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Columbia engineers build biologically powered chip

System combines biological ion channels with solid-state transistors to create a new kind of electronics

New York, NY - Columbia Engineering researchers have, for the first time, harnessed the molecular machinery of living systems to power an integrated circuit from adenosine triphosphate (ATP), the energy currency of life.

They achieved this by integrating a conventional solid-state complementary metal-oxide-semiconductor (CMOS) integrated circuit with an artificial lipid bilayer membrane containing ATP-powered ion pumps, opening the door to creating entirely new artificial systems that contain both biological and solid-state components.

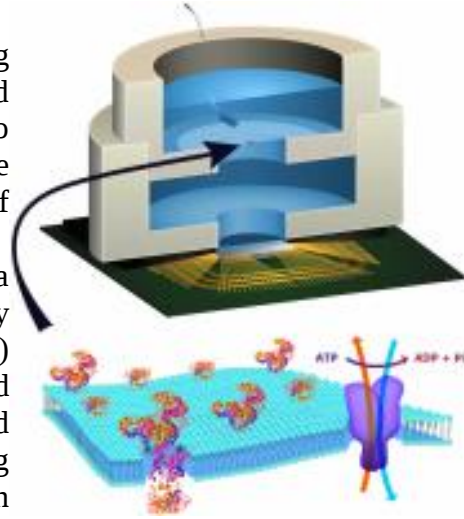


Image depicting biocell attached to CMOS integrated circuit with membrane containing sodium-potassium pumps in pore.

Trevor Finney and Jared Roseman/Columbia Engineering

The study, led by Ken Shepard, Lau Family Professor of Electrical Engineering and professor of biomedical engineering at Columbia Engineering, is published online Dec. 7 in Nature Communications.

"In combining a biological electronic device with CMOS, we will be able to create new systems not possible with either technology alone," says Shepard.

"We are excited at the prospect of expanding the palette of active devices that will have new functions, such as harvesting energy from ATP, as was done here, or recognizing specific molecules, giving chips the potential to taste and smell.

This was quite a unique new direction for us and it has great potential to give solid-state systems new capabilities with biological components."

Shepard, whose lab is a leader in the development of engineered solid-state systems interfaced to biological systems, notes that despite its overwhelming success, CMOS solid-state electronics is incapable of replicating certain functions natural to living systems, such as the senses of taste and smell and the use of biochemical energy sources.

Living systems achieve this functionality with their own version of electronics based on lipid membranes and ion channels and pumps, which act as a kind of

'biological transistor.' They use charge in the form of ions to carry energy and information -- ion channels control the flow of ions across cell membranes.

Solid-state systems, such as those in computers and communication devices, use electrons; their electronic signaling and power are controlled by field-effect transistors.

In living systems, energy is stored in potentials across lipid membranes, in this case created through the action of ion pumps.

ATP is used to transport energy from where it is generated to where it is consumed in the cell.

To build a prototype of their hybrid system, Shepard's team, led by PhD student Jared Roseman, packaged a CMOS integrated circuit (IC) with an ATP-harvesting 'biocell.' In the presence of ATP, the system pumped ions across the membrane, producing an electrical potential harvested by the IC.

"We made a macroscale version of this system, at the scale of several millimeters, to see if it worked," Shepard notes.

"Our results provide new insight into a generalized circuit model, enabling us to determine the conditions to maximize the efficiency of harnessing chemical energy through the action of these ion pumps.

We will now be looking at how to scale the system down."

While other groups have harvested energy from living systems, Shepard and his team are exploring how to do this at the molecular level, isolating just the desired function and interfacing this with electronics.

"We don't need the whole cell," he explains.

"We just grab the component of the cell that's doing what we want.

For this project, we isolated the ATPases because they were the proteins that allowed us to extract energy from ATP."

The ability to build a system that combines the power of solid-state electronics with the capabilities of biological components has great promise.

"You need a bomb-sniffing dog now, but if you can take just the part of the dog that is useful -- the molecules that are doing the sensing -- we wouldn't need the whole animal," says Shepard.

"With appropriate scaling, this technology could provide a power source for implanted systems in ATP-rich environments such as inside living cells," added Roseman.

The work is funded by the Keck Foundation and the Office of Naval Research.

PAPER -- The DOI for this paper will be 10.1038/NCOMMS10070. Once the paper is published, it will be available to view online at <http://www.nature.com/naturecommunications>.

<http://www.nature.com/ncomms/index>. <http://www.bioee.ee.columbia.edu/~shepard/>

<http://www.engineering.columbia.edu/>

<http://bit.ly/1NFULiN>

Twin civilisations? How life on an exoplanet could spread to its neighbour

Could this ever happen between close planetary neighbours?

David Rothery Professor of Planetary Geosciences, The Open University

Imagine two nearby exoplanets orbiting the same sun, each with its own indigenous civilisation.

They're going through history either as companionable neighbours or deadly rivals.

This is a familiar situation in science fiction, but could it ever happen?

With the rapidly growing number of habitable exoplanets being discovered, this scenario may seem plausible.

Now a new scientific study, to be published in the *Astrophysical Journal*, explores this issue by examining some of the conditions affecting life in a solar system with two habitable planets.

The researchers were inspired by NASA's discovery of Kepler 36b and Kepler 36c, the two known planets of the star Kepler 36.

The orbital distances of these planets from their star differ by only 10%, making them extremely close neighbours.

The inner planet completes seven orbits in the time that it takes the outer planet to complete six orbits (a situation described as 7:6 mean motion resonance).

This means that once in every six or seven of your years (depending on which planet you live on), your neighbouring planet passes close by.

Wild wobbles?

The researchers first of all wondered if these periodic close passages would affect the tilt of either planet's axis.

This is important in the context of life because large fluctuations in axial tilt would lead to drastic variations in climate.

While not fatal for microbial life, it could reduce the chances of complex life emerging and make it very hard for any intelligent life that did evolve to establish a long-lasting civilisation.

In the case of Kepler 36b or Kepler 36c, it is highly unlikely that life could exist, because they are too close to their star and have surface temperatures approaching 1000°C.

The researchers therefore analysed a hypothetical pair of Earth-like planets in 3:2 resonance, both within their star's habitable zone where liquid water would be stable on their surfaces.

Reassuringly for the prospects of complex life, they found that neither planet's axial tilt was driven to vary wildly as a result of their closeness.

Hitching a ride in a rock

Assuming that life existed on one of them, they then wanted to find out whether it could spread to the other.

It is well established that rock-dwelling microbes can survive the shock of an impact that would throw them off a planet, followed by periods of years in space, and then passage down to the ground on another world. Indeed in an experiment on the Long Duration Exposure Facility, retrieved by the Space Shuttle in 1990 after six years in space, 30% of bacteria embedded in salt crystals survived.

The theoretical concept of life spreading from world to world is called "panspermia", and because this variant involves travel encased within rock it is referred to as "lithopanspermia".

The study found that lithopanspermia should be remarkably easy between planets sharing 7:6, 6:5, 4:3 or 3:2 orbital resonance.

They would frequently pass so close to each other that impact debris flung off one would stand a good chance of raining down on the other after a relatively brief journey through space.

This, they speculate, would mean that if life emerged on either one of a habitable pair of planets then it would easily spread to the other.

But what kind of organisms would survive? Although tiny invertebrates called tardigrades have been successfully revived after exposure to the vacuum of space, they would be unlikely to survive impact shock or long durations in space, and so it seems that single-celled microbes are the most likely to make successful natural interplanetary travellers.

I'm prepared to accept all this.

Indeed, [the animation below](#) that I led three years ago argued that if we ever find life on Mars then it will be vital to establish whether it arose independently of life on Earth, or whether life spread from one to another inside meteorites..

However, the leap from microbial ancestors to indigenous intelligence on twin worlds would be enormous. Life on Earth took two billion years to go from microbes to multi-cellular organisms, and a further billion years for intelligence and space-faring capability to emerge.

Given these enormous time scales, it would be an amazing coincidence if intelligence and technology were to emerge on both worlds in the same million-year period, despite common ancestry and/or an ongoing exchange of microbes.

So the dream, or nightmare, of indigenous civilisations on sister worlds is unlikely to occur.

