficial...but strictly [only] if the patient has requested the joint prayer. [But] I believe that it may be borderline unethical and potentially detrimental to the doctor/patient relationship for the doctor to suggest a prayer.

The full discussion of this topic is available at Should Physicians Pray With Patients?.

http://bit.ly/2K5YOLx

'Walking molecules" haul away damaged DNA to the cell's emergency room

The cell has its own paramedic team and emergency room to aid and repair damaged DNA, a new USC Dornsife study reveals.

The findings are timely, as scientists are delving into the potential of genome editing with the DNA-cutting enzyme, CRISPR-Cas9, to treat diseases or to advance scientific knowledge about humans, plants, animals and other organisms, said Irene Chiolo, Gabilan Assistant Professor of biological sciences at the USC Dornsife College of Letters, Arts and Sciences.

Genome editing has arrived before scientists have thoroughly studied the significance and impact of DNA damage and repair on aging and disease, such as cancer. Chiolo's work has been revealing more about those processes.

For the study published today in *Nature*, Chiolo and her team of researchers at USC Dornsife, using fluorescent markers, tracked what happened when DNA was damaged in fruit fly cells and mouse cells. They saw how the cell launches an emergency response to repair broken DNA strands from a type of tightly-packed DNA, heterochromatin.

"Heterochromatin is also referred to as the 'dark matter of the genome,' because so little is known about it," said Chiolo. "But DNA

damage in heterochromatin is likely a major driving force for cancer formation."

Don't call it junk

Repeated DNA sequences have had a bad nickname, "junk DNA," for about 20 years. Scientists decoding the genome called it junk because they were initially focused on understanding the functions of individual genes. Since then, studies have shown that repeated DNA sequences are in fact essential for many nuclear activities, but their defective repair is also linked to aging and disease.

"Heterochromatin is mostly composed of repeated DNA sequences," Chiolo said. "The low gene content is part of the reason why these sequences are less characterized."

In fact, mutations that compromise heterochromatin repair result in massive chromosome rearrangements affecting the entire genome.

First responders take a walk

The scientists found that after the DNA strands are broken, the cell prompts a series of threads— nuclear actin filaments— to assemble and create a temporary highway to the edge of the nucleus. Then come the paramedics—proteins known as myosins.

"Myosins are conveyed as a walking molecule because they have two legs. One is attached and the other moves. It's like a molecular machine that walks along the filaments." The myosins pick up the injured DNA, walk along the filament road and then reach the emergency room, a pore at the periphery of the nucleus.

"We knew, based on our prior study, that there was an emergency room—the nuclear pore where the cell fixes its broken DNA strands. Now, we have discovered how the damaged DNA travels there" Chiolo said. "What we think is happening here is that the damage triggers a defense mechanism that quickly builds the road, the actin filament, while also turning on an ambulance, the myosin."

The researchers plan further studies examining the repair of DNA in heterochromatin.

"I'm excited to see how the molecular mechanisms we uncovered work in humans, as well as in plants that have much larger heterochromatin. It will be fascinating to see how such a complex repair mechanism functions and evolves over time and what aspects of the mechanisms may be adapted for other functions," said Christopher Caridi, a co-lead author for the study and a postdoctoral researcher in Chiolo's lab at USC Dornsife.

More: *Christopher P. Caridi et al, Nuclear F-actin and myosins drive relocalization of heterochromatic breaks, Nature (2018).* *DOI: 10.1038/s41586-018-0242-8*

https://wb.md/2KcBYOd

Five Types of Diabetes: Will New Classification Make Management Easier?

Continuing our series, Everyday Diabetes: Practical Management for Primary Care

Jay H. Shubrook, DO; Sumera Ahmed, MD

Jay H. Shubrook, DO: Hi. I am Jay Shubrook, diabetologist and professor at Touro University College of Osteopathic Medicine in California. We are continuing our series, Everyday Diabetes: Practical Management for Primary Care.

