http://bit.ly/2DsEUXF

Genes that aid spinal cord healing in lamprey also present in humans, MBL team discovers

Genes involved in repair of the lamprey spinal cord are also active in repair of the peripheral nervous system in mammals

Woods Hole, Mass.-- Many of the genes involved in natural repair of the injured spinal cord of the lamprey are also active in the repair of the peripheral nervous system in mammals, according to a study by a collaborative group of scientists at the Marine Biological Laboratory (MBL) and other institutions. This is consistent with the possibility that in the long term, the same or similar genes may be harnessed to improve spinal cord injury treatments.

"We found a large overlap with the hub of transcription factors that are driving regeneration in the mammalian peripheral nervous system," says Jennifer Morgan, director of the MBL's Eugene Bell Center for Regenerative Biology and Tissue Engineering, one of the authors of the study published this week in Scientific Reports.

Lampreys are jawless, eel-like fish that shared a common ancestor with humans about 550 million years ago. This study arose from the observation that a lamprey can fully recover from a severed spinal cord without medication or other treatment.

"They can go from paralysis to full swimming behaviors in 10 to 12 weeks," says Morgan.

"Scientists have known for many years that the lamprey achieves spontaneous recovery from spinal cord injury, but we have not known the molecular recipe that accompanies and supports this remarkable capacity," says Ona Bloom of the Feinstein Institute for Medical Research and the Zucker School of Medicine at Hofstra/Northwell, a former MBL Whitman Center Fellow who collaborated on the project.

"In this study, we have determined all the genes that change during the time course of recovery and now that we have that information, we can use it to test if specific pathways are actually essential to the process," Bloom says.

The researchers followed the lampreys' healing process and took samples from the brains and spinal cords at multiple points in time, from the first hours after injury until three months later when they were healed. They analyzed the material to determine which genes and signaling pathways were activated as compared to a non-injured lamprey.

As expected, they found many genes in the spinal cord that change over time with recovery. Somewhat unexpectedly, they also discovered a number of injury-induced gene expression changes in the brain. "This reinforces the idea that the brain changes a lot after a spinal cord injury," says Morgan. "Most people are thinking, 'What can you do to treat the spinal cord itself?' but our data really support the idea that there's also a lot going on in the brain."

They also found that many of the genes associated with spinal cord healing are part of the Wnt signaling pathway, which plays a role in tissue development. "Furthermore, when we treated the animals with a drug that inhibits the Wnt signaling pathway, the animals never recovered their ability to swim," says Morgan. Future research will explore why the Wnt pathway seems particularly important in the healing process.

The paper is the result of a collaboration between Morgan, Bloom and other scientists including Jeramiah Smith of University of Kentucky and Joseph Buxbaum of Icahn School of Medicine at Mount Sinai, both former Whitman Center Fellows. The collaboration was made possible by the MBL Whitman Center Fellowship program.

"[This study] involved several different labs located in different parts of the country with different types of expertise, but it absolutely could not and would not have been done without the support of the MBL that allows us to to work collaboratively in a shared laboratory setting," says Morgan.

Citation:
Paige E. Herman et al (2018) Highly conserved molecular pathways, including Wnt signaling, promote functional recovery from spinal cord injury in lampreys. Scientific Reports,

http://bit.ly/2FYFWbx

Little 'Rainbow' Dinosaur Discovered by Farmer in China

Iridescent feathers glistened on the dinosaur's head, wings and tail

By Laura Geggel, Senior Writer | January 15, 2018 10:09am ET

Despite its fearsome, Velociraptor-like skull, a 161-million-year-old dinosaur the size of a duck would have been a shining, shimmering and splendid sight to behold — mostly because it sported gleaming, iridescent feathers that were rainbow-colored, a new study finds.

Iridescent feathers glistened on the dinosaur's head, wings and tail, according to an analysis of the shape and structure of the creature's melanosomes, the parts of cells that contain pigment.

"The preservation of this dinosaur is incredible — we were really excited when we realized the level of detail we were able to see on the feathers," study co-researcher Chad Eliason, a postdoctoral researcher at the Field Museum in Chicago, said in a statement. [See images and illustrations of the iridescent dinosaur]

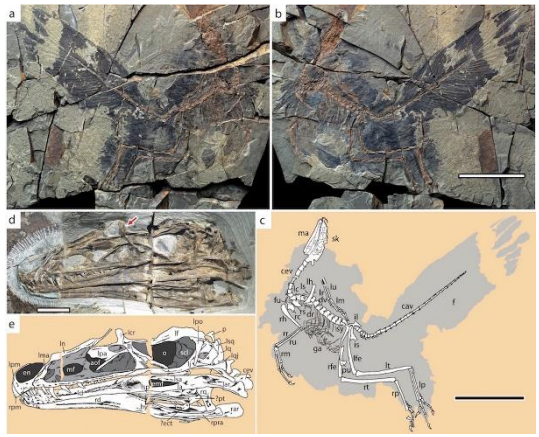
***C. juji* prepares to snatch its prey. Zhao Chuang**

A farmer in northeastern China's Hebei Province discovered the fossil, and the Paleontological Museum of Liaoning in China acquired the find in 2014. After discovering its iridescence and noting the unique bony crest on top of the dinosaur's head, researchers gave it a colorful name — *Caihong juji* — which is Mandarin for "rainbow with the big crest."

Dazzling discovery

The scientists discovered the dinosaur's iridescence and colorful nature by examining its feathers using a scanning electron microscope (SEM). Incredibly, the SEM analysis showed imprints of melanosomes in the fossil. The organic pigment once contained in the melanosomes is long gone, but the structure of the cell parts revealed the feathers' original colors, the researchers said. That's because differently shaped melanosomes reflect light in different ways.

"Hummingbirds have bright, iridescent feathers, but if you took a hummingbird feather and smashed it into tiny pieces, you'd only see black dust," Eliason said. "The pigment in the feathers is black, but the shapes of the melanosomes that produce that pigment are what make the colors in hummingbird feathers that we see."



Photos and drawings of the incredibly detailed *C. juji* fossil. Yu et al., 2018

The pancake-shaped melanosomes in *C. juji* matched those in hummingbirds, indicating that the Jurassic-age dinosaur had iridescent feathers, the researchers said.

C. juji isn't the first dinosaur on record to have iridescent feathers; *Microraptor*, a four-winged dinosaur also sported gleaming feathers, Live Science previously reported. But that dinosaur lived about 40 million years after *C. juji*, so the newly identified dinosaur is by far the oldest dinosaur on record to flaunt iridescent plumage, the researchers said.

C. juji is also the oldest animal on record to have asymmetrical feathers, which help modern birds steer while flying. However, unlike modern birds, whose asymmetrical feathers are on their wing tips, *C. juji* sported these lopsided feathers on its tail. That, combined with the fact that *C. juji* likely couldn't fly, led the researchers to conclude the dinosaur likely used its feathers to attract mates and keep warm.

This "bizarre" feature has never been seen before in either dinosaurs or birds, which evolved from dinosaurs, said study co-researcher Xing Xu, a researcher at the Institute of Vertebrate Paleontology and

Paleoanthropology at the Chinese Academy of Sciences. This suggests that tail feathers may have played a role in early, controlled flight, Xu said.

But not all of *C. juji's* features are out of the blue. Some of its traits, such as its bony head crest, resemble those on other dinosaurs, researchers said.

"This combination of traits is rather unusual," study co-researcher Julia Clarke, a professor of vertebrate paleontology at the University of Texas at Austin, said in the statement. "It has a Velociraptor-type skull on the body of this very avian, fully feathered, fluffy kind of form."

This mixture of old and new traits is an example of mosaic evolution, when some parts of an animal evolve, but others stay the same, the researchers said.

The study was published online today (Jan. 15) in the journal Nature Communications.

http://bbc.in/2DXirPH

Black Death 'spread by humans not rats'

Rats were not to blame for the spread of plague during the Black Death, according to a study.

By Victoria Gill Science correspondent, BBC News

The rodents and their fleas were thought to have spread a series of outbreaks in 14th-19th Century Europe.

But a team from the universities of Oslo and Ferrara now says the first, the Black Death, can be "largely ascribed to human fleas and body lice".

The study, in the Proceedings of the National Academy of Science, uses records of its pattern and scale.

The Black Death claimed an estimated 25 million lives, more than a third of Europe's population, between 1347 and 1351.

"We have good mortality data from outbreaks in nine cities in Europe," Prof Nils Stenseth, from the University of Oslo, told BBC News.

"So we could construct models of the disease dynamics [there]."

He and his colleagues then simulated disease outbreaks in each of these cities, creating three models where the disease was spread by:

- ***rats***
- ***airborne transmission***
- ***fleas and lice that live on humans and their clothes***

In seven out of the nine cities studied, the "human parasite model" was a much better match for the pattern of the outbreak.

It mirrored how quickly it spread and how many people it affected.

"The conclusion was very clear," said Prof Stenseth. "The lice model fits best."

"It would be unlikely to spread as fast as it did if it was transmitted by rats.

"It would have to go through this extra loop of the rats, rather than being spread from person to person."

'Stay at home'

Prof Stenseth said the study was primarily of historical interest - using modern understanding of disease to unpick what had happened during one of the most devastating pandemics in human history.

But, he pointed out, "understanding as much as possible about what goes on during an epidemic is always good if you are to reduce mortality [in the future]".

Plague is still endemic in some countries of Asia, Africa and the Americas, where it persists in "reservoirs" of infected rodents.

According to the World Health Organization, from 2010 to 2015 there were 3,248 cases reported worldwide, including 584 deaths.

And, in 2001, a study that decoded the plague genome used a bacterium that had come from a vet in the US who had died in 1992 after a plague-infested cat sneezed on him as he had been trying to rescue it from underneath a house.

"Our study suggests that to prevent future spread hygiene is most important," said Prof Stenseth.

"It also suggests that if you're ill, you shouldn't come into contact with too many people. So if you're sick, stay at home."

http://bit.ly/2BilfUd

Starting periods before age of 12 linked to heightened risk of heart disease and stroke

Along with early menopause, pregnancy complications, and hysterectomy

Starting periods early--before the age of 12--is linked to a heightened risk of heart disease and stroke in later life, suggests an analysis of data from the UK Biobank study, published online in the journal Heart.

It is one of several reproductive risk factors, including early menopause, complications of pregnancy, and hysterectomy, that seem to be associated with subsequent cardiovascular disease, the findings show.

Previous research has suggested that certain reproductive risk factors may be linked to an increased risk of heart disease or stroke, but the findings have been somewhat mixed.

In a bid to clarify any potential associations, the research team drew on data from the UK Biobank, a large population based study of more than half a million men and women up to the age of 69, and recruited between 2006 and 2010.

Participants filled in questionnaires on their lifestyle, environment, and medical history, which included a wide range of reproductive factors. They also took tests to assess their physical and functional health, and provided urine, blood, and saliva samples.

In all, the health of 267,440 women and 215,088 men--none of whom had cardiovascular disease when they entered the study--was tracked up to March 2016 or until they had their first heart attack or stroke, whichever came first.

The average age of the women at the start of the study was 56, and around half (51%) came from the most affluent third of the UK population. Six out of 10 had never smoked.

The average age at which they had started having periods was 13; most (85%) had been pregnant, and nearly half (44%) had had two kids. On average, they were 26 when they had had their first child.

One in four of the women had miscarried, and 3 percent had had a stillbirth. Nearly two thirds of them had gone through the menopause, at an average age of 50.

Some four out of 10 of the men (42%) had fathered two kids before the start of the study.

During a monitoring period spanning around 7 years, 9054 cases of cardiovascular disease were recorded, a third (34%) of which were in women. This included 5782 cases of coronary artery disease (28% women) and 3489 cases of stroke (43% women).

Analysis of the data showed that after taking account of potentially influential factors, women who had started having periods before the age of 12 were at 10 percent greater risk of cardiovascular disease than those who had been 13 or older when they started.

Similarly, those who went through the menopause early (before the age of 47) had a 33 percent heightened risk of cardiovascular disease, rising to 42 percent for their risk of stroke, after taking account of other potentially influential factors.