Beings from the first world that are able to develop space travel are likely to go to the other and find an atmosphere and climate that they could tolerate, and maybe food that they could eat – but they won't find anyone to have a conversation with.

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Drug shows potential as safe and effective for most prevalent form of adult leukemia

Phase I/II clinical trial data shows up to 95 percent response rate in relapsed chronic lymphocytic leukemia

COLUMBUS, Ohio - Clinical results published in the OnLine First edition of New England Journal of Medicine show that the new drug acalabrutinib (ACP-196) promotes high response rates that are durable in patients with chronic lymphocytic leukemia (CLL) while producing minimal side effects.

ACP-196 is a second-generation Bruton's tyrosine kinase (BTK) inhibitor.

The drug works by permanently binding BTK, which is part of a chain of proteins that relays growth signals from the surface of CLL cells to genes in the cell nucleus enabling cancer cells to survive and grow. By blocking BTK, the drug halts the flow of these growth signals and the CLL cells die.

Unlike the first generation BTK inhibitor (ibrutinib, marketed as IMBRUVICA), preclinical and phase I/II data reported in this new NEJM suggests that acalabrutinib more selectively blocks the BTK pathway without disrupting other key molecular pathways important for preserving platelet and immune function, thereby avoiding/minimizing certain side effects associated with cancer treatment.

The pre-clinical and clinical efforts of this project reported with ACP-196 were led by John C. Byrd, MD, The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James) hematology division director and D. Warren Brown Chair of Leukemia Research and Amy J. Johnson, PhD, associate professor and OSUCCC - James leukemia researcher.

The work of developing ACP-196 was done in close collaboration with investigators at Acerta Pharma, the University of California-Irvine and Cornell Medical Center.

This NEJM study integrates both pre-clinical results supporting the selectivity of ACP-196 and a phase I/II clinical trial where 61 relapsed CLL patients (median age 62) were enrolled and treated at six sites across the United States and United Kingdom.

Other sites have since joined this study based upon the success of the treatment.

The goal of this first-in-human clinical trial was to determine the recommended dose, safety, efficacy, pharmacokinetics and pharmacodynamics of ACP-196 in relapsed CLL.

Researchers report an overall patient response rate (complete and partial) of 95 percent at a median follow-up of 14.3 months.

Of the 61 patients who participated in this first-in-human testing of the agent, 87 percent were able to complete the trial treatment.

No patients experienced Richter's transformation, a rare condition where CLL morphs into an aggressive form of lymphoma, and only one patient's cancer progressed.

"This data is very exciting because it illustrates that acalabrutinib is a highly potent and selective oral BTK inhibitor that can be given safely in patients with relapsed CLL.

What is particularly remarkable is how well patients are tolerating this therapy," says Byrd, corresponding author of the study and principal investigator of the phase I/II acalabrutinib trials.

Patients enrolled to the phase I portion of the study received escalating dosages of ACP-196, with a maximum dosage of 400 mg once daily.

Patients involved in the phase II portion of the study were treated with a 100 mg dose of ACP-196 twice daily.

Patient response rates were evaluated through regular clinical assessments, imaging tests and blood work.

"It is nice to see such selectivity of a drug which we demonstrated in our pre-clinical models translate to the clinic for the benefit of patients and predicted improved tolerability" says Bonnie Harrington, DVM, Ohio State University postdoctoral student and co-first author of the study.

In November 2013, the U.S. Food and Drug Administration (FDA) granted accelerated approval of the drug ibrutinib, the first BTK inhibitor drug -- for the treatment of mantle cell lymphoma.

In February 2014, the FDA expanded the approval to chronic lymphocytic leukemia (CLL), primarily based on clinical and preclinical work conducted at the OSUCCC - James.

"BTK inhibitors are transforming CLL from an incurable to a chronic disease, especially considering that standard CLL therapies typically produce a 35-40 percent response rate in this disease setting," adds Byrd.

Clinical trials continue to evaluate ACP-196 in CLL, including a phase 3 head-to-head comparison of ibrutinib and ACP-196 led by Jeffrey Jones, MD, of The OSUCCC - James.

This research was funded with support from the Four Winds Foundation, D. Warren Brown Foundation, The Sullivan Chronic Lymphocytic Leukemia Research Fund, Mr. and Mrs. Michael Thomas, Al and Midge Lipkin, National Cancer Institute (P01 CA095426, T32 CA09338, K23 CA178183, R35 CA197734, R01 CA169162, R01HD081281 and R01 CA177292), and Leukemia and Lymphoma Society. Byrd has no financial interest in Acerta Pharma, manufacturer of ACP-196, or Janssen, manufacturer of the drug Imbruvica.

http://www.eurekalert.org/pub_releases/2015-12/su-gfe120215.php

Global fossil-fuel emissions could decline in 2015, Stanford-led study finds

Annual global carbon dioxide emissions from fossil fuels could drop slightly in 2015, according to a report from the Global Carbon Project led by a Stanford University researcher.

This surprising result contrasts with the rapid growth in emissions before 2014, underlining the need for action to stabilize and permanently lower global CO₂ emissions, the researchers conclude.

"In 2014, global CO₂ emissions from burning fossil fuels grew by just 0.6 percent," said lead author Rob Jackson, a professor of Earth system science at Stanford. "This year we expect total emissions to flatten or drop slightly, despite strong growth in gross domestic product worldwide." While CO₂ emissions have slowed during times of economic recession, this would be the first decline during a period of strong global economic growth, Jackson said.

The new report, titled "Reaching Peak Emissions," was published on Dec. 7 in the journal *Nature Climate Change*, with detailed data published simultaneously in *Earth System Science Data*.

"Decreased coal use in China was largely responsible for the decline in global CO₂ emissions," said report co-author Corinne Le Quéré of the University of East Anglia in the United Kingdom. "After a decade of rapid growth, China's emissions rate slowed to 1.2 percent in 2014 and is expected to drop by 3.9 percent in 2015."

The researchers identified China as the world's top CO₂ emitter in 2014, responsible for 27 percent of global emissions, followed by the United States (15.5 percent), the European Union (9.5 percent) and India (7.2 percent).

"Whether a slower growth in emissions will be sustained depends on the use of coal in China and elsewhere, and where new sources of energy will come from," said co-author Pep Canadell of Australia's Commonwealth Scientific and Industrial Research Organization (CSIRO). "In 2014, more than half of new energy needs in China were met from non-fossil fuel sources, such as hydro, nuclear, wind and solar power."

This trend was also accompanied by slower global growth in petroleum use and faster growth in renewables, with wind and solar capacities achieving record increases in 2014. "The most promising finding in our report is the coupling of lower carbon emissions with a strong economic growth of more than 3 percent," said Jackson, a senior fellow at the Stanford Woods Institute for the Environment and at the Precourt Institute for Energy. "But even if we reach peak global

emissions within a decade or two, we'll still be emitting massive amounts of CO₂ from burning fossil fuels." Achieving climate stabilization will require reducing emissions to near zero, he added. "Reaching zero emissions will require long-term commitments from countries attending the climate meeting in Paris this week and beyond," Jackson said.

Other co-authors of the report are Robbie Andrew, Jan Ivar Korsbakken and Glen Peters, Center for International Climate and Environmental Research (Norway); and Nebojsa Nakicenovic, International Institute for Applied Systems Analysis (Austria). The Global Carbon Project, part of the International Council for Science and Future Earth, addresses climate change by providing regular analyses of the global carbon cycle.

http://www.eurekalert.org/pub_releases/2015-12/aes-pc120115.php

Pharmaceutical CBD (cannabidiol) shows promise for children with severe epilepsy

Significant seizure reduction in studies using CBD in combination with AEDs

PHILADELPHIA - Around the globe there is high interest in the use of cannabidiol (CBD), a type of cannabinoid, for the treatment of people with epilepsy, especially children who have treatment-resistant forms of the disorder such as Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS). Three studies presented at the American Epilepsy Society's 69th Annual Meeting in Philadelphia highlight emerging efficacy and safety data of Epidiolex, a pharmaceutical liquid formulation of cannabidiol, which is currently undergoing U.S. Food and Drug Administration (FDA) authorized Phase 3 pivotal clinical trials in the United States and across the globe by GW Pharmaceuticals. A fourth study highlights possible interactions of CBD with existing anti-epileptic drugs (AEDs) in animal models of seizures.