Today, Dr Sumera Ahmed joins us. Dr Ahmed is an internist and diabetologist who is a new faculty member at Touro University California. Dr Ahmed, I want to talk a bit about types of diabetes. I believe that people think of type 1 and type 2, but there are actually several more types of diabetes. Could you tell the audience how you see the general groups of diabetes?

Sumera Ahmed, MD: The common, very broad classifications we traditionally think of are type 1 and type 2 diabetes. As we all know, type 1 diabetes is usually characterized by autoimmunity and absolute insulin deficiency. Patients with type 1 diabetes are insulin dependent and very insulin sensitive. They characteristically have a low body mass index (BMI) and are very carbohydrate sensitive.

Patients with type 2 diabetes have insulin resistance or a related insulin deficiency over a prolonged period of time. Patients with type 2 diabetes typically have a higher BMI and features of insulin resistance, such as acanthosis nigricans. They also have a strong family history of diabetes.

There are other diabetes types. Nowadays, we see atypical diabetes, such as ketosis-prone diabetes, formerly called Flatbush diabetes. We also see latent autoimmune diabetes of adult onset (LADA) and other subtypes under the broad classifications of type 1 and type 2 diabetes.

Shubrook: And, of course, gestational diabetes is also quite common and closely associated with type 2. Research by investigators from Lund University in Sweden, recently published in *The Lancet Diabetes and Endocrinology*, proposed a new classification system.[1] Tell me about this.

Ahmed: This study was conducted with a Scandinavian cohort. Patients with diabetes were categorized into five clusters, based on the severity of diabetes. Patients with severe diabetes were placed in the first three clusters, and those with milder diabetes were placed in clusters 4 and 5. The first cluster comprises severe autoimmune diabetes. Here is included the typical patient with type 1 diabetes, with severe insulin deficiency secondary to autoimmunity. These patients were insulin dependent and required insulin to survive. They also had very low BMIs.

Patients in cluster 2 also had severe insulin deficiency, but without evidence of autoimmunity. These patients had low BMIs and required insulin injections to survive.

Cluster 3 is severe insulin-resistant diabetes; in addition, these patients had the typical metabolic or physical features of what we currently call type 2 diabetes—they had higher BMIs and severe insulin resistance; hence, they were also insulin dependent. These patients had a high propensity for chronic diabetic nephropathy, in contrast to patients with severe insulin-deficient diabetes, who had a high propensity for retinopathy. That was a difference that the investigators noticed in these cohorts.

Clusters 4 and 5 are the milder forms of diabetes; cluster 4 is obesity-related diabetes and cluster 5 is the mild, age-related diabetes. Cluster 4 patients had higher BMIs, but they did not exhibit the high insulin resistance that was seen in the cluster 3 patients. Cluster 5 patients had a milder form of diabetes, with the onset at an older age. Thus, the five clusters were based on severity, the presence of GAD (glutamic acid decarboxylase) antibodies, HbA1c, and the presence of insulin and beta-cell function.

Why Does New Classification Matter?

Shubrook: This study looked at a known population of patients with diabetes to tease out the different types. Why is this important?

Ahmed: I believe they felt that it helped to individualize the treatment plan; they could personalize the treatment based on the patient's classification. For example, if patients had severe insulin resistance and thus were perhaps more prone to develop diabetic nephropathy, could the treatment plan be personalized to account for that? In my opinion, this classification is more clinically and practically useful.

Shubrook: As you have described these clusters, type 1 is cluster 1; type 1B or LADA could be included in cluster 2; cluster 3 is classic insulin resistance; cluster 4 is probably an emerging type where people have not so much the genetics of insulin resistance but obesity-related type 2 diabetes. Cluster 5 is what I would call "old-fashioned diabetes." Some of us have been in practice long enough to remember when some people had a very indolent course of diabetes in their 80s. It was not a bad disease, and it probably needs to be treated differently.

Ahmed: It is interesting that you say that. As a hospitalist, I also see many patients for whom we may not have access to medical records.