Previous miscarriages were associated with a higher risk of heart disease, with each miscarriage increasing the risk by 6 percent. And stillbirth was associated with a higher risk of cardiovascular disease in general (22%) and of stroke in particular (44%).

Hysterectomy was linked to a heightened risk of cardiovascular disease (12%) and of heart disease (20%). And those who had had their ovaries removed before a hysterectomy were twice as likely to develop cardiovascular disease as those who hadn't had these procedures.

Young age at first parenthood seemed to be another risk factor, with each additional year of age lessening the risk of cardiovascular disease by around 3 percent.

But the association between the number of children and cardiovascular disease was similar for men and women, suggesting that social, psychological, and behavioural factors may be more important than biological ones.

This is an observational study, so no firm conclusions can be drawn about cause and effect, added to which the information on reproductive factors was based on recall, so may not have been completely accurate. Nevertheless, the study was large, and the researchers were able to account for a range of potentially influential factors.

"More frequent cardiovascular screening would seem to be sensible among women who are early in their reproductive cycle, or who have a history of adverse reproductive events or a hysterectomy, as this might help to delay or prevent their onset of [cardiovascular disease]" they advise.

http://bbc.in/2DSA7f0

'Staggering' trade in fake degrees revealed

Thousands of UK nationals have bought fake degrees from a multi-million pound "diploma mill" in Pakistan, a BBC Radio 4's File on Four programme investigation has found.

By Helen Clifton, Matthew Chapman and Simon Cox File on 4

Buyers include NHS consultants, nurses and a large defence contractor. One British buyer spent almost £500,000 on bogus documents.

The Department for Education said it was taking "decisive action to crack down on degree fraud" that "cheats genuine learners".

Axact, which claims to be the "world's largest IT company", operates a network of hundreds of fake online universities run by agents from a Karachi call centre.

With names such as Brooklyn Park University and Nixon University, they feature stock images of smiling students and even fake news articles singing the institution's praises.

According to documents seen by BBC Radio 4's File on Four programme, more than 3,000 fake Axact qualifications were sold to UK-based buyers in 2013 and 2014, including master's degrees, doctorates and PhDs.

A trawl through the list of Axact UK buyers, seen by the BBC, reveals various NHS clinical staff, including an ophthalmologist, nurses, a psychologist, and numerous consultants also bought fake degrees.

A consultant at a London teaching hospital bought a degree in internal medicine from the fake Belford University in 2007.

The doctor - who had previously been disciplined by the General Medical Council (GMC) for failing to report a criminal conviction - told the BBC he had not used the certificates because they "had not been authenticated".

An anaesthetist who bought a degree in "hospital management" said he had not used the qualification in the UK. And a consultant in paediatric emergency medicine, who bought a "master of science in health care technology", claimed it was an "utter surprise" when the BBC told him it was fake. There is no suggestion any of these clinicians do not hold appropriate original medical qualifications.

Large-scale problem

The General Medical Council (GMC) said it was up to employers to verify any qualifications additional to medical degrees.

But Higher Education Degree Datacheck (HEDD) chief executive Jayne Rowley said only 20% of UK employers ran proper checks on applicants' qualifications.

And while purchasing a fake diploma was not illegal in the UK, using one to apply for employment constituted fraud by misrepresentation and could result in a 10-year prison sentence.

"[The GMC] are correct in that [doctors] are licensed to practice medicine if they have a legitimate medical degree. But [by buying a fake degree], they have still committed fraud and could still be prosecuted," she said.

Danny Mortimer, chief executive of NHS Employers, said all NHS trusts operated rigorous primary checks. Verification was "achieved through a variety of channels" and fraudulent activity would be reported to police, he said.

In 2015, Axact sold more than 215,000 fake qualifications globally, through approximately 350 fictitious high schools and universities, making $51m (£37.5m) that year alone.

Former FBI agent Allen Ezell, who has been investigating diploma mills since the 1980s, said: "We live in a credential conscious society around the world. "So as long as paper has a value, there's going to be somebody that counterfeits it and prints it and sells it.

"Employers are not doing their due diligence in checking out the papers, so it makes it work. It's the damnedest thing we've ever seen."

'Very serious issue'

Defence contractor FB Heliservices bought fake Axact degrees for seven employees, including two helicopter pilots, between 2013 and 2015.

One of these employees, speaking anonymously to the BBC, said soon after he had been given a contract to work on the Caribbean island of Curacao, the local government decided all those working in the territory had to have a degree.

"We looked into distance learning, and contact was made with this online university. It was just something that needed to be done to keep working in the country.

"Everyone knew they were not bona fide. But no-one had a problem with it."

Parent-company Cobham held an internal investigation into the incident, but decided the purchase was a "historic issue" that "had no impact upon the safety of any of its operations or the training of any individuals in the UK or elsewhere". "Procedural and disciplinary actions have been taken to address all the issues raised," it added.

But MP James Frith, a member of the Education Select Committee, said the decision was a "very serious issue".

"I am amazed that a business would put itself and its very existence at risk by having fraudulent qualifications to, by the sounds of it, get into a new market."

Following a New York Times expose in 2015, Axact's chief executive was arrested and an investigation launched by the Pakistani authorities. Senior manager Umair Hamid was sentenced to 21 months in a US prison in August 2017 for his part in Axact's fraud.

Yet the Pakistani investigation has ground to a halt amid claims of government corruption.

Allan Ezell said Axact continued to launch new online universities all the time - and had now branched out into extortion and blackmail.

"It's a whole new game," he said. "Normally a diploma mill is finished with you by the time you get your degree. That's just the beginning now.

"You get a telephone call that looks like it's coming from your embassy or local law enforcement, threatening to arrest or deport you unless you get some additional documents to help support the phony diploma you already have. We've never seen that before."

Cecil Horner, a British engineer based in Saudi Arabia, was still getting threatening calls from Axact agents after paying nearly £500,000 for fake documents.

Mr Horner's son Malcolm said he believed his father, who died in 2015, had bought the qualifications because of the fear of losing his job.

"It makes me so angry," he said.

"It's unfathomable these websites still exist and they can't be shut down."

Action Fraud, the UK's national cybercrime reporting centre, said it did not have the power to close fake Axact websites but instead had to provide evidence to domain registries and registrars, which could take months.

MP James Frith said he was "staggered" by the "aggressive tactics" used by Axact and would ask the Education Selection Committee to look into the issue.

The Department of Education said HEDD was taking a proactive approach.

"Degree fraud cheats both genuine learners and employers, so we've taken decisive action to crack down on those seeking to profit from it," a spokesman said.

Axact did not respond to a request for an interview from the BBC.

File on 4: Degrees of Deception *is on BBC Radio 4 on Tuesday 16 January at 20:00 GMT and on the iPlayer.*

http://wb.md/2DVeI50

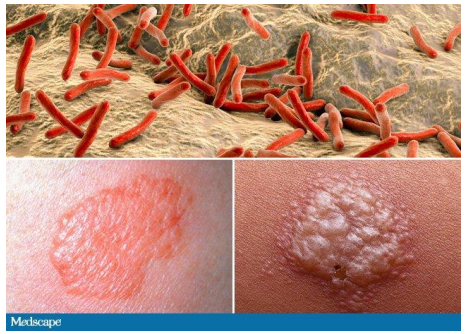
Four Old Antimicrobials That Still Work Best

Let's not forget older time-tested agents for treatment of a variety of infections

Douglas S. Paauw, MD; Joanna M. Pangilinan, PharmD; Laurie Scudder, DNP, NP

Old, but Still Good, Antimicrobials

Although attention is often paid to the newest and most expensive blockbuster drugs, let's not forget older agents that have stood the test of time for treatment of a variety of infections. These four antimicrobials should enter the new year with you and your prescription pad.



Images from Dreamstime, Alamy

Isoniazid

Isoniazid was first synthesized in 1912, and activity against tuberculosis was identified in 1945. More than 100 years later, and despite growing drug resistance, isoniazid is still a standard component of multidrug treatment regimens for both pulmonary and extrapulmonary disease, although drug susceptibility testing should be performed for previously treated patients.[1] *For more, refer to our Drugs & Diseases discussion of tuberculosis therapy.*

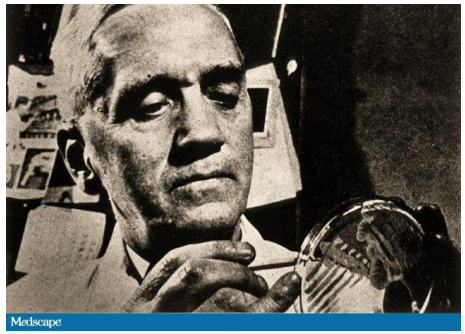


Image courtesy of National Institutes of Health

Penicillin

Penicillin was discovered in 1928, when Alexander Fleming observed that the mold *Penicillium notatum* destroyed colonies of *Staphylococcus aureus*. Use as an antibiotic began in the 1940s. Today, penicillin still has activity against many microbes and is recommended as first-line treatment for group A beta-hemolytic streptococcal (GABHS) pharyngitis.[2] Pneumococcal resistance to penicillin varies substantially by region,[3] but to date, no clinical isolate of penicillin-resistant GABHS penicillin has been reported.[4] In fact, the much larger concern is the reported overdiagnosis of penicillin allergy, particularly in children.[5,6] *For more, refer to our special report on penicillin allergy.*

Image courtesy of Wikimedia Commons

Sulfa

In 1932, a German pathologist found that prontosil, a chemical derivative from azo dyes, had antibacterial activity, which was later attributed to its metabolism to sulfanilamide.[7] In the hands of the Nazi regime, experiments using sulfanilamide were carried out at the all-female Ravensbrück concentration camp[8]—an ordeal recently chronicled in the novel *Lilac Girls.*

Sulfonamides are effective against many gram-positive and gram-negative bacteria and protozoa. Although sulfas remain a backbone of antimicrobial therapy, adverse effects, drug allergy, introduction of newer antibiotics, and resistance have reduced their utility.[9] Resistance to one sulfonamide means resistance to all.[10]

Trimethoprim/sulfamethoxazole has had a resurgence, because it is a first-line treatment for the ever-growing problem of community-acquired methicillin-resistant *S aureus* (MRSA).[11] It must be used carefully, especially in elderly persons, because of the risk for hyperkalemia. *For more, refer to our case challenge on hyperkalemia.*

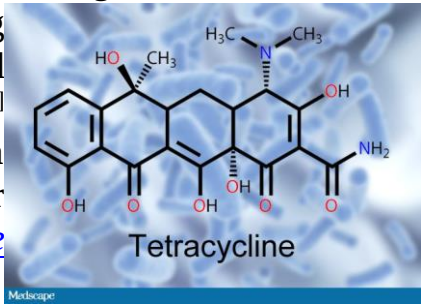


Image from Shutterstock

The Tetracyclines

Tetracycline was patented in 1955, and within 3 years, it was the most prescribed broad-spectrum antibiotic in the United States.[12] Although tetracyclines continue to be used for the treatment of chlamydia, spirochetal infections, anthrax, plague, tularemia, and other infections,[13] widespread use, particularly in veterinary medicine, has led to rising rates of resistance.[14] In particular, some pneumococcal strains and many GABHS, gram-negative bacillary uropathogens, and penicillinase-producing gonococci are resistant to tetracycline.[13] However, most community-acquired MRSA isolates are sensitive to both doxycycline and minocycline,[15] and these two drugs are also used for the treatment of acne. Recent research has focused on the anti-inflammatory properties of tetracyclines, particularly minocycline, and the potential for neuroprotection against Alzheimer disease,[16] stroke,[17] and neuromuscular disorders.[18]

For more, refer to our Drugs & Diseases discussion of tetracycline.

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http://bit.ly/2EZf4Ha

Chemical evolution: Progenitors of the living world

Alternation of wet and dry conditions could have sufficed to drive the prebiotic synthesis of RNA nucleosides

RNA was probably the first informational molecule. Now chemists from Ludwig-Maximilians-Universitaet (LMU) in Munich have demonstrated that alternation of wet and dry conditions could have sufficed to drive the prebiotic synthesis of the RNA nucleosides found in all domains of life.