The largest CBD study presented efficacy and safety data on GW Pharmaceutical's investigational medicine, Epidiolex (cannabidiol) from open-label Expanded Access programs at 16 sites. The study (abstract 3.034) involves 261 people, predominantly children, who have severe epilepsy that had not responded adequately to other treatments. The average age of the participants was 11. Over the course of 12 weeks, the study participants were given Epidiolex in gradually increasing doses. In all cases, Epidiolex was added to current AED treatment regimes. On average, patients were taking approximately three other AEDs. Participants and their families/caregivers recorded the number of seizures prior to taking CBD and during the 12 weeks of treatment. Clinicians also tested hematologic, liver and kidney function as well as AED levels before treatment and then at four, eight and 12 weeks during the study.

After three months of treatment, the frequency of all seizures was reduced by a median of 45 percent in all participants. Almost half (47%) of the participants in the study experienced a 50 percent or greater reduction in seizures and nine percent of patients were seizure-free. Among specific patient populations, DS patients had a 62 percent reduction in seizures and 13 percent were seizure-free. Patients with LGS experienced a 71 percent reduction in atonic seizures.

Adverse events occurred in more than 10 percent of participants with the most common being somnolence, diarrhea and fatigue and led to discontinuation in 4 percent of patients. Thirty-four percent of participants reported serious adverse events of which 5 percent were considered treatment related including altered liver enzymes (n=4), status epilepticus (n=4), diarrhea (n=4) and others. Twelve percent withdrew from the study for lack of efficacy.

"We are pleased to report these promising data on significant numbers of children," said lead author Orrin Devinsky, M.D., of New York University Langone Medical Center's Comprehensive Epilepsy Center. "These data reinforce and support the safety and efficacy we have shared in previous studies. Most importantly it is providing hope to the children and their families who have been living with debilitating seizures."

However, Devinsky cautions that "these results are from an uncontrolled study. Further study is needed before results can be confirmed. Randomized controlled studies are now underway to help us better understand the effectiveness of the drug. We very much look forward to the results from these studies during 2016," he said.

A related study (abstract 2.296) authored by Michael Oldham, M.D., MPH, formerly at the University of California San Francisco (UCSF) and currently at the University of Louisville, explored the long-term efficacy of Epidiolex. This study followed a subset of the first population (n=25) at UCSF Benioff Children's Hospital San Francisco, with an average age of 9, for one year. The patients took CBD in addition to their regular AED regimen. After 12 months, treatment with CBD resulted in a 50 percent reduction in seizures for 10 participants (40%). One participant with DS remained seizure-free. Twelve of the participants discontinued CBD because the treatment did not work for them. One participant suffered a marked increase in seizure frequency due to CBD.

"The CBD as an add-on therapy reduced seizures by half for a third of the patients in the first 12 weeks of the study," Oldham said. "This substantial improvement was maintained by 40 percent of participants for the entire 12-month period showing strong promise that CBD can be effective in controlling seizures."

A third preclinical study (abstract 3.397) explored the anticonvulsant and tolerability profile of CBD in animal models. Using the Anticonvulsant Screening

Program (ASP), the researchers used four well-established acute seizure models and found that CBD exerted significant anticonvulsant effects and was well-tolerated in rodents. This study, provided as a free service by the National Institute of Neurological Disorders and Stroke ASP, was conducted at the University of Utah.

A fourth study, led by Misty D. Smith, Ph.D. at the University of Utah (abstract 1.215), explores how CBD interacts with five different AEDs in animal models of seizure. The study helps determine the effects of CBD in combination with common AEDs, including carbamazepine, valproate, levetiracetam, clobazam and lacosamide. The interactions between these drugs could be additive, meaning the drugs work well together; synergistic, meaning the drugs enhance each other's effects; or antagonistic, which occurs when the combination of drugs seems to reduce overall effectiveness.

Smith used isobolographic analysis of three fixed dose ratio combinations of CBD with each AED in order to rapidly assess the effectiveness of each combination against limbic seizure activity. The study found a significant synergistic interaction of CBD with levetiracetam and significant antagonistic interactions with some of the fixed dose-ratio combinations of CBD with clobazam and CBD with carbamazepine.

"By identifying the synergistic, additive or antagonistic interactions between CBD and other ASDs, we are gaining a better understanding of the nature of these interactions. This will help optimize therapeutic safety and efficacy for CBD going forward," said Smith.

http://www.eurekalert.org/pub_releases/2015-12/w-mtm120715.php

Migraine triggers may all act through a common pathway
Migraines can be triggered by a variety of factors, including stress, sleep disruption, noise, odors, and diet.

The findings of a new Headache review indicate that many of these factors converge on a common pathway involving oxidative stress.

When Dr. Jonathan Borkum at the University of Maine examined studies on migraine triggers published between 1990 and 2014, he found that nearly all traditional triggers had a propensity to generate oxidative stress, an imbalance between the production of free radicals and the ability of the body to counteract their harmful effects. The findings suggest that antioxidants might help prevent or preempt migraines.

"These data hint that an acute migraine attack may be an attempt by the brain to protect itself, and possibly--when you look at certain chemicals released during an attack--to heal itself," said Dr. Borkum. "Understanding migraines may ultimately teach us how we, too, can protect the brain."

<http://www.bbc.com/news/blogs-news-from-elsewhere-35027464>

Japan: Ham-giving tradition hit by WHO cancer report

Some Japanese consumers seem to be avoiding ham as gifts this year

By News from Elsewhere... ...as found by BBC Monitoring

Sales of one of Japan's more popular seasonal gifts have reportedly been hit in the wake of a World Health Organisation (WHO) report on cancer.

Hams are among items traditionally sent during the oseibo gift-giving season in December, but the WHO's report linking processed meats with bowel cancer mean that sales are lower than in previous years, The Japan Times newspaper says. According to one department store in Osaka, sales of ham - which usually spike in December - have fallen as shoppers opt for alternatives. "Customers might switch to other products, such as beer," an unnamed store official tells the paper.

Producers have sought to reassure customers that "moderate" consumption of ham and sausages carries a much lower cancer risk, but opinion seems to be split among shoppers who spoke to The Japan Times. While some say they've refrained from sending processed meats this year, one elderly consumer ordered a box of hams, saying: "I don't think the risks are huge."

Oseibo is one of two traditional gift-giving seasons in Japan, where people send presents to thank others for kindness they have shown during the year. Gifts are mainly consumables or premium foods, and ham, beer, desserts and cooking oil are popular choices. However, the festival appears to have merged with the Western idea of giving Christmas presents, and as Japanese cultural expert Rochelle Kopp writes, oseibo is now more likely to be observed by the older generation.

http://www.eurekalert.org/pub_releases/2015-12/mgh-awn120315.php

Antidepressant with novel action appears safe and effective in phase 1b clinical trial

A small clinical trial of a novel antidepressant that stimulates neurogenesis - the production of new brain cells - shows that the compound appears to be safe and may be effective against depression.

Results of the phase 1B trial, led by Massachusetts General Hospital (MGH) investigators, show that treatment with the drug currently identified as NSI-189 improved both depressive and cognitive symptoms in study participants and that its effects appear to persist for several months after treatment discontinuation. The study was supported by the pharmaceutical company Neuralstem.

"All currently approved antidepressant drugs modulate changes in the levels of monoamine neurotransmitters," says Maurizio Fava, MD, executive director of the Clinical Trials Network & Institute (CTNI) in the MGH Department of

Psychiatry, lead author of the study published online in the journal *Molecular Psychiatry*. "Our study finds that this novel compound promotes neurogenesis in a specific part of the brain, is well tolerated and may have robust antidepressant effects. If its efficacy is confirmed in larger trials, this drug could be an important new option for patients not helped by currently available medications."