When you ask the patients about type of diabetes, those taking insulin will often say that they have type 1, when in fact they actually have an advanced type 2 diabetes or a prolonged period of type 2 diabetes and now require insulin.

My dad was diagnosed with diabetes when he was much older, over 65 years of age, and he did not have a higher BMI. He has type 2 diabetes with a strong family history, but I always wondered, where do I place him? Now I have the answer. I can place him into cluster 5. He has mild age-related diabetes, with an indolent course. He is doing great on metformin.

I love this new classification. It will help me categorize my patients more easily and will help me individualize the treatment.

Shubrook: So you are a proponent for a new classification.

Ahmed: Yes, absolutely.

Shubrook: The researchers also highlighted the finding that many people in cluster 3 were not receiving metformin, and this is probably one of the most important groups to get it. This brings us back to your focus of giving the right treatment to the right people.

Ahmed: Yes. If patients in cluster 2 have a high risk for retinopathy and patients in cluster 3 have a high risk for nephropathy, we need to make sure that they are screened appropriately. Of course, patients with diabetes do need all of their screenings, but perhaps this helps us focus on patients in these two clusters, to make sure that they get the appropriate screenings and follow-up care.

Shubrook: I very much appreciate your insights. I have learned something from this. For our listeners, stay tuned because there may be a new classification coming. Thank you very much.

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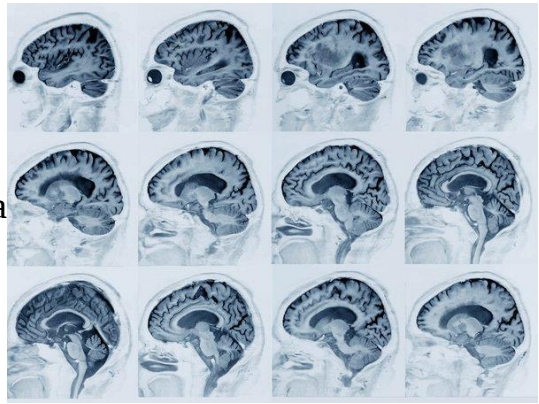
https://nyti.ms/2K7HkOA

A Common Virus May Play Role in Alzheimer's Disease, Study Finds

It has long been a controversial theory about Alzheimer's disease, often dismissed by experts as a sketchy cul-de-sac off the beaten path from mainstream research.

By Pam Belluck June 21, 2018



But a new study by a team that includes prominent Alzheimer's scientists who were previously skeptics of this theory may well change that. The research offers compelling evidence for the idea that viruses might be involved in Alzheimer's, particularly two types of herpes that infect most people as infants and then lie dormant for years.

New research suggests that certain viral infections could accelerate an immune response increasing the accumulation of amyloid, the protein in human brains which forms the plaques of Alzheimer's. **Zephyr/Science Source**

The study, published Thursday in the journal Neuron, found that viruses interact with genes linked to Alzheimer's and may play a role in how Alzheimer's develops and progresses.

The authors emphasized they did not find that these viruses cause Alzheimer's. But their research, along with another soon-to-be-published study, suggests that viruses could kick-start an immune response that might increase the accumulation of amyloid, a protein in human brains which clumps into the telltale plaques of Alzheimer's.

"These viruses are probably significant players in driving the immune system in Alzheimer's," said Joel Dudley, the study's senior author and an associate professor of genetics and genomic sciences at the Icahn School of Medicine at Mount Sinai in New York. "I think they're like gas on the flames of some pathology that may be immune-driven."

If so, that could change the course of research and possibly lead to treatments and new ways of screening for the disease.

"This definitely brings up the potential role of infection or infectious particles in the pathology of Alzheimer's," said Dr. John Morris, director of the Knight Alzheimer's Disease Research Center at Washington University School of Medicine in St. Louis.

Dr. Morris, who was not involved in the research, said it provided the strongest evidence to date for a viral role. The study analyzed samples from nearly 950 human brains in four different brain banks and found links to the genetic, molecular and clinical symptoms of Alzheimer's.