"And the Earth was without form and void" - before the emergence of life. Meanwhile, we know rather more about the early Earth, but how

might the chemical structures that provide the basic subunits of today's hereditary molecules - RNA and DNA - have formed from simpler starting materials some 4 billion years ago? Under what conditions could these building blocks have then been linked into long chains that could not only encode information but also propagate it by self-reproduction? Many possible scenarios have been proposed for the phase of chemical evolution that preceded the emergence of the first biological cells. Now, researchers led by LMU chemist Professor Thomas Carell have extended these models by demonstrating a plausible route for the prebiotic synthesis of the 'nucleosides' that constitute the informational components of RNA.

Specifically, Carell and his colleagues have shown that nucleosides can be formed in a continuous process by exposing simple chemicals to the kinds of fluctuating physical conditions that would have prevailed in geothermally active areas characterized by volcanic activity on the early Earth. They begin with a mixture of formic acid, acetic acid, sodium nitrite and a few nitrogen-containing compounds, all of which have previously been shown to form from even simpler precursors under prebiotic conditions. The reaction mixture also contained nickel and iron, which are found in large amounts in the Earth's crust. The driving force for the chemical reactions is supplied by fluctuations in temperature and pH, together with wet/dry cycles, such as those that occur in the vicinity of periodically active hot springs or in strongly seasonal climates with alternating periods of precipitation and evaporation.

The core of the process is a series of reactions that gives rise to compounds called formamidopyrimidines, which can in turn be converted into the canonical purines (adenosine and guanosine) found in RNA. In a paper published last year, Carell and his team first described this FaPy pathway as a possible chemical scenario for the prebiotic synthesis of nucleosides. "This time around, we not only began with simpler precursor compounds, but chose conditions that would be expected to prevail in a plausible geological setting, such as hydrothermal springs on land," explains Sidney Becker, a PhD student in Carell's group and first author of the study. The paper has now appeared in one of the leading online, open-access journals, Nature Communications.

Notably, not only the canonical purine nucleosides found in RNA were synthesized in the new experiments, but also a whole series of closely related molecules. Even more strikingly, all of the modifications observed are known to occur in RNAs in all three domains of life - Eukaryota (animals and plants), Bacteria and Archaea - and are therefore essential components of functional genetic systems. Hence, they were most probably already present in the last common ancestor of all life forms. This in turn argues, says Becker, that these compounds must have been available on early Earth when biological evolution began. Indeed, the authors of the new study suggest that the non-canonical nucleosides could have played a crucial role in the phase of chemical evolution that preceded the emergence of the 'RNA world' (the term refers to a hypothetical period during which RNA molecules are thought to have served as chemical catalysts, in addition to storing genetic information, in primordial cells). Seen in this light, the RNA modifications found in today's organisms represent molecular fossils that have continued to participate in vital biological functions for billions of years.

http://bit.ly/2FYxeKi

The early bits of life

How can life originate before DNA and genes?

One possibility is that there are natural processes that lead to the organisation of simple physical objects such as small microcapsules that undergo rudimentary forms of interaction, self-organisation and information processing.

An inter-disciplinary team from the University of Bristol involving Rich Carter, Dr Karoline Wiesner and Professor Stephen Mann from the Bristol Centre for Complexity Sciences, School of Mathematics and School of Chemistry has developed computer simulations that

demonstrate how interactions between simple mathematical "objects" (automata) can lead to the self-organisation of robust, cooperative networks of interacting populations capable of mutual reproduction, competition and selective extinction.

Each community represents an information niche, which remains stable under fixed conditions but transforms into a new niche when the environmental conditions are changed.

By determining the information required to generate each niche, the team demonstrate that the population adapts and transitions only where an equal or increased level of information is generated by the system.

The team's findings may be relevant to understanding how inanimate systems such as chemically communicating protocells can initiate the transition to living matter prior to the onset of contemporary evolutionary and genetic mechanisms.

The new work brings together theoretical and experimental approaches currently being investigated in the Centre for Protolife Research in the School of Chemistry.

Professor Mann, who led the study, said: "Although the new work is far away from life as we know it, the spontaneous emergence of information niches suggests a possible pathway to initiating the first steps in the transition from inanimate to living matter prior to the onset of Darwinian evolution."

More information: Richard J. Carter et al. Emergence and dynamics of self-producing information niches as a step towards pre-evolutionary organization, Journal of The Royal Society Interface (2018). DOI: 10.1098/rsif.2017.0807

http://bit.ly/2Du9RLh

How did we evolve to live longer?

Researchers at Newcastle University show that a collection of small adaptations in proteins that respond to stress, accumulated over millennia of human history, could help to explain our increased natural defences and longer lifespan.

Publishing in *Nature Communications*, the team of collaborators from the UK, France and Finland and lead by researchers at Newcastle University, UK explain the importance of a protein called p62.

Many cells in our body, such as those which make up our brain need to last us a lifetime. To do this our cells have developed ways of protecting themselves. One way is through a process called autophagy, which literally means self-eating, where damaged components are collected together and removed from the cell.

This is very important as accumulation of damage in cells has been linked to several diseases including dementia.

Lead author, Dr Viktor Korolchuk explains: "As we age, we accumulate damage in our cells and so it is thought that activating autophagy could help us treat older people suffering from dementia. In order to be able to do this we need to understand how we can induce this cell cleaning."

The importance of protein, p62

In this study the authors were able to identify how a protein called p62 is activated to induce autophagy. They found that p62 can be activated by reactive oxygen species (ROS). ROS are by-products of our metabolism that can cause damage in the cell. This ability of p62 to sense ROS allows the cell to remove the damage and to survive this stress. In lower organisms, such as fruit flies, p62 is not able to do this.

The team identified the part of the human p62 protein which allows it to sense ROS and created genetically modified fruit flies with 'humanised' p62. These 'humanised' flies survived longer in conditions of stress. Dr Korolchuk adds: "This tells us that abilities like sensing stress and activating protective processes like autophagy may have evolved to allow better stress resistance and a longer lifespan."

Indeed, in the study, the authors found that specific mutations in human p62, which cause a neurodegenerative disease called amyotrophic lateral sclerosis (ALS), can prevent activation of p62 by ROS. These cells are then unable to induce protective autophagy, and the authors explain that this could underlie the premature death of neurons in patients with this devastating age-related disease.

In contrast, 'humanised' p62 fruit flies did not live longer suggesting that other mechanisms may be required.

The research demonstrates that a collection of small adaptations like that of human p62 could have accumulated over time and these adaptations could underlie our increased natural defences and longer lifespans.

The discovery of these adaptations allows a better understanding of how we can protect against and treat age-related diseases.

Reference: *Oxidation of SQSTM1/p62 mediates the link between redox state and protein homeostasis. Bernadette Carroll et al. doi:10.1038/s41467-017-02746-z*

http://bit.ly/2mWpfEQ

Can mice really mirror humans when it comes to cancer?

Just how close are mice to people when it comes to researching cancer

EAST LANSING, Mich. -- A new Michigan State University study is helping to answer a pressing question among scientists of just how close mice are to people when it comes to researching cancer.

The findings, now published in PLOS Genetics, reveal how mice can actually mimic human breast cancer tissue and its genes, even more so than previously thought, as well as other cancers including lung, oral and esophagus.

According to the Centers for Disease Control, cancer is the second leading cause of death among Americans next to heart disease.

"Just like human breast cancer, there are many subtypes that can be found in mice," said Eran Andrechek, co-author and physiology professor whose work focuses on the genetic makeup of cancer. "Our work outlines the genetic similarities of the tissue and cells in different types of tumors and shows the strong relationships mice can have to other human cancers too."

Different tumor subtypes can include glandular, which include the mammary glands, as well as squamous, which are very rare and involve epithelial cells that line the inside of the breast.

Andrechek's federally funded study looked at mice containing all subtypes and compared the makeup of the rodent tumors and the way the genes acted, known as gene expression, to human tumor data.

He found that not only did the genes act the same in certain breast cancers but the gene similarities were active in other cancers as well.

"Groups of genes were also being expressed similarly in the lung, oral and esophageal tumors," Andrechek said. "For example, mouse mammary tumors shared a signaling pathway that is found in human lung cancer and controls how cells reproduce and move from one location to another."

Because tumors have distinct genes, the way they act or send signals can help scientists identify and define the specific kind of cancer they're dealing with in hopes of finding the right treatment.

"Our work will help scientists understand in part what makes the various tumors so unique and such a challenge to treat," Andrechek said. "But even more importantly, for patients, our ability to identify the similarities could allow treatments for other cancers like lung to be used for certain breast cancers down the road."

The study was funded by the National Institutes of Health and Worldwide Cancer Research.

http://nyti.ms/2BiMKqx

Fed Up With Drug Companies, Hospitals Decide to Start Their Own

A group of large hospital systems plans to create a nonprofit generic drug company to battle shortages and high prices.

By REED ABELSON and KATIE THOMAS JAN. 18, 2018

For years, hospital executives have expressed frustration when essential drugs like heart medicines have become scarce, or when prices have skyrocketed because investors manipulated the market.

Now, some of the country's largest hospital systems are taking an aggressive step to combat the problem: They plan to go into the drug business themselves, in a move that appears to be the first on this scale.

"This is a shot across the bow of the bad guys," said Dr. Marc Harrison, the chief executive of Intermountain Healthcare, the nonprofit Salt Lake City hospital group that is spearheading the effort. "We are not going to lay down. We are going to go ahead and try and fix it."

While Intermountain executives would not name the drugs they intend to make, hospitals have long experienced shortages of drugs like morphine or encountered sudden price increases for old, off-patent products like the heart medicine Nitropress. Hospitals have also come under criticism for overcharging for their services, including for some drugs.

Several major hospital systems, including Ascension, a Catholic system that is the nation's largest nonprofit hospital group, plan to form a new nonprofit company, that will provide a number of generic drugs to the hospitals. The Department of Veterans Affairs is also expressing interest in participating.

Generic drugs at Intermountain Medical Center in Murray, Utah. Intermountain Healthcare is spearheading an effort by a group of hospitals to create a nonprofit generic drug company. **Kim Raff for The New York Times**

In all, about 300 hospitals are now included in the group. Other hospitals are expected to join.

Dr. Harrison said they planned to focus only on certain drugs. "There are individual places where there are problems," he said. "We are not indicting an entire industry."

Dr. Kevin A. Schulman, a professor of medicine at the Duke University School of Medicine who has studied the generic drug market and is advising the effort, said: "If they all agree to buy enough to sustain this effort, you will have a huge threat to people that are trying to manipulate the generic drug market. They will want to think twice."

The idea is to directly challenge the host of industry players who have capitalized on certain markets, buying up monopolies of old, off-patent drugs and then sharply raising prices, stoking public outrage and prompting a series of Congressional hearings and federal investigations.

The most notorious example is of Martin Shkreli, the former hedge fund manager who raised the price of a decades-old drug, Daraprim, to $750 a tablet in 2015, from $13.50.

Hospitals have also struggled to deal with shortages of hundreds of vital drugs over the past decade, ranging from injectable morphine to sodium bicarbonate (the medical form of baking soda), shortfalls that are exacerbated when only one or two manufacturers make the product.

Intermountain Medical Center, the flagship hospital of Intermountain Healthcare. The new generic drug company will sell to major health groups. **Kim Raff for The New York Times**

"We're seeing an acceleration of both shortages and escalation of prices," said Dr. Richard Gilfillan, the chief executive of Trinity Health, a large Catholic system that operates in nearly two dozen states and is part of the group. "There's not been any effective push back on either of these."

Intermountain executives would not discuss many details of the project, citing fears that competitors could shut them out of the market by quickly dropping the price of the drugs in question, then raising them again later. They said they would focus on drugs whose prices have risen sharply or that have been in short supply.