The study authors note that only one third of patients with major depressive disorder can be adequately treated with today's antidepressant drugs. For some, the drugs do not provide sufficient symptom relief; for others, unpleasant side effects - including gastrointestinal symptoms, weight increase, sleep disorders and sexual dysfunction - can lead them to discontinue treatment. While the primary mechanism of current antidepressants is alteration of neurotransmitters like serotonin, these drugs also induce neurogenesis in the brain structure called the hippocampus, suggesting that increasing neurogenesis could be an alternate strategy for treating depression.

Animal studies of NSI-189 conducted by Neuralstem, which is developing the drug for clinical use, showed that it stimulated hippocampal neurogenesis and improved behavioral symptoms in a mouse model of depression. A phase 1a trial in healthy volunteers was conducted in 2011, and the current phase 1b trial - designed primarily to address safety and identify the maximum safe dose - was designed and guided by investigators from the MGH CTNI. The trial enrolled 24 adult patients diagnosed with major depressive disorder, who were randomized into three treatment groups. In each group of 8 participants, 6 received the active drug and 2 received a placebo; those assigned to the active drug in the double-blinded study received 40 mg doses either once, twice or three times daily. After 28 days of treatment, which was conducted in an inpatient clinical trials unit, patients were followed for another 56 days.

Reports of adverse effects - none of them serious - were similar in both the control group and in participants receiving the active drug, even those who took the maximum daily dose. EEG readings taken prior to and at several times during treatment showed some changes, primarily an increase in high-frequency alpha waves, and MRI scans suggested the possibility of increased hippocampal volume in those taking the active drug. On four measures of depressive or cognitive symptoms, participants receiving the active drugs showed improvement after the 28-day treatment period, with significant differences from the placebo group on two measures based on participants' self-reports. Symptom improvement was maintained throughout the follow-up period, which the authors indicate is particularly notable since the effects of current antidepressants typically only last as long as they are taken. The MGH team has also helped to design and is

involved in implementing the larger phase 2 trial of NSI-189 that has recently been initiated

Along with Fava, who is the Slater Family Professor of Psychiatry at Harvard Medical School, co-authors of the Molecular Psychiatry paper are Bettina Hoeppner, PhD, Martina Flynn, David Mischoulon, MD, PhD, Gustavo Kinrys, MD, and Marlene Freeman, MD, MGH Psychiatry; Bradford Dickerson, MD, and Nikolaos Makris, MD, MGH Neurology; Karl Johe, PhD, Neuralstem; Larry Ereshefsky, PharmD, FCCP, BCPP, and Brett English, PharmD, PhD, PAREXEL International; Lev Gertsik, MD, California Clinical Trials Medical Group; J.A. Bilello and L.M. Thurmond, Ridge Diagnostics; and Jack Johnstone, Q-Metrx, Inc.

http://www.eurekalert.org/pub_releases/2015-12/ki-lbp120415.php

Link between PCOS in the mother and autism in the child

Children born to mothers with polycystic ovarian syndrome are at an increased risk of developing autism spectrum disorders

Children born to mothers with polycystic ovarian syndrome, PCOS, are at an increased risk of developing autism spectrum disorders, according to a new epidemiological study from Sweden's Karolinska Institutet. The findings, which are published in the journal *Molecular Psychiatry*, support the notion that exposure to sex hormones early in life may be important for the development of autism in both sexes.

The new study is the first report that demonstrates a link between maternal polycystic ovarian syndrome, PCOS, and autism spectrum disorders, ASD, in children. ASD represent a range of neurodevelopmental disorders characterised by impairments in language and social interaction, as well as stereotypic, repetitive behaviours. The underlying causes are not entirely clear, but there are several lines of evidence that indicate that exposure to certain sex hormones early in life may play a role in the development of ASD. These sex hormones, known as androgens, are responsible for development of male-typical characteristics.

Androgens also affect the development of the brain and central nervous system. Since women with PCOS have increased levels of androgens even during pregnancy, the investigators hypothesised that the disorder might affect the risk of ASD in the children. 5-15 per cent of women of child-bearing age are affected by PCOS, making it one of the most common endocrine disorders.

The researchers used the extensive nationwide Swedish health and population register databases and studied all children aged 4-17 who were born in Sweden from 1984 to 2007. The researchers used an anonymised dataset where all personal identifiers had been removed. They identified around 24 000 ASD cases and compared them to 200 000 controls.

"We found that a maternal diagnosis of PCOS increased the risk of ASD in the offspring by 59 per cent", says Kyriaki Kosidou, lead researcher on the study, at

the Department of Public Health Sciences. "The risk was further increased among mothers with both PCOS and obesity, a condition common to PCOS that is related to more severely increased androgens."

ASD are about four times more common in boys than girls, but there were no observed differences in risk between boys and girls in the study. The mechanisms that explain the association between maternal PCOS and ASD in the children were not explored in this epidemiological study. In addition to increased exposure to maternal androgens, other possibilities are that shared genetic influences between the two conditions, or other metabolic problems common to PCOS, might partly explain the relationship. Further studies are necessary to explore and replicate the finding.

"It is too early to make specific recommendations to clinicians in terms of care for pregnant women with PCOS, though increased awareness of this relationship might facilitate earlier detection of ASD in children whose mothers have been diagnosed with PCOS", says Renee Gardner, senior investigator on the study, also at the Department of Public Health Sciences.

Several of the investigators are also affiliated to the Stockholm County Council (SLL) Centre for Epidemiology and Community Medicine. This work was financially supported by Autism Speaks, the Stiftelsen Sunnerdahls Handikappfond Foundation, the Swedish Regional agreement on medical training and clinical research (ALF), and the Swedish Research Council.

Publication: 'Maternal polycystic ovary syndrome and the risk of autism spectrum disorders in the offspring: A population-based nationwide study in Sweden', Kyriaki Kosidou, Christina Dalman, Linnea Widman, Stefan Arver, Brian K. Lee, Cecilia Magnusson, Renee M. Gardner, Molecular Psychiatry, online Dec. 8, 2015, doi: org/10.1038/MP.2015.183

<http://read.bi/1Nip7UT>

How to beat anyone at rock-paper-scissors, according to a Chinese mathematician

The question of how to win at rock-paper-scissors has, believe it or not, plagued mathematicians and game theorists for some time.

Harrison Jacobs

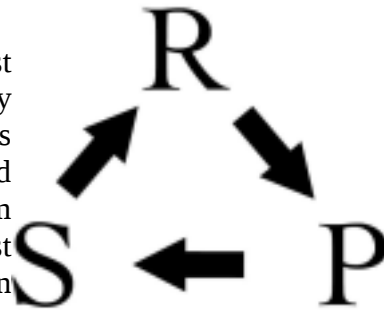
While they previously had devised a theoretical answer to the question, an experiment by Zhijian Wang at Zhejiang University in China that used real players has revealed an interesting wrinkle to the original theory.

In the experiment, Zhijian noticed that winning players tended to stick with their winning strategy, while losers tended to switch to the next strategy in the sequence of rock-paper-scissors, following what he calls "persistent cyclic flows." Here's how it works in practice: Player A and Player B both start by using random strategies. If Player A uses rock and Player B uses paper, Player A loses. In the next round, Player A can assume that Player B will use paper again and should

therefore use scissors to win. In the round after that, because Player B lost, Player A can assume that Player B will use the next strategy in the sequence — scissors — and Player A should then use rock, thus winning again.

If you take the game on a theoretical level, the most mathematically sound way to play rock-paper-scissors is by choosing your strategy at random. Because there are three outcomes — a win, a loss, or a tie — and each strategy has one other strategy that it can beat and one other strategy that can beat it, and we don't care what strategy we win with, it makes the most sense to pick paper, rock, and scissors each one-third of the time. This is called the game's [Nash Equilibrium](#).

While the Nash Equilibrium should be the best strategy in real life, Zhijian found a decidedly different pattern when he and some other researchers recruited 72 students to play the game. They divided the pupils into 12 groups of six players and had them each play 300 rounds of rock-paper-scissors against each other. Zhijian also added a payout in proportion to the number of victories.



Losing players choose the next strategy in the sequence. Harrison Jacobs

When Zhijian reviewed the results, he found that students chose each strategy close to one-third of the time, suggesting the Nash Equilibrium theory. But when he looked closer, he noticed a more unusual pattern.