"It's a very complex disease, and the answer's not going to be one thing," he said. "If viruses are a part of that, we definitely need to take a look at it."

The virus theory is far from being accepted by most Alzheimer's experts. Some raise the chicken-or-egg question: Could viruses found in greater amounts in Alzheimer's brains be consequences of the disease or even, as Dr. Lennart Mucke, director of the Gladstone Institute of Neurological Disease in San Francisco said, "innocent bystanders"?

Dr. Mucke called the new study "impressive and very well designed." But, he noted, "there have been many speculations and even outright claims that infections contribute to the development of Alzheimer's disease."

"None of them has held up after rigorous cause-effect evaluations," he added.

Still, the new findings will be bolstered by another upcoming study in Neuron, led by Rudolph Tanzi and Robert Moir, neuroscientists at Massachusetts General Hospital and Harvard, who have broken ground on the virus idea for years.

Their new experiments, performed in mice and three-dimensional brain cells in a dish, found that the same herpes species ignited a protective reaction in amyloid, a protein present in all human brains. Dr. Tanzi describes this as "seeding" the amyloid, causing it to ensnare the virus in fibrous nets that form plaques.

In this way, he said, viruses and other microbes are the "prequel" to the prevailing theory that Alzheimer's is caused by amyloid accumulation the brain cannot clear out.

For the study published Thursday, Dr. Dudley, who described himself as a "big data guy," not an Alzheimer's expert, was asked by the National Institutes of Health to help generate new Alzheimer's ideas by analyzing information from a consortium involving many brain banks and researchers.

Dr. Dudley was interested in whether existing drugs could be repurposed to treat Alzheimer's, which has so far resisted all drugs tested in hundreds of clinical trials. To start, he and colleagues created computer models mapping the molecular and genetic networks disrupted as Alzheimer's progresses.

What the scientists found surprised them. Genes that were active in Alzheimer's pathology also turned out to be active in fighting viruses. "I went looking for drugs, and all I found were these stupid viruses," Dr. Dudley joked.

Then the researchers searched in about 2,000 samples from 944 brains of people who had died — some with Alzheimer's, some with other types of neurological problems, and some without cognitive impairment. The idea was to see if any viral gene sequences were more abundant in Alzheimer's brains.

Although some previous Alzheimer's studies had focused on herpes, "we had no horse in the race and said, 'We're going to look across all viral genes known to man,'" Dr. Dudley said.

Out of 515 viruses, Alzheimer's brains consistently had more of two herpes species: 6A and 7. These belong to a family of roseoloviruses that affect almost every baby, sometimes causing a pinkish rash and fever. They then go dormant, but can later get reactivated for various reasons, including illness or stress.

These herpes species have the ability to enter brain cells. And, said Dr. Dudley, "The viruses have a direct sort of push-pull with lots of known Alzheimer's genes."

In fact, people with the gene most known to increase the risk of getting Alzheimer's, ApoE4, had even more of herpes 6A, said Ben Readhead, the study's first author, affiliated with the Icahn School of Medicine and the Arizona State University-Banner Neurodegenerative Disease Research Center.

And genes that seemed to make tissues more susceptible to harm from the herpesviruses were expressed most strongly in two brain areas that are especially damaged in Alzheimer's, Dr. Dudley said.

But herpes may not be the only infection that triggers the brain's immune response, Dr. Tanzi said. Bacteria, parasites and other microbes might, too.

"It could lead to new therapeutic strategies down the road," said Dr. Eric Reiman, executive director of the Banner Alzheimer's Institute in Phoenix and one of several Alzheimer's experts and longtime virus-theory skeptics who were co-authors on the study.

For example, experts said, it might make sense to develop vaccines or drugs to pre-empt infections most linked to Alzheimer's and to screen people for genes that increase vulnerability to those infections. The goal, said Dr. Reiman, is to "find better ways to understand and treat the disease — including ways that may defy preconceived notions."

Dr. Dudley said he is unsure whether many mainstream Alzheimer's researchers will endorse the virus idea anytime soon.