"We're going to have to hold that very close to our vest," Dr. Harrison said. The company will either rely on third-party manufacturers or decide to make the drugs themselves.

The new company will initially focus on selling to hospitals, but officials said they may eventually expand to offer the products more broadly.

Dr. Carolyn Clancy, the executive in charge of the Veterans Health Administration, said its pharmacy experts have consulted with the other systems about the project and is now working out the details of its possible involvement. "Our strong interest here is minimizing the impact of any shortages of generic drugs," she said. While she said the agency is able to negotiate good prices for veterans, "we don't

necessarily control supply" and have experienced many of the same shortages, including the recent lack of saline fluids, as the other health groups.

"We are constantly scanning the horizon and constantly attentive to interruptions of supply chains of medicines," she said.

In addition to Daraprim, several old, off-patent drugs have seen sharp price increases over the past several years. In 2015, Valeant Pharmaceuticals International became a Wall Street darling after it sold investors on its business model of buying up old drugs, then raising the prices precipitously. That year, it sharply raised the prices of two heart drugs, Nitropress and Isuprel, adding millions to hospitals' drug bills almost overnight. Valeant's practices led to a series of investigations and Congressional hearings as well as a shake-up of the company's leadership.

Representatives for the generic drug industry have noted that many of the most high-profile cases have involved old, off-patent drugs for which there has been no generic competition.

The trade group for generic manufacturers, the Association for Accessible Medicines, said its members generally welcome competition. "The whole generic industry is premised on competition, and that competition brings dramatic savings for patients," said Allen Goldberg, a spokesman for the group.

But generic drug makers have also come under scrutiny.

The hike in the price of doxycycline hyclate, an antibiotic, which increased to $3.65 a pill in 2013 from 5.6 cents in 2012, led to a congressional investigation as well as state and federal price-fixing inquiries into some of the industry's biggest players. Last fall, a coalition of state attorneys general broadened a lawsuit over price fixing, accusing 18 companies of engaging in illegal practices involving 15 drugs.

Anthony R. Tersigni, the chief executive of Ascension, said he and other hospital executives felt they had little choice but to try to solve the problem themselves. "We took the position collectively rather than waiting and hoping for the generic drug companies to address it," he said. "We have to address it head on."

Intermountain executives said that they would seek approval to manufacture the products from the Food and Drug Administration, which has vowed to give priority to companies that want to make generics in markets for which there is little competition.

The project boasts a high-profile list of advisers, ranging from Bob Kerrey, the former Democratic senator of Nebraska, to Dr. Donald Berwick, a former administrator for the Centers of Medicare and Medicaid Services, as well as two former executives with Amgen, the drug manufacturer.

Erin Fox, a drug shortage expert at the University of Utah, said the idea of creating a nonprofit drug company is promising. "I think anything that increases the number of suppliers will help," she said. She added that the trick will be in selecting the right third-party manufacturer to ensure good quality.

Correction: January 18, 2018

An earlier version of a picture caption with this article erroneously gave a name to a new generic drug company. The company does not yet have a name; it is not called Project Rx.

http://bit.ly/2DzivqT

Single blood test screens for eight cancer types

Provides unique new framework for early detection of the most common cancers

Johns Hopkins Kimmel Cancer Center researchers developed a single blood test that screens for eight common cancer types and helps identify the location of the cancer.

The test, called CancerSEEK, is a unique noninvasive, multianalyte test that simultaneously evaluates levels of eight cancer proteins and the presence of cancer gene mutations from circulating DNA in the blood.

The test is aimed at screening for eight common cancer types that account for more than 60 percent of cancer deaths in the U.S. Five of the cancers covered by the test currently have no screening test.

"The use of a combination of selected biomarkers for early detection has the potential to change the way we screen for cancer, and it is based on the same rationale for using combinations of drugs to treat cancers," says Nickolas Papadopoulos, Ph.D., senior author and professor of oncology and pathology.

The findings were published online by Science on Jan. 18, 2018.

"Circulating tumor DNA mutations can be highly specific markers for cancer. To capitalize on this inherent specificity, we sought to develop a small yet robust panel that could detect at least one mutation in the vast majority of cancers," says Joshua Cohen, an M.D.-Ph.D. student at the Johns Hopkins University School of Medicine and the paper's first author. "In fact, keeping the mutation panel small is essential to minimize false-positive results and keep such screening tests affordable."

The investigators initially explored several hundred genes and 40 protein markers, whittling the number down to segments of 16 genes and eight proteins. They point out that this molecular test is solely aimed at cancer screening and, therefore, is different from other molecular tests, which rely on analyzing large numbers of cancer-driving genes to identify therapeutically actionable targets.

In this study, the test had greater than 99 percent specificity for cancer. "Very high specificity was essential because false-positive results can subject patients to unnecessary invasive follow-up tests and procedures to confirm the presence of cancer," says Kenneth Kinzler, Ph.D., professor of oncology and co-director of the Ludwig Center. The test was used on 812 healthy controls and produced only seven false-positive results.

The test was evaluated on 1,005 patients with nonmetastatic, stages I to III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung or breast. The median overall sensitivity, or the ability to find cancer, was 70 percent and ranged from a high of 98 percent for ovarian cancer to a low of 33 percent for breast cancer. For the five cancers that have no screening tests--ovarian, liver, stomach, pancreatic and esophageal cancers--sensitivity ranged from 69 percent to 98 percent.

"A novelty of our classification method is that it combines the probability of observing various DNA mutations together with the levels of several proteins in order to make the final call," says Cristian Tomasetti, Ph.D., associate professor of oncology and biostatistics, who developed the algorithm. "Another new aspect of our approach is that it uses machine learning to enable the test to accurately determine the location of a tumor down to a small number of anatomic sites in 83 percent of patients."

Although the current test does not pick up every cancer, it identifies many cancers that would likely otherwise go undetected. "Many of the most promising cancer treatments we have today only benefit a small minority of cancer patients, and we consider them major breakthroughs. If we are going to make progress in early cancer detection, we have to begin looking at it in a more realistic way, recognizing that no test will detect all cancers," says Bert Vogelstein, M.D., co-director of the Ludwig Center, Clayton Professor of Oncology and Howard Hughes Medical Institute investigator.

To zero in on the analytes they included in their CancerSEEK test, the research team pulled data from more than three decades of cancer genetics research generated at their Ludwig Center at Johns Hopkins, where the first genetic blueprints for cancer were created, as well as data from many other institutions.

To precisely determine the optimal number of DNA bases to assess in the CancerSEEK test, the researchers used a method based on diminishing returns. "The more DNA bases you assay, the more mutations you are capable of finding, but eventually you reach a point of diminishing returns," explains Cohen. "We designed our test to reflect this point of diminishing returns, including the DNA markers that were useful to detecting the cancers and eliminating those that did not add benefit." The result was a relatively small panel of highly selective DNA markers.

"This test represents the next step in changing the focus of cancer research from late-stage disease to early disease, which I believe will be critical to reducing cancer deaths in the long term," says Vogelstein. CancerSEEK is noninvasive and can, in principle, be administered by primary care providers at the time of other routine blood work.

"This has the potential to substantially impact patients. Earlier detection provides many ways to improve outcomes for patients. Optimally, cancers would be detected early enough that they could be cured by surgery alone, but even cancers that are not curable by surgery alone will respond better to systemic therapies when there is less advanced disease," says Anne Marie Lennon, M.D., Ph.D., associate professor of medicine, surgery and radiology, clinical director of gastroenterology and director of the Multidisciplinary Pancreatic Cyst Program.

The investigators feel that a test that will be used routinely for cancer screening must have a cost in line with or less than other currently available screening tests for single cancers, such as colonoscopy. They envision that the CancerSEEK test will eventually cost less than $500. Larger studies of the test are currently under way.

In addition to Cohen, Papadopoulos, Lennon, Tomasetti, Kinzler and Vogelstein, other participants include Lu Li, Yuxuan Wang, Christopher Thorburn, Bahman Afsari, Ludmila Danilova, Christopher Douville, Ammar Javed, Fay Wong, Austin Mattox, Ralph Hruban, Christopher Wolfgang, Michael Goggins, Marco Dal Molin, Tian-Li Wang, Richard Roden, Alison Klein, Janine Ptak, Lisa Dobbyn, Joy Schaefer, Natalie Silliman, Maria Popoli, Joshua Vogelstein, James Browne, Robert Schoen, Randall Brand, Jeanne Tie, Peter Gibbs, Hui-Li Wong, Aaron Mansfield, Jin Jen, Samir Hanash, Massimo Falconi, Peter Allen, Shibin Zhou, Chetan Bettegowda and Luis Diaz.

The research was supported by the Lustgarten Foundation for Pancreatic Cancer Research, the Virginia and D.K. Ludwig Fund for Cancer Research, The Commonwealth Fund, the John Templeton Foundation, the Clinomics Program, Mayo Clinic Center for Individualized Medicine, the Mayo Clinic Biobank, the Sol Goldman Center for Pancreatic Cancer Research, The Michael Rolfe Pancreatic Cancer Research Foundation, the Benjamin Baker Scholarship, the Gray Foundation, the Early Detection Research Network, Susan Wojcicki and Dennis Troper, the Marcus Foundation, the Conrad N. Hilton Foundation, the Howard Hughes Medical Institute, and National Institutes of Health Grants P50-CA62924, P50-CA102701, CA06973, GM-07309, and U01CA152753.

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Did Researchers Just Take a Big Step Toward a Universal Flu Vaccine?

New vaccine candidate might bring researchers one step closer to universal flu protection

By Brandon Specktor, Senior Writer | January 18, 2018 01:51pm ET

With more than a dozen different strains of influenza circulating the world at any given time, flu season is a bit like a box of chocolates: you never know what you're going to get. That's one reason why you need a flu shot every year. Different flu strains are constantly adapting different ways of evading your immune system's defenses, and, so far, there is no single vaccine that can protect you from them all.

But scientists are making progress: A new vaccine candidate developed at the University of California, Los Angeles (UCLA), might bring researchers one step closer to universal flu protection. Engineered from multiple strains of the influenza virus, all of which have vulnerabilities to a specific type of protein in the immune system, the vaccine successfully protected test animals from two different strains of the flu in the lab.

Interferin' with interferons

The basis for the new vaccine candidate lies in a component of the immune system called interferons. When your immune system detects an infection, interferons are among the first responders on the scene, according to the study, published today (Jan. 18) in the journal Science. True to their name, the main function of these antiviral proteins is to interfere with the spread of viruses. They do this by signaling the danger to surrounding host cells, turning on multiple protective genes to promote a swift immune response that will, hopefully, kill the virus, and help the immune system adapt to the virus for long-lasting protection.

"If viruses do not induce interferons, they will not be killed in the first-line defense, and without interferons, the adaptive immune response is limited," said senior study author Ren Sun, a professor of molecular and

medical pharmacology at the David Geffen School of Medicine at UCLA, in a statement. "For these reasons, viruses have evolved strategies to evade detection and limit the production of interferons by host organisms."

With this in mind, Sun and his colleagues spent four years researching the entire influenza genome in order to identify any mutations that either inhibit or enhance the host's interferon response. Previous studies showed that it was possible to disable individual genetic sequences responsible for blocking interferons, but Sun and his colleagues were determined to go further, targeting multiple interferon-blocking sites to inhibit the virus as much as possible.

This research entailed sequencing every amino acid in the influenza genome, and ultimately allowed the researchers to identify eight mutations that made various influenza genes particularly sensitive to interferons. They combined these eight mutations into a new, "hyper-interferon-sensitive" (HIS) strain of influenza that would, theoretically, stimulate a strong immune response in infected hosts. This new strain could become the basis of a broader, more effective flu vaccine, the researchers wrote.

A step toward universal protection

The researchers tested the vaccine on several lab mice and ferrets (common test subjects for influenza infection, the authors noted). The vaccine proved safe: "[Test subjects showed] no increase in copy number, no pathology, and no body weight loss or death with the vaccination," lead study author Yushen Du, a recent doctoral graduate at UCLA, told Live Science in an email.