The pattern that Zhijian discovered - winners repeating their strategy and losers moving to the next strategy in the sequence - is called a "conditional response" in game theory. The researchers have theorized that the response may be hard-wired into the brain, a question they intend to investigate with further experiments.

For now, Zhijian suggests that exploiting the knowledge that most people use the conditional strategy may result in winning a lot more games of rock-paper-scissors.

<http://bit.ly/1IGVkJT>

Learning and Brain Activity Are Boosted by a Dose of a Small-Molecule Compound

In people, a molecule called d-cycloserine improved test performance and strengthened brain cell connections

By Michael M. Torrice, Chemical & Engineering News

We learn from experience: It sounds like a trite sentiment posted by a friend on Facebook, but neuroscientists would agree. Our interactions with the world around us strengthen and weaken the connections between our neurons, a process that neuroscientists consider to be the cellular mechanism of learning.

Now researchers report that boosting signaling of a certain receptor in the brain with a small molecule can enhance these cellular changes and improve learning in people. The findings could lead to new treatments for patients with disorders associated with deficits in learning, such as Alzheimer's disease and schizophrenia.

Through decades of research on how synapses change in animal brains, scientists have found that the N-methyl-d-aspartate receptor (NMDAR) plays a critical role in strengthening synapses during learning. Compounds that increase NMDAR signaling can drive such changes and, as a result, help animals learn new tasks.

Robert F. Asarnow at UCLA and colleagues wanted to test whether one such compound, d-cycloserine, would act similarly in people. But neuroscientists measure synapse changes in animals by sticking electrodes into slices of brain tissue to record electrical signals. "Obviously, we don't do that to our friends," Asarnow says.

So his team used electroencephalography (EEG) to record electrical activity through electrodes stuck to the scalps of its subjects. The team monitored this activity as the subjects watched a certain pattern flash on a screen at high frequency for a couple minutes. Afterward, the subjects showed a spike in EEG activity in their visual cortex when they viewed the pattern at a later time. This suggested a population of neurons had wired themselves together by strengthening their synapses.

People given a single dose of d-cycloserine showed greater activity spikes than subjects not taking the compound, a sign that it enhanced the bolstering of those connections. The compound also led to better performance in two tests of experience-dependent learning (Proc. Natl. Acad. Sci. USA 2015, DOI: [10.1073/pnas.1509262112](https://doi.org/10.1073/pnas.1509262112)). The results are exciting, says Stefan G. Hofmann of Boston University. This is the first evidence that d-cycloserine can enhance forms of cognition relevant to some psychiatric disorders, he says.

http://www.eurekalert.org/pub_releases/2015-12/uoc-irp120815.php

International research partnership yields discovery of a new fossil species

An international research partnership is revealing the first mosasaur fossil of its kind to be discovered in Japan.

Not only does the 72-million-year-old marine reptile fossil fill a biogeographical gap between the Middle East and the eastern Pacific, but also it holds new revelations because of its superior preservation. This unique swimming lizard, now believed to have hunted on glowing fish and squids at night, is detailed in an article led by Takuya Konishi, a University of Cincinnati assistant professor of

biological sciences. The article is published in the Journal of Systematic Palaeontology, a publication of the Natural History Museum in London.

The fossil marine reptile, *Phosphorosaurus ponpetelegans* (a phosphorus lizard from an elegant creek), existed during the Late Cretaceous Period just before the last of the dinosaurs such as *Tyrannosaurus* and *Triceratops*. Compared with some of their mosasaur cousins that could grow as large as 40 feet, this species is relatively small, about 3 meters, or 10 feet long. This unique discovery in a creek in the town of Mukawa in northern Japan reveals that they were able to colonize throughout the northern hemisphere.



An international research partnership is revealing the first mosasaur fossil of its kind to be discovered in Japan. Not only does the 72-million-year-old marine reptile fossil fill a biogeographical gap between the Middle East and the eastern Pacific, but also it holds new revelations because of its superior preservation. Takuya Konishi/University of

Cincinnati

"Previous discoveries of this particular rare mosasaur have occurred along the East Coast of North America, the Pacific Coast of North America, Europe and North Africa, but this is the first to fill the gap between the Middle East and the Eastern Pacific," explains Konishi, a member of the research team that also was represented by the Royal Tyrrell Museum of Palaeontology (Canada), University of Alberta, Brandon University, Hobetsu Museum (Japan), Fukuoka University and the town of Mukawa.

Because the fossil was so well preserved, the creature revealed it had binocular vision - its eyes were on the front of the face, providing depth perception. This was a new discovery for this fossil species. The discovery reveals that the eye structure of these smaller mosasaurs was different from their larger cousins, whose eyes were on either side of their large heads, such as the eye structure of a horse. The eyes and heads of the larger mosasaurs were shaped to enhance streamlined swimming after prey that included fish, turtles and even small mosasaurs.

"The forward-facing eyes on *Phosphorosaurus* provide depth perception to vision, and it's common in birds of prey and other predatory mammals that dwell among us today," says Konishi. "But we knew already that most mosasaurs were pursuit predators based on what we know they preyed upon - swimming animals. Paradoxically, these small mosasaurs like *Phosphorosaurus* were not as adept

swimmers as their larger contemporaries because their flippers and tailfins weren't as well developed."

As a result, Konishi says it's believed these smaller marine reptiles hunted at night, much like the owl does compared with the daytime birds of prey such as eagles. The binocular vision in nocturnal animals doubles the number of photoreceptors to detect light. And, much like owls with their very large eyes to power those light receptors, the smaller mosasaur revealed very large eye sockets.

Also, because fossils of lantern fish and squid-like animals have been found from the Late Cretaceous Period in northern Japan, and because their modern counterparts are bioluminescent, the researchers believe that *Phosphorosaurus* may have specifically targeted those glowing fish and squids at night while their larger underwater cousins hunted in daytime.

"If this new mosasaur was a sit-and-wait hunter in the darkness of the sea and able to detect the light of these other animals, that would have been the perfect niche to coexist with the more established mosasaurs," says Konishi.

Painstaking Preservation

The fossil, enclosed in a rock matrix, was first discovered in 2009, in a small creek in northern Japan. Revealing what was inside the matrix while protecting the fossil was a painstaking process that took place at the Hobetsu Museum in Mukawa. The calcareous nodule would be dipped at night in a special acid wash, and then carefully rinsed the next day, as the two-year process freed the bones from the matrix. To further protect the fossil, special casts were made of the bones so that the researchers could piece together the remains without damaging the fossil.

"It's so unusually well-preserved that, upon separating jumbled skull bones from one another, we were able to build a perfect skull with the exception of the anterior third of the snout," says Konishi. "This is not a virtual reality reconstruction using computer software. It's a physical reconstruction that came back to life to show astounding detail and beautiful, undistorted condition."

Future Research

Konishi says future research will examine how this new mosasaur fits in the evolutionary family tree of mosasaurs.

Additional researchers on the project were Michael W. Caldwell, Department of Biological Sciences and Earth and Atmospheric Sciences, University of Alberta, Edmonton; Tomohiro Nishimura and Kazuhiko Sakurai, Hobetsu Museum; and Kyo Tanoue, Fukuoka University.

The research was supported by the Japanese town of Mukawa; the Hobetsu Museum in Mukawa; Brandon University; the National Sciences and Engineering Research Council (NSERC) Discovery Grant (23858); an NSERC Accelerator Grant (412275); a Chairs Research Allowance; and funding from the Central Research Institute of Fukuoka University (105008).

http://www.eurekalert.org/pub_releases/2015-12/uoo-hts120815.php

Human trials suggest 'rescued' drug could be safer treatment for bipolar disorder

Initial human trial promising for 'failed' drug ebselen

A drug destined for the scrap heap has been rescued by Oxford scientists, who may have found it a new role in treating bipolar disorder.

A team from Oxford University, led by Dr Grant Churchill and Dr Sridhar Vasudevan of the Department of Pharmacology, in collaboration with Professor Phil Cowen of the Department of Psychiatry, used a database of 'failed' drugs, found to be safe but ineffective for their proposed use, to identify ebselen as a possible alternative to lithium, the main treatment for people who are bipolar.