"It's very unpopular," he said. "I'm sure there's a lot of people who are secretly unhappy about it."

Still, he said, Alzheimer's researchers "come up to me at conferences and say in hushed tones, 'Oh, I also have a data set that shows viruses, but I'm afraid to publish it.'"

http://bit.ly/2tnWxko

Psychiatric disorders share an underlying genetic basis

Psychiatric disorders may have important molecular similarities that are not reflected in current diagnostic categories

Psychiatric disorders such as schizophrenia and bipolar disorder often run in families. In a new international collaboration, researchers explored the genetic connections between these and other disorders of the brain at a scale that far eclipses previous work on the subject. The team determined that psychiatric disorders share many genetic variants, while neurological disorders (such as Parkinson's or Alzheimer's) appear more distinct.

Published today in Science, the study takes the broadest look yet at how genetic variation relates to brain disorders. The results indicate that psychiatric disorders likely have important similarities at a molecular level, which current diagnostic categories do not reflect.

The study was led by co-senior authors Ben Neale, director of population genetics in the Stanley Center at Broad Institute of MIT and Harvard and a faculty member in the Analytical and Translational Genetics Unit at Massachusetts General Hospital, and Aiden Corvin, professor at Trinity College Dublin, with first author Verneri Anttila, a postdoctoral research fellow in Neale's lab. The team further includes researchers from more than 600 institutions worldwide.

"This work is starting to re-shape how we think about disorders of the brain," says Neale. "If we can uncover the genetic influences and

patterns of overlap between different disorders, then we might be able to better understand the root causes of these conditions -- and potentially identify specific mechanisms appropriate for tailored treatments."

Exploring these biological connections is challenging. The brain is a tricky organ to study directly, difficult to scan in detail or ethically biopsy. And, because brain disorders often co-occur, it's hard to untangle when one might be affecting the development of another.

To examine the biological overlap between these disorders, researchers must rely on genetics. For the current study, international consortia pooled their data to examine the genetic patterns across 25 psychiatric and neurological diseases. Because each genetic variant only contributes a tiny percentage of the risk for developing a given disorder, the analyses required huge sample sizes to separate reliable signals from noise.

The researchers measured the amount of genetic overlap across the disorders using genome-wide association studies (GWAS) of 265,218 patients and 784,643 controls. They also examined the relationships between brain disorders and 17 physical or cognitive measures, such as years of education, from 1,191,588 individuals. The dataset ultimately included all GWAS consortia studying common brain disorders that the team could identify with sufficient sample sizes. "This was an unprecedented effort in sharing data, from hundreds of researchers all around the world, to improve our understanding of the brain," says Anttila.

The final results indicated widespread genetic overlap across different types of psychiatric disorders, particularly between attention-deficit/hyperactivity disorder (ADHD), bipolar disorder, major depressive disorder, and schizophrenia. The data also indicated strong overlap between anorexia nervosa and obsessive-compulsive disorder (OCD), as well as between OCD and Tourette syndrome.

In contrast, neurological disorders such as Parkinson's and multiple sclerosis appeared more distinct from one another and from the psychiatric disorders -- except for migraine, which was genetically correlated to ADHD, major depressive disorder, and Tourette syndrome.

According to the researchers, the high degree of genetic correlation among the psychiatric disorders suggests that current clinical categories do not accurately reflect the underlying biology. "The tradition of drawing these sharp lines when patients are diagnosed probably doesn't follow the reality, where mechanisms in the brain might cause overlapping symptoms," says Neale.

As a hypothetical example, a single mechanism regulating concentration could drive both inattentive behavior in ADHD and diminished executive function in schizophrenia. Further exploration of these genetic connections could help define new clinical phenotypes and inform treatment development and selection for patients.

Additionally, within the cognitive measures, the researchers were surprised to note that genetic factors predisposing individuals to certain psychiatric disorders -- namely anorexia, autism, bipolar, and OCD -- were significantly correlated with factors associated with higher childhood cognitive measures, including more years of education and college attainment. Neurological disorders, however, particularly Alzheimer's and stroke, were negatively correlated with those same cognitive measures.