Even more exciting, Du said, the vaccine also proved effective. When the test animals were injected with the vaccine, they produced potent immune responses when they were exposed to various strains of the flu. And while the vaccine was derived from an H1N1 strain of influenza, animals that were exposed to the H3N2 strain also showed an effective immune response — suggesting that the interferon-stimulating vaccine was doing its job.

The protective effects of the new vaccine are likely due to the generation of "cross-reactive T-cells" — immune cells that can "react with multiple viral strains," John Teijaro, an assistant professor in the Department of Immunology and Microbiology at The Scripps Research Institute, and Dennis Burton, co-chair of the same department, wrote in a commentary that appeared alongside the study in the journal Science. In other words, the vaccine appears to lead to the release of powerful T-cells that can fight off multiple strains of the flu.

"In addition to increasing [vaccine] safety, the use of mutations scattered throughout the viral genome should provide a barrier to the development of viral resistance," Teijaro and Burton wrote. This is important, because if a virus becomes resistant to a vaccine, the vaccine is no longer useful.

This new method of engineering viruses with specific immune vulnerabilities could be applied to other diseases besides influenza, according to the study. But despite this new success, many challenges line the path toward a universal flu vaccine. For one, the new study tested exposure to only two strains of flu — H1N1 and H3N2 — while many other dangerous strains remain. "It would be valuable to test additional viruses, including highly virulent avian subtypes such as H5N1 and H7N9, in subsequent studies," Teijaro and Burton wrote.

According to Du, the team will continue their research by extending the study to a type of flu virus called influenza B virus, which infects only humans, ferrets, and seals. "We are also thinking about performing large-scale animal tests before going into clinic trials [in humans] of the current vaccine strain," she said.

http://bit.ly/2FZMM0o

World's oldest known oxygen oasis discovered

Layers in South Africa's Pongola Basin bear witness to oxygen production by bacteria as early as 2.97 billion years ago

In the Earth's early history, several billion years ago, only traces of oxygen existed in the atmosphere and the oceans. Today's air-breathing organisms could not have existed under those conditions. The change

was caused by photosynthesizing bacteria, which created oxygen as a by-product – in vast amounts. 2.5-billion-year-old rock layers on several continents have yielded indications that the first big increase in the proportion of oxygen in the atmosphere took place then.

Now, working with international colleagues, Dr. Benjamin Eickmann and Professor Ronny Schönberg, isotope geochemists from the University of Tübingen have discovered layers in South Africa's Pongola Basin which bear witness to oxygen production by bacteria as early as 2.97 billion years ago. That makes the Basin the earliest known home to oxygen-producing organisms – known as an oxygen oasis. The study has been published in the latest *Nature Geoscience*.

Conditions on Earth some three billion years ago were inhospitible to say the least. The atmosphere contained only one-one hundred thousandth of the oxygen it has today. The primeval oceans contained hardly any sulfate; but they did contain large amounts of ferrous iron. When bacteria started producing oxygen, it could initially bond with other elements, but began to enrich the atmosphere in a massive oxygen emission event around 2.5 billion years ago.

"We can see that in the disappearance of reduced minerals in the sediments on the continents. Certain sulfur signatures which can only be formed in a low-oxygen atmosphere are no longer to be found," says Benjamin Eickmann, the study's lead author. This event, which could be described as global environmental pollution, went down in the Earth's history as the Great Oxygenation Event. It was a disaster for the early bacteria types which had evolved under low-oxygen conditions; the oxygen poisoned them. "However, after the first big rise, the atmosphere only contained 0.2 percent oxygen; today it's around 21 percent," Eickmann explains. Exposed to an atmosphere which contained increasing amounts of oxygen, the continents were subject to enhanced erosion. That led to more trace elements entering the oceans. The improved supply of nutrients in turn led to more life forms in the seas.

Sulfur signatures as an archive of Earth history

In their current study the researchers investigated the 2.97-bilion-year-old sediments deposited in the Pongola Basin in what is now South Africa. From the proportions of sulfur isotopes (particularly the of $^{34}S/^{32}S$ ratio), in the sediments, the researchers are able to conclude that the bacteria used the sulfate in the primeval seas as a source of energy, reducing it chemically.

"Sulfate is a form of oxidized sulfur. A higher concentration of sulfate in the water indicates that sufficient free oxygen must have been present in the shallow sea of the Pongola Basin," Ronny Schönberg says. This free oxygen must have been produced by other, photosynthesizing bacteria. At the same time, another sulfur isotope signature (the $^{33}S/^{32}S$ ratio) in these sediments indicates a continued reduced, very low-oxygen atmosphere.

"That makes the Pongola Basin the oldest oxygen oasis known to date. The oxygen was building up in the water long before the Great Oxygenation Event, Schönberg explains. Several hundred million years later, the steadily rising levels of oxygen led to the oxidation of the atmosphere, and that is what made life on Earth – in all its variety as we know it today – even possible.

More information: *Benjamin Eickmann et al. Isotopic evidence for oxygenated Mesoarchaean shallow oceans, Nature Geoscience (2018). DOI: 10.1038/s41561-017-0036-x*

http://bit.ly/2Ds2a8e

Tumour behaviour calls Cambrian-oxygen link into question

Swedish study suggests multicellular life might have needed low, not high, oxygen levels in order to thrive.

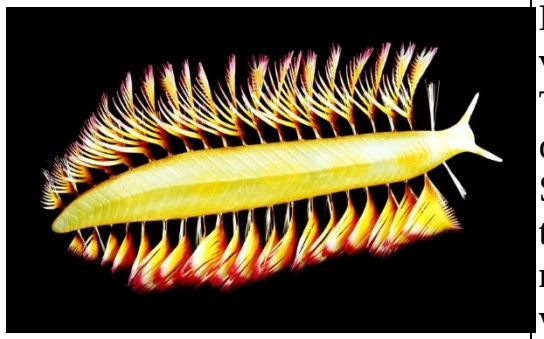
Stephen Fleischfresser reports.

Exploration of the relationship between oxygen, stem cells and cancer might just challenge the story of how life as we know it came to be, according to new research published in *Nature Ecology & Evolution*.

About 543 million years ago, the most spectacular evolutionary event in the Earth's history began: the Cambrian explosion. During this period, multicellular animal life began first to appear and diversify in

staggering ways, producing such oddities as the aptly named *Hallucigenia* and the spiky Wixwaxia.

The fossil record bears out this abrupt explosion of biodiversity, most clearly seen in the Burgess Shale in British Columbia, Canada. This vast fossil bed, holding within it the first appearance of modern animal phyla, seemingly without precursors, led the great Stephen Jay Gould to postulate his theory of 'punctuated equilibrium' – the idea that evolution is not always gradual, as Darwin imagined, but can sometimes undergo sharp leaps and bounds.



Did Cambrian lifeforms, such as this polychaete worm from the Burgess Shale, arise because of low, not high, oxygen levels? **Studio - Chase/Getty Images**

However, the cause of the Cambrian explosion has been much debated. Previous hypotheses have centred around the idea that an increase in available oxygen may have triggered biological diversification. One 2013 paper published in the *Proceedings of the National Academy of Sciences* found that high oxygen environments promote greater ecological complexity, and argued on this basis that environmental oxygenation then satisfactorily explains the explosion of life in the Cambrian.

However, Emma Hammarlund, a geobiologist working at the division for translational cancer research at Sweden's' Lund University and guest researcher at the Nordic Centre for Earth Evolution at the University of Southern Denmark, is not convinced by this account. She notes that recent research has questioned the correlation between the Cambrian explosion and increasing atmospheric oxygen.

"A heated hunt for the geochemical evidence that oxygen increased when animals diversified goes on," she says, "but, after decades of discussion, it seems worthwhile to consider the development of multicellularity also from other angles."

Instead, Hammarlund thinks a biological innovation might be key. Hammarlund enlisted the expertise of Kristoffer von Stedingk and Sven Påhlman, both medical tumour biologists from Lund University.

"I wanted to learn what tumour scientists observe on a daily basis, in terms of tissue growth and how it relates to oxygen," explains Hammarlund. "Tumours are after all, and unfortunately, successful versions of multicellularity."

Together they investigated the relationship between oxygen and stem cell biology.

Stem cells, the pluripotent cells that can become any type of biological tissue, require specific oxygen levels, as do the cancer stem cells responsible for tumour growth. In particular, too much oxygen can wreak havoc with successful stem cell function.

Stem cells, and cells that maintain similar properties, such as the tissues responsible for healing, as well as those responsible for tumours, generally require hypoxic, or low oxygen, environments. Certain vertebrate tissues even simulate hypoxia to allow them to work normally.

The team therefore hypothesises that the evolution of the biological innovation of stem cell properties might well have played a role in the diversification of life in the Cambrian. Such innovation not only could easily have happened in low oxygen environments, but might even have required them.

"Therefore, we flip the perspective on the oxic setting," says Sven Påhlman, "While low oxygen is generally unproblematic for animal cells, the oxic settings pose a fundamental challenge for complex multicellularity.

"Surely, many people would intuitively disagree. But once you flip the perspective on the oxic niche and start to consider it as challenging for stem cell properties and tissue renewal, then puzzling observations from distant fields starts to fit together. And you can't turn back."

http://nyti.ms/2rmabpq

Yes, Lots of People Are Getting Flu Symptoms. No, This Season Isn't So Unusual. Here's Why.

How bad is this flu season?

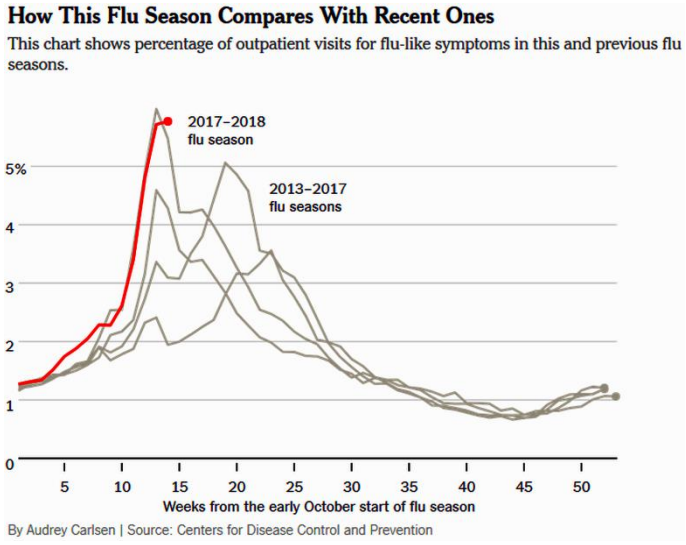
By DONALD G. McNEIL Jr. JAN. 18, 2018

At the moment, the 2017-2018 flu season is considered "moderately severe." Large numbers of Americans have fallen ill, and every state except Hawaii has reported widespread flu activity. But some regions have been hit harder than others. More important, the number of people hospitalized or dying from flu nationwide is not unusually high. This season is closely paralleling the 2014-2015 season, which was dominated by the same H3N2 flu strain and was also "moderately severe."

Is this year's flu strain unusually dangerous?

H3N2 is the most dangerous of the four seasonal flu strains, but it is not new nor uniquely lethal. A typical season mixes two Type A strains - H1N1 and H3N2, and two Type B strains - Victoria and Yamagata. (The B strains normally arrive later and are rarer.)

As of Jan. 7, about 78 percent of all samples genetically sequenced have been H3N2, according to the Centers for Disease Control and Prevention. That strain first emerged in Hong Kong in 1968 and killed an estimated 1 million people around the world that year. But it has circulated ever since, constantly undergoing small mutations. Many people have had it, and an H3N2 strain is a component of every season's flu shot, so partial immunity is widespread.



How many people are ill, and how do we know?

Almost 6 percent of all Americans seeking medical care now have flu symptoms. That is tracked by the C.D.C.'s Outpatient Influenza-like Illness Surveillance Network, to which about 2,000 doctors' offices and clinics around the country report weekly how many of their patients have fevers of at least 100 degrees plus a cough or sore throat. The 2014-15 and 2012-13 flu seasons also peaked at close to 6 percent. By contrast, the mildest recent season, 2011-2012, barely surpassed 2 percent. In 2009, during the H1N1 "swine flu" pandemic, almost 8 percent of visits were flu-related, but they peaked in October, not in January. That never happens in seasonal flu but is typical of pandemic flus.