Ebselen was under development as a treatment for stroke, but was abandoned by its manufacturer in the final phase of clinical trials. However, those trials proved that the drug was safe for use in humans. Initial tests of ebselen as a treatment for bipolar disorder were carried out in mice. That research, reported in early 2014, found that results were promising, so the researchers were able to use the existing safety information to fast track an initial trial of ebselen in people.

Dr Grant Churchill explained: 'Lithium has been used for over 60 years and remains the most effective treatment for bipolar disorder, but suffers from toxicity and has many side effects. It is toxic at only twice the right dose and can cause weight gain and thirst. Long-term lithium use can lead to kidney damage. The side effects also encourage people to stop taking it, which means they can relapse.

'An alternative treatment that has fewer side effects would be safer and would likely have a lower rate of people stopping taking their prescribed drug. Lower toxicity also means fewer medical appointments to get the dose right and fewer visits to monitor for side effects.'

In a small trial, healthy adult volunteers were given a course of ebselen. They carried out a number of tests of brain function, provided blood samples and also went through an MRI scan .

The results showed that ebselen had similar effects on the brain to lithium. The next stage will be a full clinical trial to test the effectiveness of ebselen as a treatment. The researchers have obtained funding from the Stanley Medical Research Institute in the United States to conduct a 'proof of concept' study for ebselen in patients with bipolar disorder. It is hoped that the study will start in later in 2016

Should these successes continue, ebselen will be one of only a few examples of a 'rescued drug', where a new use has been found for a failed drug compound.

Dr Sridhar Vasudevan said: 'By rescuing a drug, we benefit from the earlier research and the work of the earlier researchers has a new value. Rather than remaining unused on the shelf of a pharmaceutical company or academic laboratory, drug compounds become available for other uses.

'Recently, there has been more focus on encouraging researchers to share these compounds so that others can find new uses for them. Even so, this is one of the first handful of examples of drug repurposing.'

The paper, Effect of the putative Lithium mimetic ebselen on brain myo-Inositol, is published in the journal Neuropsychopharmacology (doi:10.1038/npp.2015.343).

http://www.eurekalert.org/pub_releases/2015-12/nrts-dp120815.php

Dogs (and probably many other animals) have a conscience too!

Self-consciousness: beyond the looking-glass and what dogs found there

The article has been published in the journal Ethology, Ecology and Evolution, with a title the researcher Roberto Cazzolla Gatti borrowed from the novel by Lewis Carroll: "Self-consciousness: beyond the looking-glass and what dogs found there".

That man's best friend has a conscience is what every owner would be willing to bet, without even thinking about it for a moment. This means that dogs have self-consciousness. But the problem in science is that ideas and assumptions must be demonstrated. It is not enough for someone to have an inkling of something for it to be considered a scientific fact. Self-awareness, or self-consciousness, has been studied mainly by examining the responses of animals and children to their reflection in the mirror. The ultimate proof of possession of a consciousness of self, of one's body and one's own identity, is evaluated based on the individual's ability to use his own reflection to notice and touch a mark (usually a red dot) applied under anaesthesia or during a period of distraction on the face, head, or other parts of the body. This test is known as the "mirror test" and many have observed experiments with children or chimpanzees that easily identify themselves in the mirror and repeatedly touch the mark placed by the investigator on their body.

The basis of the test is that the subject who understands the concept of "self" and "the other" is able to distinguish between the two entities and, therefore, to recognize himself or herself in the reflection. The most interesting result arising from the confirmation of a consciousness of self is that, based on these results, other behavioral traits may be deduced such as, for example, empathy.

In fact, the ability to differentiate oneself from others is often considered a prerequisite for understanding that someone else may be happy or sad, even if the viewer is not.

- When I became interested in this aspect of ethology I went through the scientific literature and I discovered that, however, the ability to recognize their own image in the mirror is a skill extremely rare in the animal kingdom, - Roberto Cazzolla Gatti said. - Until now, only humans and great apes (gorillas excluded), a single Asian elephant, some dolphins, Eurasian magpies, and some ants have passed the test of mirror self-recognition (MSR). A wide range of species has been observed to fail the test, including several species of monkeys, giant pandas, sea lions, birds, and dogs.

Dogs, in particular, show no interest in looking in the mirror, but usually sniff or urinate around it. Dogs and wolves, like dolphins, show a high level of cognitive complexity, but previous attempts to demonstrate the self-recognition of these animals have been inconclusive.

- I believed that because dogs are much less sensitive to visual stimuli with respect to what, for example, humans and many apes are, it is likely that the failure of this and of other species in the mirror test is mainly due to the sensory modality chosen by the investigator to test the self-awareness and not, necessarily, to the absence of this latter, - Roberto Cazzolla Gatti continued.

Attempts to verify this idea have been made before, but most of them were only observational, lacked empirical evidence, or had been carried out only with a single individual and not repeated systematically with other dogs of different sex and age (for example Marc Bekoff in 2001 used a "yellow snow test" to measure how long his dog was sniffing his scent of urine and those of the other dogs in the area). Therefore, the final test of self-recognition in a species as phylogenetically distant from apes (thus with different sensory modalities and communication behavior) as the dog was not obtained.

- So I imagined a new test able to move beyond the mirror version and I called it the "sniff test of self-recognition (STSR)", - the researcher said. - I demonstrated that even when applying it to multiple individuals living in groups and with different ages and sexes, this test provides significant evidence of self-awareness in dogs and can play a crucial role in showing that this capacity is not a specific feature of only great apes, humans, and a few other animals, but it depends on the way in which researchers try to verify it.

This research was conducted with a test performed on 4 dogs, all strays grown in semi-freedom. Dr. Gatti collected urine samples from each dog and divided and stored them in containers labeled to each dog. Then he submitted the animals to the sniff test of self-recognition. The tests were repeated four times a year, at the beginning of each season. This test is nothing more than a modified version of the mirror test, carried out to check the sense of smell, and not the sight, as the main way to determine self-awareness.

- Then I placed within a fence 5 urine samples containing the scent of each of the four dogs and a "blank sample", filled only with cotton wool odorless, - Dr. Gatti said. - The containers were then opened and each dog was individually introduced to the inside of the cage and allowed to freely move for 5 minutes. The time taken by each dog to sniff each sample was recorded.

The result was surprising: all dogs devoted more time to smell the urine samples of the others rather than their own, and this behavior confirmed the hypothesis that dogs seem to know their own smell exactly, they are less interested in their own, and they are therefore self-aware.

In addition, this study shows a correlation between the age of the individual dogs and the time spent to sniff the urine samples, a result that strongly supports the idea that self-awareness increases with age, as demonstrated in other species, such as chimpanzees and humans.

The innovative approach to test the self-awareness with a smell test highlights the need to shift the paradigm of the anthropocentric idea of consciousness to a species-specific perspective. We would never expect that a mole or a bat can recognize themselves in a mirror, but now we have strong empirical evidence to suggest that if species other than primates are tested using chemical or auditory perception, we could get really unexpected results.

From now on, according to the results of this study, it will be more difficult to establish, watching our dog, whether in that moment we are thinking about him or he is thinking about us. Maybe both. It will be, however, easier to recognize that the age of empathy that was anticipated by the great ethologist Frans de Waal has finally arrived.

<http://bit.ly/1QxUFut>

Japanese Akatsuki probe enters Venus orbit after inspired hack *Japanese Akatsuki probe enters Venus orbit after inspired hack*

It's a reunion of astronomical proportions. A damaged satellite that missed its rendezvous with Venus was finally sent into orbit around the planet yesterday – exactly five years late – after mission controllers came up with a successful hack to get it back on course.

On 21 May 2010, the Japanese space agency JAXA launched the Akatsuki satellite to study Venus's atmosphere. Researchers hoped that the mission would reveal, among other things, why the planet's surface is subject to extreme winds at up to 400 kilometres per hour.

But disaster struck on 7 December 2010, when the satellite attempted to fire its thrusters. Instead of entering into orbit around Venus, it cruised off into space and wound up travelling around the sun. Later analysis suggested the thruster nozzles had been damaged, causing a safety valve to cut in before Akatsuki had properly

changed course. Over the next few years, JAXA tested the various thrusters and found the main ones to be unusable. So the team came up with a last-ditch strategy for a second attempt on Venus.