"We were surprised that genetic factors of some neurological diseases, normally associated with the elderly, were negatively linked to genetic factors affecting early cognitive measures. It was also surprising that the genetic factors related to many psychiatric disorders were positively correlated with educational attainment," says Anttila. "We'll need more work and even larger sample sizes to understand these connections."

The consortia have made their GWAS data accessible online, either freely available for download or by application. They plan to examine additional traits and genetic variants to explore these patterns further, aiming to discover the relevant mechanisms and pathways that underlie and potentially link these disorders.

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http://bit.ly/2KdvKkv

Research team discovers drug compound that stops cancer cells from spreading

Via a mouse model, OHSU physician-scientists lead effort to hone a drug that inhibits cancer cells from spreading to other areas in the body

PORTLAND, Oregon - Fighting cancer means killing cancer cells. However, oncologists know that it's also important to halt the movement of cancer cells before they spread throughout the body. New research, published today in the journal Nature Communications, shows that it may be possible to freeze cancer cells and kill them where they stand.

Raymond Bergan, M.D., Division Chief of Hematology and Medical Oncology and professor of medicine at OHSU, says that the majority of cancer treatment therapies today are directed toward killing cancer. To date, he says, no one has developed a therapy that can stop cancer cells from moving around the body.

"For the vast majority of cancer--breast, prostate, lung, colon, and others--if it is detected early when it is a little lump in that organ and it has not spread, you will live. And generally, if you find it late, after it has spread throughout your body, you will die," says Bergan, also the associate director of medical oncology in the OHSU Knight Cancer Institute and director of the OHSU Bergan Basic Research Laboratory. "Movement is key: the difference is black and white, night and day. If cancer cells spread throughout your body, they will take your life. We can treat it, but it will take your life."

For that reason, the study of cancer cell movement, or motility, has been the focus of his group's research for several decades.

Stopping cancer cell movement

In 2011, Bergan and team took a novel approach to their research by working with chemists to jointly discover a drug that will inhibit the movement of cancer cells. The Nature Communications paper outlines the multidisciplinary team's work with KBU2046, a compound that was found to inhibit cell motility in four different human cell models of solid cancer types: breast, prostate, colon and lung cancers.

"We used chemistry to probe biology to give us a perfect drug that would only inhibit the movement of cancer cells and wouldn't do anything else," Bergan says. "That basic change in logic lead us to do everything we did."

A multidisciplinary team

The team of investigators includes Bergan's team at OHSU, a chemist from Northwestern University as well as researchers from Xiamen University in China, the University of Chicago, and the University of Washington. Ryan Gordon, Ph.D., research assistant professor in the OHSU School of Medicine and co-director of the Bergan lab, says drawing upon the strengths of this cross-functional group was key to the research's success. "As we identified areas we were lacking, we looked at new cutting-edge technologies, and if there was something that didn't meet our needs, we developed new assays to address our needs," he says.

The lab of Karl Scheidt, Ph.D., professor of chemistry and professor of pharmacology; director of the Center for Molecular Innovation and Drug Discovery; and executive director of the NewCures accelerator at Northwestern University, was responsible for the design and creation of new molecules which were then evaluated by

Bergan's team for their ability to inhibit cell motility. Using chemical synthesis approaches, Scheidt and team accessed new compounds that minimized motility in tumor cells, with few side effects and very low toxicity.

"We've taken a clue provided by nature and through the power of chemistry created an entirely new way to potentially control the spread of cancer," Scheidt says. "It's been a truly rewarding experience working together as a team toward ultimately helping cancer patients."

Refining the drug

Bergan notes the process for narrowing down the specific drug compound was a process of refinement. "We started off with a chemical that stopped cells from moving, then we increasingly refined that chemical until it did a perfect job of stopping the cells with no side effects," he says. "All drugs have side effects, so you look for the drug that is the most specific as possible. This drug does that."