Are hospitals overwhelmed?

In some places, including Southern California and central Texas, some hospitals have seen so many flu patients that they had to set up triage tents or turn other patients away. But overall there have not been reports of regional shortages of antiviral medications, patients dying because a city ran out of respirators, or other signs of a major crisis.

Where is the flu spreading?

This year's outbreak began in Louisiana and Mississippi, then spread across Texas to California and up the West Coast from San Diego to Seattle. It also stretched into the Midwest. Kinsahealth, which makes internet-connected thermometers and builds its database from 25,000 daily fever readings, says the current hot spot is the St. Louis area. The Northeast has been largely spared so far, as have Minnesota, the Dakotas and some Rocky Mountain states.

Are large numbers of people dying?

No, although it may appear so right now. The deaths of a few apparently healthy people — notably those of a 21-year-old fitness buff in Latrobe, Pa., a mother of three in San Jose, Calif., and a 10-year-old hockey player in New Canaan, Conn. — have been widely publicized, and

some areas, like San Diego, have reported record numbers of deaths. But it is still too early to say how high mortality will be nationally. It can take weeks to confirm all flu-related deaths. As of now, the mortality rate for victims under age 18, a bellwether C.D.C. category, is well below that seen in the 2014-15 season.

How many usually die?

Even in a mild year, flu kills about 12,000 Americans, the C.D.C. estimates. In a bad year, it kills up to 56,000. Most of those deaths are among the elderly, but flu also kills middle-aged adults with underlying problems like heart or lung disease, diabetes, immune suppression or obesity. It is also dangerous for pregnant women, children under age 5 and children with asthma. And, every season, flu and its complications, including pneumonia, meningitis and sepsis, kill some apparently healthy people.

Does this year's flu shot work?

Its H3N2 component is a bad match for the circulating strain. Australia just had a severe flu season with many deaths, and the vaccine there had the same mismatch. Experts estimated that the vaccine prevented infection only 10 percent of the time. The shot's efficacy here has not yet been calculated because the virus is still spreading, but experts expect it to be about 30 percent. In Australia, vaccination failed partially because it is urged for only the most vulnerable, while in the United States millions of healthy people are vaccinated.

Is it worth getting the flu shot anyway?

Experts say yes, because even when the shot does not prevent you from catching the flu, it may save you from dying of it. And while getting it in October is best, because it takes about two weeks to build immunity, it is still not too late, because the virus persists all winter and into spring.

Are antiviral flu medicines working?

Yes. Of all the samples tested so far by the C.D.C., only 1 percent were resistant to oseltamivir, zanamivir, and peramivir, the ingredients in Tamiflu, Relenza and Rapivab. But to be effective, these medicines should be taken as early as possible after symptoms appear. (Rapivab is given intravenously, usually in hospitals.)

http://bit.ly/2EYMyVY

Breakthrough study shows how plants sense the world

This understanding could help commercial crops resist pathogens and drought.

BIRMINGHAM, Ala. - Plants lack eyes and ears, but they can still see, hear, smell and respond to environmental cues and dangers -- especially to virulent pathogens. They do this with the aid of hundreds of membrane proteins that can sense microbes or other stresses.

Only a small portion of these sensing proteins have been studied through classical genetics, and knowledge on how these sensors function by forming complexes with one another is scarce. Now, an international team of researchers from four nations -- including Shahid Mukhtar, Ph.D., and graduate student Timothy "TC" Howton at the University of Alabama at Birmingham -- has created the first network map for 200 of these proteins. The map shows how a few key proteins act as master nodes critical for network integrity, and the map also reveals unknown interactions.

"This is a pioneering work to identify the first layer of interactions among these proteins," said Mukhtar, an assistant professor of biology in the UAB College of Arts and Sciences. "An understanding of these interactions could lead to ways to increase a plant's resistance to pathogens, or to other stresses like heat, drought, salinity or cold shock. This can also provide a roadmap for future studies by scientists around the world."

The international team, based in Europe, Canada and the United States, was led by Youssef Belkhadir, Ph.D., Gregor Mendel Institute of Molecular Plant Biology, Vienna, Austria. The study has been published in the journal Nature.

The novel comprehensive interaction network map focused on one of the most important classes of these sensing proteins -- the leucine-rich

repeat receptor kinases, or LRR-receptor kinases, which are structurally similar to human toll-like receptors.

The LRR-receptor kinases are a family of proteins in both plants and animals that are largely responsible for sensing the environment. In plants, they have an extracellular domain of the protein, extending beyond the cell membrane, which can recognize chemical signals, such as growth hormones or portions of proteins from pathogens. The receptor kinases then initiate responses to these signals inside the cell, using an intracellular domain of the protein.

The model plant Arabidopsis thaliana contains more than 600 different receptor kinases -- 50 times more than humans -- that are critical for plant growth, development, immunity and stress response. Until now, only a handful had known functions, and little was known about how the receptors might interact with each to coordinate responses to often-conflicting signals.

For the Nature study, the Belkhadir lab tested interactions between extracellular domains of the receptors in a pairwise manner, working with more than 400 extracellular domains of the LRR-receptor kinases and performing 40,000 interaction tests.

Positive interactions were used to produce an interaction map displaying how those receptor kinases interact with one another, in a total of 567 high-confidence interactions.

Laboratories of David Guttman, Ph.D., and Darrell Desveaux, Ph.D., at the University of Toronto, Canada, analyzed the receptor interaction map using algorithms to generate diverse hypotheses, and those predictions were validated in the labs of Belkhadir and Cyril Zipfel, Ph.D., The Sainsbury Laboratory, Norwich, United Kingdom.

At UAB, Mukhtar and Howton tested 372 intracellular domains of the LRR-receptor kinases whose extracellular domains had shown high-confidence interactions, to see if the intracellular domains also showed strong interactions. More than half did, suggesting that the formation of these receptor complexes is required for signal perception and downstream signal transduction. This also indicates a validation of the biological significance of the extracellular domain interactions.

The Mukhtar lab at UAB has cloned nearly all of the intracellular domains of the LRR-receptor kinases of Arabidopsis. "This is part of an effort to understand how plants react to pathogens or how pathogens hijack the immune system, an area of our interest," Mukhtar said.

The Nature study included two major surprises, says Adam Mott, Ph.D., University of Toronto. LRR-receptor kinases that have small extracellular domains interacted with other LRR-receptor kinases more often than those that have large domains. This suggests that the small receptor kinases evolved to coordinate actions of the other receptors. Second, researchers identified several unknown LRR-receptor kinases that appear critical for network integrity.

The most important one, dubbed APEX, was predicted to cause severe disruptions to the rest of the network if removed. Researchers found that removal of APEX, and several other known LRR-receptor kinases, indeed did impair plant development and immune responses, even though those responses are controlled by receptor kinases several network steps away from the APEX node.

This new understanding of how receptor kinases interact may help researchers identify important receptor kinases that can modify stress responses in commercial crops to make them resistant to environmental stresses like global warming and pathogens.

"The network developed in this study allows future researchers to comprehend the previously unknown connectivity of these receptors," Howton said. "This knowledge can be used to better understand how plants are sensing their environment within the complete context of the plant cell surface receptors."

Support for the Nature paper, "An extracellular network of Arabidopsis leucine-rich repeat receptor kinases," came from grants from the Austrian Academy of Sciences, the Natural Sciences and Engineering Research Council of Canada Discovery Grants, a Canada Research Chair, and the Centre for the Analysis of Genome Evolution and Function. Funding also came from the Gatsby Charitable Foundation, the European Research Council, the Hertha Firnberg Programme, the Deutsche Forschungsgemeinschaft, the National Science Foundation IOS-

1557796, the Austrian Federal Ministry of Science, Research & Economy, and the City of Vienna.

http://bit.ly/2n2xFeP

Scientists discover how treating eczema could also alleviate asthma

Scientists from VIB-UGent have discovered insights for a possible new therapy for eczema that also reduces the severity of asthma.

The findings are an important next step in understanding the relationship between the two inflammatory diseases and to developing effective therapies. The results of the study are published in the Journal of Investigative Dermatology.

Children with atopic dermatitis (AD), a type of eczema of the skin, show an increased risk of developing asthma later in life. This phenomenon, also known as atopic march, raises questions on whether therapies can be developed that not only tackle AD, but also prevent the onset of other allergic diseases. Intrigued by this possibility, a team of VIB scientists took to the lab.

Marching from the skin to the lungs

House dust mites are known culprits in the development of both AD and asthma, as exposure to the mites induces inflammation. Dr. Julie Deckers, Prof. Karolien De Bosscher and Prof. Hamida Hammad (all VIB-UGent Center for Inflammation Research) created a mouse model to look further into the relationship between the two diseases.

Dr. Julie Deckers (VIB-UGent): "As predicted, our test showed that house dust mite-induced skin inflammation leads to aggravated levels of allergic airway inflammation. Yet, to our surprise, this response significantly differs from the reaction to direct exposure of house dust mites in the lungs without prior skin inflammation. These results have given us a deeper understanding of the complexity of the atopic march."

One therapy to rule them all

The real challenge, however, was to investigate whether the relief of skin inflammation might influence the subsequent development of asthma. The team therefore combined two anti-inflammatory compounds - corticosteroids and PPAR? agonists - into one potential treatment in mice.

Dr. Julie Deckers (VIB-UGent Center for Inflammation Research): "The combined therapy effectively alleviated AD, but was insufficient at preventing allergic asthmatic response in the lungs. However, the treatment did significantly reduce the severity of the asthma by counteracting one aspect of the specific immune response in the lungs. In this way, the therapy represents a potent remedy against allergic skin inflammation and the aggravation of atopic march."

The team is now looking for industrial partners to develop clinical trials for the therapy, making the leap from mouse to man. At the same time, they plan to further investigate the exact mechanisms driving the progression from AD to asthma in order to develop alternative therapies that can halt the atopic march.

Funding *Fund for Scientific Research (FWO)*

Publication *Co-activation of GR and PPARγ in murine skin prevents worsening of atopic march, Deckers et al., Journal of Investigative Dermatology, 2017*

http://bit.ly/2DqsmvM

Creation of synthetic horsepox virus could lead to more effective smallpox vaccine

Synthetic technology breakthrough points to safer vaccines and targeted cancer treatments

UAlberta researchers created a new synthetic virus that could lead to the development of a more effective vaccine against smallpox. The discovery demonstrates how techniques based on the use of synthetic DNA can be used to advance public health measures.

Virologist David Evans and his research associate Ryan Noyce produced an infectious horsepox virus, which they synthetically reconstructed using a published genome sequence and DNA fragments manufactured entirely by chemical methods. The team went on to show that the synthetic horsepox virus could provide vaccine protection in a mouse model of poxvirus infection.

"This application of synthetic DNA technology has the potential to revolutionize how we manufacture complex biologicals including

recombinant viruses," said Evans, a professor of microbiology and member of the Li Ka-Shing Institute of Virology. "These methods advance the capacity to produce next-generation vaccines and offer special promise as a tool for constructing the complicated synthetic viruses that will likely be needed to treat cancer," said David Evans.

The horsepox virus U of A researchers synthesized is the largest virus assembled to date using chemically synthesized DNA. Horsepox -an equine disease caused by horsepox virus -is not a hazard to humans. It is closely related to vaccinia virus, the virus that was used as a vaccine to eradicate human smallpox 40 years ago. While there have been no cases of naturally occurring smallpox since 1977, it remains a concern to public health agencies.

Tonix Pharmaceuticals Holding Corp. is developing the synthetic version of horsepox as a potential vaccine to prevent smallpox (variola virus) infection in humans. Seth Lederman, President and Chief Executive Office of Tonix, is co-investigator on the research and co-inventor on the designated TNX-801 patent. "Tonix's goal is to develop a vaccine that has a better safety profile than the current vaccines for broader usage and to provide greater protection to the public," said Lederman.