Fuel jettisoned

In October 2011, they dumped all the fuel for the broken thrusters, making the satellite lighter. Then they used secondary attitude control thrusters, intended to orient the probe, to put Akatsuki on course to rendezvous with Venus in 2015.

On Monday, that moment arrived. After firing its secondary thrusters for a full 20 minutes, Akatsuki appears to have gone into orbit around Venus, JAXA announced. However, it will take a few days to properly pin down the orbit. JAXA expects to release an update at 6 pm Japan time (9 am GMT) tomorrow.

Concerns linger over the condition of Akatsuki's instruments: it was never built to fly as close to the sun as it has, and they could have been damaged by the heat. As a result, JAXA decided to attempt the Venus rendezvous now instead of next year, even though the later date would have put the satellite into a better orbit for collecting data.

"If it is successful in getting into orbit, it will be our only opportunity to study Venus from orbit in the next few years," says Jeremy Bailey from the University of New South Wales in Sydney, Australia. Since the European Venus Express orbiter ended its mission in 2014, we have not had any probes gathering data from Venus's atmosphere, he says.

The probe's observations could yield insights into what Earth might be like in a billion years or so, when the greenhouse effect could have run away and the sun's output may be higher than today. "On Earth, if you took all the carbonate rocks out and put all that carbon dioxide in the atmosphere, you'd basically get Venus," Bailey says.

<http://www.bbc.com/news/health-35039306>

Molecule clears Alzheimer's plaques in mice

A molecule can clear Alzheimer's plaques from the brains of mice and improve learning and memory, Korean scientists have found in early tests.

Exactly how it gets rid of the abnormal build-up is not understood.

The small Nature Communications study hints at a way to tackle the disease even once its in full swing, dementia experts say. But there is no proof the same method would work in people - many more years of animal trials are needed first.

Plaque-busting

Currently, there is no cure for Alzheimer's disease. Treatments can lessen the symptoms, but scientists are looking for ways to prevent, halt or reverse the disease. As the dementia progresses, more plaques (clumps of abnormal proteins and chemicals) form in the brain and healthy brain cells die off.

Scientists reason that preventing or removing the plaques might help, and many drug candidates are in development. Some drugs still being tested appear to stop the plaques from forming - but that is if it taken early enough, before the disease has advanced.

However, the South Korean researchers believe they may have found a molecule, called EPPS, that could work even if plaques have already formed. They gave EPPS to mice (bred to have the Alzheimer's plaques) by spiking their drinking water for two weeks, and then monitored them over the next three months to see what effect it might have. Compared with a control group of mice who received only normal water, the EPPS mice performed better on memory and learning problems (running through a maze).

The EPPS mice also had far fewer plaques in their brain at the end of the trial than they had had at the beginning. The same could not be said for the control group.

The Alzheimer's Society and Alzheimer's Research UK said it was important to remain cautious - animal study findings may never apply to humans.

Prof Tom Denning, an expert in dementia research at the University of Nottingham, said: "From a clinician's point of view, this research is of interest, but we still don't know if removing amyloid plaques is useful in humans.

"It may well be that the appearance of plaques is too far down the chain of molecular processes to be beneficial. "We don't know if this animal work will lead to any useful agent that can be used for clinical trials."

<http://bit.ly/1xcTkx>

Dinosaurs Evolved in a Startlingly Short Time

New fossil dates show beasts arose from their ancestors in half the time researchers previously thought

By [Laura Geggel](#), [LiveScience](#) on December 8, 2015

Dinosaurs took less than 5 million years to evolve from their reptile predecessors, the early dinosauromorphs, a new study finds.

The finding revamps the time line between the dinosaurs and early dinosauromorphs. Until now, researchers thought that it took at least 10 million to 15 million years for the early dinosauromorphs to evolve into dinosaurs.

"It really narrows the amount of time between the appearance of these early dinosauromorphs and the first dinosaurs," said study co-researcher Randall Irmis, a paleontologist at the University of Utah and a curator of paleontology at the Natural History Museum of Utah. "Rather than there being 10 [million] or 15 million years between when the first dinosauromorphs show up and the first dinosaurs, now it's just 5 million years." [[See Photos of the Early Dinosauromorph Site in Argentina](#)]

Early dinosauromorphs were just like dinosaurs, except for a few key features. For instance, dinosaurs had a ball-and-socket hip that could rotate easily, and additional sacral vertebrae (a vertebra at the end of the spine), which helped strengthened the hips. This allowed dinosaurs to develop stronger leg muscles, which, along with their forward-hinging feet, helped them run faster than their competitors. They also developed an extra hole in their skulls, which let them cool off after vigorous activity.



*Animals escaping from an erupting volcano 235 million years ago in northwestern Argentina. These species, found as fossils in the Chanares Formation, include early mammal relatives (the dicynodont *Dinodontosaurus* in the left background, and the cynodont *Massetognathus* in the left foreground) and early dinosaur precursors (*Lewisuchus* in the right background, and *Lagerpeton* in the right foreground). By measuring radioactive isotopes in zircons crystals from the volcanic ash, scientists were able to determine the precise age of this fossil assemblage.*

Victor Leshyk

Even though paleontologists had studied these predecessors previously, they still haven't been certain about the age of the rocks containing early dinosauromorph [fossils](#), Irmis said. He and his colleagues gave the matter a closer look, investigating the Chanares Formation in northwestern Argentina, a site known for containing the fossils of early dinosauromorphs and early dinosaurs.

The researchers relied on a handy mineral called zircon to help them date the early dinosauromorph-containing rock layer. When zircon crystals form, they trap [the radioactive element uranium](#) within them. Over time, uranium decays into lead.

"We know the exact rate at which uranium decays into lead," Irmis told Live Science. By measuring the [ratio of uranium to lead](#), researchers can determine how long ago the zircon crystal formed.

However, zircon isn't present in all rocks. So the researchers looked for volcanic ash, where the mineral is more commonly found. Luckily, they found zircon crystals in a rock layer that contained early dinosauromorphs. The scientists took

a sample from that layer, as well as from the younger layer above it, so they could bookend the finding.

Dating the rock

The researchers crushed the rock samples so they could isolate the zircon crystals, which are as small as grains of sand, Irmis said. Then, the scientists analyzed about 20 zircon crystals from each sample, using a [mass spectrometer](#), an instrument that separates elements and isotopes (a variation of an element) by mass and concentration, the researchers said.

What's more, the zircon crystals contained a helpful cross-check: They have different uranium isotopes that decay at different rates, and "we're fairly confident we've got the right age if they all agree with each other," Irmis said.

The results show that the rock layer is between 234 million and 236 million years old, from the Late Triassic period, he said, meaning the early dinosauromorphs within the layer are the same age. This new date is 5 million to 10 million years younger than previously thought, Irmis said.

Dinosaurs may have evolved rapidly (geologically speaking), but it appears they came to [dominate paleo-Earth in a smooth and gradual manner](#), Irmis said. That is, they didn't suddenly wrest power from their early dinosauromorph relatives.

"When we look at the ecosystems of [the] first dinosauromorphs and the ecosystems with the first dinosaurs, it's interesting that we don't see much difference in how the ecosystems are put together," Irmis said. "You don't seem to see dinosaurs showing up and immediately taking over."

He added, "it really emphasizes that there wasn't much special about the first dinosaurs. They were pretty similar to their early dinosauromorph relatives and probably doing very similar things." [[Image Gallery: 25 Amazing Ancient Beasts](#)]

Dinosaurs move forward

Some dinosauromorphs persisted for another 20 million years after dinosaurs emerged, Irmis said. But the dinosaurs' adaptations appear to have been advantageous in the long run, Irmis said. These changes helped dinosaurs prosper until the 6-mile-long (10 kilometers) asteroid wiped them out 66 million years ago, Irmis said.

But dinosaurs took a while to spread throughout the world, the researchers note. The dinosaurs didn't dominate the mid to high latitudes—such as present-day Argentina, Brazil and South Africa—until the late Triassic, about 215 million years ago. It took dinosaurs [even longer to dominate the lower latitudes](#), such as present-day western and eastern North America, areas that were closer to the equator at that time, Irmis said.