Bergan says the key to this drug was engaging the heat shock proteins--the "cleaners" of a cell. "The way the drug works is that it binds to these cleaner proteins to stop cell movement, but it has no other effect on those proteins." He says it is a very unusual, unique mechanism that "took us years to figure out."

"Initially, nobody would fund us," Bergan says. "We were looking into a completely different way of treating cancer."

Next step: testing the drug in humans

Ultimately, Gordon says the goal of this research is to look for a new therapeutic to benefit humans.

"The eventual promise of this research is that we're working toward developing a therapeutic that can help manage early stage disease, preventing patients from getting the more incurable later-stage disease," he says. He's quick to note this work has not been tested in humans, and doing so will require both time and money. The team's best estimate is that will take about two years and five million dollars of funding. They are currently raising money to do IND (investigational new drug) enabling studies, a requirement to conduct a clinical trial of an unapproved drug or an approved product for a new indication or in a new patient population.

In addition, Drs. Bergan and Scheidt have founded a company, Third Coast Therapeutics, aimed to bring this type of therapy to patients.

"Our eventual goal is to be able to say to a woman with breast cancer: here, take this pill and your cancer won't spread throughout your body. The same thing for patients with prostate, lung, and colon cancer," Bergan says. "This drug is highly effective against four cancer types (breast, colon, lung, prostate) in the in vitro model so far. Our goal is to move this forward as a therapy to test in humans."

Bergan says his team feels lucky to have the opportunity to conduct this challenging research at the OHSU Knight Cancer Institute, an institute dedicated to novel approaches to detecting and treating cancer. "What early detection is trying to do is detect an early, lethal lesion. Cancers are lethal because they move," he says. "This drug is designed to stop that movement."

Funding for this research was supported by the Department of Defense and the Veteran's Administration.

http://bit.ly/2lxI15o

The 'Keystone Virus' Had Never Been Seen in People, Until a Florida Teen Caught It

There's a new mosquito-borne virus to be wary of — or at least new to those of us who don't study such viruses.

By Rachael Rettner, Senior Writer | June 22, 2018 06:29am ET

A teenager in Florida is the first person known to be infected with a virus called Keystone virus, which is spread by mosquitoes. The teen visited an urgent care clinic in North Central Florida in August 2016, after he developed a fever and rash, according to a new report of his case, published June 9 in the journal Clinical Infectious Diseases.

Doctors initially thought the teen might have an infection caused by the Zika virus — after all, his visit occurred in the midst of the Zika epidemic in Florida — but tests for that virus came back negative.

But unexpectedly, researchers from the University of Florida (UF) found the Keystone virus in samples from the patient.

The Keystone virus was first discovered in 1964 in the Tampa Bay area, and has been previously found in animals, according to a statement from the University of Florida. Doctors had suspected the virus might infect people, but they hadn't found the virus in humans, until now. The researchers say there could be other, undiagnosed cases of this virus.

"Although the virus has never previously been found in humans, the infection may actually be fairly common in North Florida," Dr. J. Glenn Morris, director of the UF Emerging Pathogens Institute, said in the statement. "It's one of these instances where if you don't know to look for something, you don't find it."

Although the teen's symptoms were mild, it's possible that the Keystone virus may cause more severe symptoms in people, including brain infections. Two relatives of the Keystone virus, the Jamestown Canyon virus and La Crosse encephalitis virus, can cause inflammation of the brain, called encephalitis.

The researchers say the discovery of the Keystone virus in a person highlights the need for more research into the prevalence of mosquito-borne diseases in the U.S. "All sorts of viruses are being transmitted by mosquitoes, yet we don't fully understand the rate of disease transmission," Morris said.

http://bit.ly/2K3OPWV

Scientists discover how antiviral gene works

Finding could form the basis for potent new drugs

BRONX, NY - It's been known for years that humans and other mammals possess an antiviral gene called RSAD2 that prevents a remarkable range of viruses from multiplying. Now, researchers at Albert Einstein College of Medicine, part of Montefiore, have discovered the secret to the gene's success: The enzyme it codes for generates a compound that stops viruses from replicating. The newly discovered compound, described in today's online edition of *Nature*, offers a novel approach for attacking many disease-causing viruses.