Current smallpox vaccines are used to protect first responders and military service members but are rarely used except in special circumstances. Because of the toxicity of most modern smallpox vaccines, Canada and the United States have long discontinued immunizing whole populations, as was the policy prior to smallpox eradication.

Evans hopes the research will contribute to informed discussions relating to the potential applications of synthetic biology for the benefit of society. His U of A research team had previously used more traditional recombinant DNA technologies to engineer a vaccinia virus with the aim of improving the treatment for bladder cancer.

The virus is an oncolytic virus, which means it was modified to selectively kill rapidly-dividing cancer cells while remaining safe for surrounding healthy cells. In pre-clinical models these viruses can infect and kill cancer cells, while promoting the development of an immune response that is needed to prevents the cancer from returning. However, future generations of oncolytic viruses will require a greater degree of modification than is possible using older technologies. Synthetic biology offers a powerful tool for manufacturing these more complicated biological therapeutics.

"We are invested as a research laboratory in taking that same technology and applying it to other poxviruses," said Evans.

The work of assembling TNX-801 was funded by a research contract from Tonix Pharmaceuticals, but was made possible by a long history of grant funding from the Canadian Institutes of Health Research (CIHR) and the Natural Sciences and Engineering Research Council (NSERC). The study was published in PLOS ONE.

http://bit.ly/2F1wItG

What's that smell? Hunter-gatherer societies have the answer

Research in Malaysia overturns the notion that neurology is responsible for widespread difficulties in describing odours.

Andrew Masterson reports.

Although the argument shows little sign of dying down, recent research confirms that the Inuit people do indeed have 50 words for snow. Far less controversially, the Japanese language contains 50 words for rain. Presumably both these cultures maintain such generous vocabularies for describing inclement weather because they need it.

The same imperative, it seems, is in operation in certain hunter-gatherer societies, the members of which have a large number of words to describe smells -- a lexicon that is so lacking in industrial societies that some researchers have claimed it is a neurological impossibility.

In a paper published in the journal *Current Biology*, Asifa Majid, Radboud University in the Netherlands, and Nicole Kruspe, of Lund University in Sweden, report on the way two peoples resident on the Malay Peninsula – the hunter-gatherer Semaq Beri and the horticultural

Semelai – apply language to smell. Both communities live in similar environments and speak closely related languages. The researchers set out to see if they also shared similar ways of naming odours.

To test this, they used 20 Semaq Beri and 21 Semelai volunteers. Each was shown 80 standardised colour chips, and presented with 16 standardised smells, including fish, turpentine, clove, rose, garlic and orange. The horticultural Semelai proved adept at naming colours, but quite poor at assigning names to odours. The hunter-gatherer Semaq Beri did well at both tasks.

The results did not wholly surprise Majid, because they reinforced findings from a study she had conducted with another scientist, Niclas Burenhult, published in 2015. In this, she had worked with another Malay Peninsula hunter-gather society, the Jahai, and found that their language contained at least a dozen instances of "abstract descriptive odour categories that are basic, everyday terms".

The odour descriptions, she and Burenhult reported, appeared to be inherited from ancestral languages, suggesting that communicating about smell was a deep-seated and long-standing cultural practice.

"Contrary to the prevailing assumption in the cognitive sciences," the paper concluded, "these languages and cultures demonstrate that odour is far from vestigial in humans."

The notion that odour is poorly served by language is a common one, and seemingly supported by evidence. "There has been a long-standing consensus that 'smell is the mute sense, the one without words,' and decades of research with English-speaking participants seemed to confirm this," says Majid.

Examples are not difficult to find. A 1999 study in the journal *Neuroscience and Biobehavioral Reviews*, for instance, suggested that words to describe smells are in short supply because "odour information processing shares some of the cortical resources used in processing language and that interference between these two types of stimuli occurs when they are simultaneously processed".

Another, in Trends in *Cognitive Sciences*, in 2015, observed that "most people find it profoundly difficult to name familiar smells", an outcome that implies "deficient sensory-specific interactions with the language system".

The new work by Majid and Kruspe, however, moves the argument away from the neurological and back towards the cultural. Differences in the ability to describe odours arise not from neural networks, but necessity. "Hunter-gatherers' olfaction is superior, while settled peoples' olfactory cognition is diminished," Majid says.

http://bbc.in/2DVDIJk

'Adolescence now lasts from 10 to 24'

Adolescence now lasts from the ages of 10 to 24, although it used to be thought to end at 19, scientists say.

By Katie Silver Health reporter, BBC News

Young people continuing their education for longer, as well as delayed marriage and parenthood, has pushed back popular perceptions of when adulthood begins. Changing the definition is vital to ensure laws stay appropriate, they write in an opinion piece in the Lancet Child & Adolescent Health journal. But another expert warns doing so risks "further infantilising young people".

When puberty begins

Puberty is considered to start when the part of the brain known as the hypothalamus starts releasing a hormone that activates the body's pituitary and gonadal glands. This used to happen around the age of 14 but has dropped with improved health and nutrition in much of the developed world to around the age of 10. As a consequence, in industrialised countries such as the UK the average age for a girl's first menstruation has dropped by four years in the past 150 years.

Half of all females now have their period by 12 or 13 years of age.

When the body stops developing

There are also biological arguments for why the definition of adolescence should be extended, including that the body continues to develop. For example, the brain continues to mature beyond the age of

20, working faster and more efficiently. And many people's wisdom teeth don't come through until the age of 25.

Delaying life's milestones

Young people are also getting married and having children later.

According to the Office of National Statistics, the average age for a man to enter their first marriage in 2013 was 32.5 years and 30.6 years for women across England and Wales. This represented an increase of almost eight years since 1973.

Lead author Prof Susan Sawyer, director of the centre for adolescent health at the Royal Children's Hospital in Melbourne, writes: "Although many adult legal privileges start at age 18 years, the adoption of adult roles and responsibilities generally occurs later." She says delayed partnering, parenting and economic independence means the "semi-dependency" that characterises adolescence has expanded.

Social policy

This social change, she says, needs to inform policy, such as by extending youth support services until the age of 25. "Age definitions are always arbitrary", she writes, but "our current definition of adolescence is overly restricted". "The ages of 10-24 years are a better fit with the development of adolescents nowadays."

Prof Russell Viner, president-elect of the Royal College of Paediatrics & Child Health, said: "In the UK, the average age for leaving home is now around 25 years for both men and women." He supports extending the definition to cover adolescence up until the age of 24 and says a number of UK services already take this into account.

He said: "Statutory provision in England in terms of social care for care leavers and children with special educational needs now goes up to 24 years," as does provision of services for people with cystic fibrosis.

'Infantilising young people'

But Dr Jan Macvarish, a parenting sociologist at the University of Kent, says there is a danger in extending our concept of adolescence.

"Older children and young people are shaped far more significantly by society's expectations of them than by their intrinsic biological growth," she said. "There is nothing inevitably infantilising about spending your early 20s in higher education or experimenting in the world of work."

And we should not risk "pathologising their desire for independence".

"Society should maintain the highest possible expectations of the next generation," Dr Macvarish said.

Prof Viner disagrees with Dr Macvarish's criticism and says broadening adolescence can be seen as "empowering young people by recognising their differences". "As long as we do this from a position of recognising young people's strengths and the potential of their development, rather than being focused on the problems of the adolescent period."

http://bit.ly/2mX6u5e

Stand Back, Way Back: Flu Virus Can Be Spread Just by Breathing

Simply standing back when someone coughs or sneezes won't necessarily protect you from the flu — you also need to keep your distance when a sick person merely breathes.

By Rachael Rettner, Senior Writer | January 19, 2018 05:48pm ET

That's because the virus can be spread just by breathing, a new study confirms.

In the study, the scientists found large quantities of infectious flu virus in the exhaled breath of people with the disease, highlighting the importance of "airborne" transmission in flu spread.

"The study findings suggest that keeping surfaces clean, washing our hands all the time and avoiding people who are coughing does not provide complete protection from getting the flu," study co-author Sheryl Ehrman, dean of the College of Engineering at San José State University, said in a statement. But staying home when you're sick "could make a difference in the spread of the influenza virus," Ehrman said.

Previously, many researchers thought that flu viruses spread mainly through "large particle" droplets that are produced when people cough or sneeze. Researchers also knew that flu viruses could travel through the air through smaller particles called aerosols, released when someone

breathes. But exactly how much flu virus people "shed" by breathing, and whether these exhaled flu viruses were infectious, was unclear, the researchers said.

To examine this, the researchers enrolled 142 people who were confirmed to be sick with the flu in their study, and had the participants sit in a machine that could capture the flu viruses in their breath. The machine, called the "Gesundheit II human source bioaerosol sampler," consists of a large, cone-shaped device where participants place their head. Participants were asked to breathe, talk, cough and sneeze naturally during a 30-minute session in the machine.

The researchers found that coughing was not necessary for the sick participants to generate infectious aerosols. Of the 23 aerosol samples that were obtained without coughing, nearly half (48 percent) contained detectable levels of flu virus, and eight samples (about 35 percent) contained infectious virus.

"We found that [people with the] flu … contaminated the air around them with infectious virus just by breathing, without coughing or sneezing," lead study author Dr. Donald Milton, a professor of environmental health at the University of Maryland School of Public Health, said in the statement.

People were more likely to generate these infectious aerosols during the first few days of their illness, Milton said. "So when someone is coming down with influenza, they should go home and not remain in the workplace and infect others," he said.

The study also found that participants didn't sneeze very often, and even when they did, their sneezes didn't generate a greater number of infectious particles than coughing did. This suggests that "sneezing does not appear to make an important contribution to influenza virus shedding in aerosols," although it could play a role in spreading the virus through the contamination of surfaces, the researchers said.

The findings could be used to improve mathematical models of the risk of airborne flu transmission, the researchers said.

The study was published online Jan. 18 in the journal Proceedings of the National Academy of Sciences.

http://nyti.ms/2n17HaO

One Day Your Mind May Fade. At Least You'll Have a Plan.

When Ann Vandervelde visited her primary care doctor in August, he had something new to show her.

Paula Span THE NEW OLD AGE JAN. 19, 2018

Dr. Barak Gaster, an internist at the University of Washington School of Medicine, had spent three years working with specialists in geriatrics, neurology, palliative care and psychiatry to come up with a five-page document that he calls a dementia-specific advance directive.

Ann Vandervelde, at her home in Seattle, opted to fill out an advance directive for dementia, spelling out to doctors how she would want to be treated at various stages of the disease. **Evan McGlinn for The New York Times**

In simple language, it maps out the effects of mild, moderate and severe dementia, and asks patients to specify which medical interventions they would want — and not want — at each phase of the illness.

"Patients stumble into the advanced stage of dementia before anyone identifies it and talks to them about what's happening," Dr. Gaster told me. "At what point, if ever, would they not want medical interventions to keep them alive longer? A lot of people have strong opinions about this, but it's hard to figure out how to let them express them as the disease progresses."

One of those with strong opinions, it happens, was Ms. Vandervelde, 71, an abstract painter in Seattle. Her father had died of dementia years before, in a nursing home after her mother could no longer care for him at home. Ms. Vandervelde had also spent time with dementia patients as a hospice volunteer.

Further, caring for her mother in her final year, Ms. Vandervelde had seen how family conflicts could flare over medical decisions. “I was not going to leave that choice to my children if I could spare them that,” she said.

So when Dr. Gaster explained his directive, “it just made so much sense,” Ms. Vandervelde said. “While I could make these decisions, why not make them? I filled it out right there.”

Like a growing number of Americans over age 60, she already had a standard advance directive, designating a decision-maker (her husband) to direct her medical care if she became incapacitated.

Not all experts are convinced another directive is needed. But as Dr. Gaster and his co-authors recently argued in the journal JAMA, the usual forms don’t provide much help with dementia.

“The standard advance directives tend to focus on things like a ‘permanent coma’ or a ‘persistent vegetative state,’” Dr. Gaster said. “Most of the time, they apply to a person with less than six months to live.”

Although it’s a terminal disease, dementia often intensifies slowly, over many years. The point at which dementia patients can no longer direct their own care isn’t predictable or obvious.

Moreover, patients’ goals and preferences might well change over time. In the early stage, life may remain enjoyable and rewarding despite memory problems or difficulties with daily tasks.

“They have potentially many years in which they wouldn’t want a directive that says ‘do not resuscitate,’” Dr. Gaster said. But if severe dementia leaves them bedridden, unresponsive and dependent, they might feel differently — yet no longer be able to say so.

Whereas a persistent vegetative state occurs rarely, Dr. Gaster tells his patients, dementia strikes far more commonly.

How commonly? That’s not a simple question to answer.

Researchers often cite the long-term Framingham study, which in 1997 estimated the lifetime risk at age 65 as 10.9 percent for men and 12 percent for women.

But the participants in that study were overwhelmingly white. Among the populations facing higher dementia rates are African-Americans, Dr. Murali Doraiswamy, a neuroscientist at Duke University, pointed out.

Last year, the journal Demography published a more representative model, estimating that for the cohort born in 1940, the lifetime risk at age 70 was 30.8 percent for men and 37.4 percent for women.

Ms. Vandervelde is an abstract painter who saw firsthand how family conflicts could flare over medical decisions when her parents died. She wanted to spare her children that grief. **Evan McGlinn for The New York Times**

Dr. Gaster tells patients that “somewhere between 20 and 30 percent of us will at some point develop dementia.” Over the past year, as patients turn 65 and qualify for Medicare — which covers a visit to discuss advance care planning — he has offered them his dementia-specific directive, intended to supplement their other directives.

For each stage of dementia, the patient can choose among four options. “Full efforts to prolong my life” and “comfort-oriented care only, focused on relieving suffering” represent two ends of the spectrum.

Patients can also opt for lifesaving treatments — except when their hearts stop or they can’t breathe on their own, precluding resuscitation or ventilators.

Or they can opt to receive care where they live but avoid hospitalization. “For someone who doesn’t understand what’s happening, going to an E.R. or being hospitalized can be really traumatic,” Dr. Gaster said. The experience can lead to delirium and other setbacks.

So far, 50 to 60 patients have filled out the form. A few have declined his offer to discuss dementia; others “nod and thank me and take it home and never mail it back.”

But most appreciate the overture, Dr. Gaster said, especially if family members have experienced dementia. “It’s something they think and worry about, and they welcome the idea because they do have clear wishes.” In that case, he adds the completed form to their medical records.

We could debate whether a separate dementia form, on top of the general advance directive everyone should have, makes sense. Already, nurses and doctors lament that paperwork often winds up forgotten in a drawer, a safe deposit box or a lawyer’s office, unavailable in a crisis.

If patients haven’t updated the directive in years, their designated proxies may have moved or died. Proxies may never have learned their loved ones’ preferences in the first place. Will adding another directive clarify this process?

Other leaders in the campaign to persuade Americans to document their end-of-life wishes had questions, too.

Ellen Goodman, founder of The Conversation Project (whose dementia-related kit similarly presents choices at different stages), pointed out that the new form represents a patient-doctor agreement.

“We need to have families involved,” she said. “No checklist on earth is going to cover everything you encounter. Most important is the conversation with the decision-maker. That person has to understand what you value and what’s important to you.”

Dr. Rebecca Sudore, a geriatrician and palliative care specialist at the University of California, San Francisco, agreed. Her effort — Prepare for Your Care, an online guide — encourages users to incorporate their reasons for various decisions. “At the bedside, the ‘why’ is very important,” she said.

Both The Conversation Project and Prepare for Your Care provide links to the advance directive/durable power-of-attorney forms legal in each state.

What’s not in dispute: It’s crucial to talk to family, friends and doctors about the quality of life we find acceptable and unacceptable, which interventions we agree to or don’t — and then to document those decisions and circulate the document to designated decision-makers and everyone else who might be involved.

And yes, we should incorporate decisions about dementia into that process, whether in a separate form or not.

When Ann Vandervelde completed her dementia-specific directive, “I felt great relief,” she said. It gave her a sense of control, “and that’s really important to me, to be in the driver’s seat all the way to the end.”

http://bit.ly/2DWuP24

Health expert hopes unique spin on karuta is as infectious as the game

Want to learn more about infectious diseases in an avant-garde way? A Japanese expert on the subject has come up with a solution through a self-made version of karuta, the traditional card game.

Keen to teach the broader public about infectious diseases, Harue Okada, a specially appointed professor on public health with Hakuoh University in Tochigi Prefecture, took three years to complete the game.

A unique version of karuta, a traditional Japanese card game, has been devised to promote public awareness of infectious diseases. **KYODO**

“I created the entire karuta game to become a kind of dictionary about infectious diseases,” she said.

The karuta game contains playing cards bearing illustrations and text about 46 types of diseases ranging from common childhood diseases such as mumps and “pool fever” (pharyngoconjunctival fever) to more deadly bugs including the Ebola and Zika viruses.

The game of karuta, which uses cards with poems on them, is traditionally played during New Year’s celebrations. Each karuta game contains yomifuda (a reading card), and a torifuda (a picture card). When the Japanese text on a yomifuda is read out, players grab the

torifuda that has the corresponding image and kana (syllabic script), or the first syllable of the text, in one corner.

For Okada's game, the infectious diseases are written on every torifuda. One yomifuda, using text designed to make it rhythmical, refers to how Ebola is endemic to Africa, while another calls on preventing Rubella, the virus more commonly known as German measles, with vaccines.

There are different levels of play designed to cater to people from elementary school students to adults. The back of each torifuda contains information on the cause of a disease, its route of infection and ways to prevent it. By reading the text after grabbing the card, both the player and participants learn about each disease.

Okada has written many books including picture books about infectious diseases. But those that can be addressed in a single book are few. This inspired her to think of a more effective way to broaden the public's knowledge of diseases. Karuta, she thought, was a fun way of doing that.

http://bit.ly/2DWl4RA

Want a healthier population? Spend less on health care and more on social services

Redistributing money to social services from health care is actually a small change in health care spending

Increased social spending was associated with health improvements at the population level, while health spending increases did not have the same effect, according to a large new Canadian study in CMAJ (Canadian Medical Association Journal).

"Spending more on health care sounds like it should improve health, but our study suggests that is not the case and social spending could be used to improve the health of everyone," says Dr. Daniel Dutton, The School of Public Policy, University of Calgary, Calgary, Alberta. "Relative to health care, we spend little on social services per person, so redistributing money to social services from health care is actually a small change in health care spending."

Health care costs are expanding in many developed countries like Canada, and governments are seeking ways to contain costs while maintaining a healthy population. Treating the social determinants of health like income, education, or social and physical living environments through spending on social services can help address the root causes of disease and poor health. However, health spending continues to make up the lion's share of spending.

The study looked at data from 9 of Canada's 10 provinces over 31 years from 1981 to 2011 (Prince Edward Island and the northern territories were not included because of insufficient data) to see if social and health care spending ratios were linked to population health status. The researchers looked at three health outcomes: potentially avoidable mortality, infant mortality, and life expectancy.

Average per capita spending on social services was $930 compared with $2900 -- almost three times the amount -- for health services. Health spending per capita increased 10-fold over the study period compared with social spending. However, increased social spending per dollar spent on health care was associated with improved health outcomes at the population level by province.

"Social spending as a share of health spending is associated with improvements in potentially avoidable mortality and life expectancy," says Dr. Dutton. "If governments spent one cent more on social services per dollar spent on health by rearranging money between the two portfolios, life expectancy could have experienced an additional 5% increase and potentially avoidable mortality could have experienced an additional 3% decrease in one year."

This has implications for the way governments allocate spending.

"If social spending addresses the social determinants of health, then it is a form of preventive health spending and changes the risk distribution for the entire population rather than treating those with disease. Redirecting resources from health to social services, that is, rearranging payment without additional spending, is an efficient way to improve

health outcomes," he says. In a related commentary, http://www.cmaj.ca/lookup/doi/10.1503/cmaj.171530,

Dr. Paul Kershaw, School of Population and Public Health, University of British Columbia, Vancouver, BC, writes that the researchers found that increased health spending "is associated with lost opportunities to improve life expectancy and prevent avoidable mortality by comparison with a more even distribution between medical and social investments. These results add to evidence that should impel governments to seek better balance between medical and social expenditures."

Governments have increased health spending as the aging population has expanded. The commentary author suggests governments should allocate social spending fairly for both young and old to ensure that the younger generation is not being shortchanged.

"Effect of provincial spending on social services and health care on health outcomes in Canada: an observational longitudinal study" is published January 22, 2018.

http://bit.ly/2DprHuC

Rare prehistoric shell mound in Aichi, Japan, suggests possible mid-Jomon shell trade

Most likely served as a clam processing site approximately 4,500 years ago

An ancient heap of shells at Sakatsuji Shell Midden in the city of Toyohashi, Aichi Prefecture, most likely served as a clam processing site in the latter half of the mid-Jomon Period, approximately 4,500 years ago, an investigation conducted by the city's board of education has revealed.

While there are ruins in eastern Japan that indicate organized production during the mid-Jomon Period — including the Nakazato shell midden, or mound, which is a national historic site in Tokyo's Kita Ward — it is extremely rare to find one in the Chubu region or further west. This latest discovery will provide important clues about the culinary lifestyle and economic activities conducted in the Jomon Period.

The Sakatsuji shell mound is one of the Muro cluster of seven shell middens in Aichi Prefecture. An excavation conducted in the 1970s showed a rough scale of activities there, but details had remained unknown. The mound is located approximately 3.5 km inland of what is now Mikawa Bay. But prior to the bay being filled in to create rice fields in the Edo Period the shell mound had faced the sea, along a stretch of coastland where the shores are shallow.

As a land consolidation project is scheduled to start in the area that includes the mound, the board of education had been excavating approximately 1,000 square meters of land since May.

The mound, made almost entirely of clamshells, measures roughly 1.6 meters high, about 6 meters wide and more than 24 meters long.

At least four layers have been identified, sandwiched between soil streaked with charcoal. The team also discovered around 55 objects that looked like furnaces assembled from stones, and the members expect to find more as they continue excavating.

"We believe that the clams were boiled in the furnaces, and their meat stripped from the shells. Afterward the shells were piled up, then the ground was leveled and made into a processing site again," said a member of the excavation team. "That kind of process must have been repeated again and again."

The excavation team was not able to find any evidence of residences nearby, so it was likely the workers who dug and processed the clams lived in another area.

The volume of shells discovered was so huge it is hard to believe that they were consumed within the region, and the excavation team has said there is a possibility people dried the clams after they were boiled so that they would last longer and could be used for trading.

The shells are of various sizes. "We found many large shells similar to those seen in high-class Japanese restaurants. The clams must have become quite salty when boiled in sea water, so maybe they were used to make soup stock," a member of the excavation team said. Several hundred furnaces have been found in the other six shell mounds in Muro.

They share the same features as the Sakatsuji midden, which indicates the whole area was bustling with clam processing at the time.

However, the other six shell middens were from the late Jomon Period — approximately 2,300 to 3,800 years ago — which means the clam processing site of Sakatsuji was much older. Most of the furnaces found in the other shell middens were also without stone structures, and were constructed in such a way that earthenware was placed directly on the floor. “Perhaps they changed to a simpler furnace in order to meet the growing demand for clams,” said one of the team members.

The excavation will continue until the end of March and an on-site briefing is expected to be held in mid-February.

According to Tomonari Osada, a part-time lecturer specializing in archaeology at Chubu University, the Tokai region during the mid-Jomon Period is believed to have been less socially developed compared to the period immediately before the beginning of the Yayoi Period.

“I would be surprised if the production conducted at the Sakatsuji shell midden was for the sake of trading and distribution to other regions. We need to focus on this site and conduct further analysis to determine whether the objects made of stones were indeed furnaces for boiling (clams).”