"Nature has given us a template for creating a powerful and safe antiviral compound," says study leader Steven C. Almo, Ph.D., professor and chair of biochemistry, professor of physiology & biophysics and the Wollowick Family Foundation Chair in Multiple Sclerosis and Immunology at Einstein. Dr. Almo and his colleagues at Einstein and Pennsylvania State University found that the compound, called ddhCTP, disrupts the replication machinery of Zika virus. The next step is to test the compound against a broad array of viruses.

Dr. Almo predicts that modifications to ddhCTP could make it even more potent. Furthermore, he says, "drugs based on this compound may have a favorable safety profile. We've been living with ddhCTP for many millions of years and long ago developed mechanisms to prevent it from interfering with the replication of our own cells." Tyler Grove, Ph.D., a research assistant professor in Dr. Almo's lab, and Anthony Gizzi, who received his Ph.D. from Einstein in May, are co-lead authors on the study.

Finding How Viruses Are Vanquished

Mammalian cells that become infected by viruses and other pathogens release signaling proteins called interferons. The interferons in turn trigger the expression of hundreds of genes--one of which is RSAD2, the gene that codes for the enzyme viperin (short for "virus inhibitory protein, endoplasmic reticulum-associated, interferon-inducible"). Studies have shown that viperin's expression inhibits a broad spectrum of disease-causing viruses, including hepatitis C, rabies and HIV-1.

Researchers had proposed several theories for how viperin exerts its anti-viral effects, but precisely how it acted was a mystery. The current study reveals that viperin catalyzes the conversion of a nucleotide called CTP (cytidine triphosphate) into a structurally similar compound, or analog: the nucleotide ddhCTP--a previously undescribed molecule that sabotages viral replication.

Many viruses use CTP as a building block to synthesize the new strands of genetic material they need to replicate. The conversion of CTP to its analog, ddhCTP, throws a monkey wrench into virus' ability to copy its genome. The analogue's structure differs only slightly from CTP's--but the difference is sufficient to bring viral replication to a halt.

Dr. Almo's colleagues at Pennsylvania State University showed in laboratory studies that ddhCTP was highly effective at inhibiting the replication of three different strains of Zika virus--a mosquito-borne virus that causes an infection for which there is currently no treatment. "Based on our enzymology studies," says Dr. Almo, "we think that ddhCTP may be able to inhibit all flaviviruses, a class of viruses that includes Zika as well as dengue, West Nile, yellow fever, Japanese encephalitis and hepatitis C."

A Promising Platform for New Drugs

Dr. Almo says that ddhCTP appears to be "a completely novel drug scaffold" for designing antiviral drugs. "We are hoping we can generate variants of this molecule that will be even more effective," he adds. "Those drugs would be based on a naturally occurring molecule, so they could have few off-target effects--a common problem with manmade nucleotide analogs, which can be effective but also quite toxic."

The paper is titled "A naturally occurring antiviral ribonucleotide encoded by the human genome." The other Einstein contributors are: Rohit K Jangra, Ph.D., Scott J. Garforth, Ph.D., Quan Du, Ph.D., Sean M. Cahill, Ph.D., Natalya G. Dulyaninova, Ph.D., Kartik Chandran, Ph.D., and Anne R. Bresnick, Ph.D. Other authors include Craig E. Cameron, Ph.D., Jamie J. Arnold, Ph.D., and Joyce Jose, Ph.D., all at Pennsylvania State University, and James D. Love, Ph.D., at the Institute for Protein Innovation, Boston, MA.

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Drs. Gizzi, Grove, Arnold, Cameron, and Almo are co-inventors on a U.S. provisional patent application (No. 62/548,425) that incorporates discoveries described in this manuscript. The authors declare no other conflicts of interest.