The new research is a "solid study," said Kenneth Lacovara, a professor of paleontology and geology and the dean of the School of Earth & Environment at Rowan University in New Jersey, who wasn't involved with the study.

"The story is that there was a very rapid evolution and a very rapid achievement of dominance in the fauna as they go from [early] dinosauromorphs to [dinosaurs](#)," Lacovara said. It shows that "being a dinosaur is a really good idea. It really works. It allows them to outcompete things that aren't like dinosaurs. And if you include birds, being a dinosaur is still a pretty good thing."

The findings were published online today (Dec. 7) in the [journal Proceedings of the National Academy of Sciences](#).

http://www.eurekalert.org/pub_releases/2015-12/nu-lla120715.php

Living longer and healthier in mind but not in body

Women are now spending fewer years with cognitive impairment but more years with disability compared to 20 years ago, new research has revealed.

Experts have shown that between 1991 and 2011 women's life expectancy at age 65 increased by 3.6 years but they identified that the female body doesn't age as well as its mind.

A study by Newcastle University, UK, and the University of Cambridge, UK, published in *The Lancet*, has revealed that women lived approximately 2.5 months less with moderate or severe cognitive impairment and six months fewer with mild cognitive impairment, such as problems with memory and thinking.

However, this is balanced by the fact that at age 65 females now spend around seven months more with moderate or severe disability and 2.5 years more with mild disability.

Meanwhile, overall men's life expectancy increased by 4.5 years but they had only 1.3 years more with mild disability and there was no increase in the years spent with moderate or severe disability, or mild or worse cognitive impairment.

Professor Carol Jagger, from Newcastle University's Institute for Ageing, led the analysis of the research.

She said: "The big unanswered question is whether our extra years of life are healthy ones and the aim of our research was to investigate how health expectancies at age 65 years and over changed between 1991 and 2011. "One possibility for the increased years women are living with mild disability might be the rise in obesity levels over the decades, but there may also be particular conditions, or just more multiple diseases, which are a feature of very old age."

The research team compared two rounds of the Cognitive Function and Ageing Study, done in England in 1991 and 2011.

Health expectancy was measured in three ways: self-perceived health, life without disability, and time free from cognitive impairment. For the study a total of 7,635 people aged 65 and over were analysed in Newcastle, Cambridge and Nottingham. Analysis of the Health Survey for England for those aged 65+ over a similar time period showed problems with vision and hearing did not account for increases in disability.

Nevertheless, stability in self-care activities, like cooking, and increases in mobility limitations, such as walking 200 yards and climbing stairs, may contribute to gains in mild disability.

Professor Carol Brayne, from the University of Cambridge, was overall lead for the study. She said: "The findings suggest a compression of cognitive morbidity when comparing older people now compared to 20 years ago in England. This is very good news and consistent with our earlier reporting of a reduction in age specific prevalence of dementia across two decades."

Health expectancies are important indicators to monitor population health trends and inequalities internationally, nationally and regionally.

It is necessary for Government to get a clear indication if people are living longer, healthier lives as it can have an impact on the economy, housing and employment opportunities.

Future work will examine the reasons for the increase in years with disability. The researchers will look at which diseases and conditions are responsible for the rise in mild disability and whether patterns prevail across all the regions studied.

Professor Jagger added: "Our findings have important implications for Government, employees and individuals with respect to raising the state pension age and extending working life. "It is also necessary for community care services and family carers who predominantly support those with mild to moderate disability to enable them to continue living independently."

In most developed countries worldwide life expectancy is increasing at the rate of at least two years every decade, and, for life expectancy at age 60, shows no sign of slowing down.

Newcastle University's Institute for Ageing held a conference today (Tuesday, December 8), which focused on 'The economic and social impact of ageing' - Professor Jagger opened the event.

Reference:

A comparison of health expectancies over two decades in England: results of the Cognitive Function and Ageing Study I and II

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Published in the Lancet. DOI: [http://dx.doi.org/10.1016/S0140-6736\(15\)00947-2](http://dx.doi.org/10.1016/S0140-6736(15)00947-2)

http://www.eurekalert.org/pub_releases/2015-12/tnam-amv120715.php

After menopause, vulvovaginal troubles are common and linked with other pelvic problems

Nevertheless, over 30 percent of women haven't seen a gynecologist, and over 80 percent didn't get the standard treatment

CLEVELAND, Ohio - After menopause, more than half of women may have vulvovaginal symptoms that have a big impact on their lifestyle, emotions, and sex life. What's more, the symptoms tend to travel with other pelvic troubles, such as prolapse and urinary and bowel problems. But many women aren't getting help, shows a study published online today in *Menopause*, the journal of The North American Menopause Society (NAMS).

The researchers from Dartmouth, Yale, and the Connecticut Healthcare System recruited 358 women ages 55 and older from primary care offices and senior centers to answer questions about common symptoms after menopause. The women answered questionnaires, not only about symptoms such as vaginal and vulvar dryness and irritation and their impact, but also about other menopause symptoms, other pelvic problems such as urinary urgency and urinary and fecal incontinence, whether they had seen a gynecologist, and what sort of treatment they had received.

Vulvar and vaginal symptoms--itching, burning, stinging, pain, irritation, dryness, discharge, or odor--were very common. A little more than half of the women (51%) said they had one or more of these. The symptoms also had a significant impact on their lives. Forty percent of the women with symptoms said the symptoms posed emotional problems, and 33% said they had an impact on their lifestyle. More than three-quarters of the women who were sexually active with a partner (76%) said the symptoms posed problems in their sex lives.

But with these symptoms came others. Many women with the vulvar and vaginal symptoms also had urinary frequency (50%) or leaking because of urinary urgency (43%). That helps confirm why NAMS and other organizations gave these postmenopausal problems a new name that includes urinary symptoms--"genitourinary syndrome of menopause" or GSM. In addition to urinary problems, significantly more women with the vulvovaginal symptoms than without also had pelvic organ prolapse or fecal incontinence without diarrhea. The women with the vulvar and vaginal symptoms also tended to have more menopausal symptoms other than hot flashes.

But, despite all these symptoms and the distress they cause, nearly a third of the women with symptoms (33%) had not seen a gynecologist in the last two years.

And a huge majority--83%--were not getting the standard GSM treatment, which is low-dose estrogen in the vagina through creams, pills, or rings.

"This study demonstrates that there is an unmet need for postmenopausal women to have regular gynecologic visits where questions can be asked about vaginal and urinary health problems and assessment can be made to determine the presence of vulvovaginal atrophy, urinary symptoms of urgency or incontinence or pelvic floor disorders and offer FDA approved safe and effective therapies," says NAMS Executive Director JoAnn V. Pinkerton, MD, NCMP "Women need to tell their healthcare providers about their genitourinary symptoms, and providers need to ask."

The boxed warnings on the low-dose intravaginal estrogen therapies for GSM (also known as vulvovaginal atrophy or VVA) may have made providers reluctant to prescribe them and women to use them.

"The boxed warnings prompt a level of fear that is out of step with these low-dose, local estrogen products," said Dr. Pinkerton. That prompted experts from NAMS and leaders from other scientific organizations to go to FDA recently to request removing this warning from the label information. The NAMS experts who spoke to FDA stressed that providers should exercise caution and evaluate the uterus if women develop bleeding as well as advising women to discuss the use of low-dose intravaginal estrogen with their oncologist if they have had cancer.

"Diagnosis of these problems requires a pelvic exam and evaluation of the vaginal and vulvar tissues to look for atrophy, prolapse, or infection, noted Dr. Pinkerton. Safe and effective therapies are available and include, not only the first-line, low-dose vaginal estrogen creams, tablets, or rings, but also ospemiphene, the new oral selective estrogen receptor modulator or SERM that treats painful intercourse."

The study, which will be published in the April 2016 print edition of *Menopause*, was supported by grants from the Claude D. Pepper Older Americans Independence Center at Yale University School of Medicine and an award from the National Institutes on Aging.

<http://bit.ly/1xfWJu>

Laziness and lack of sleep — especially when combined — can shorten your life

New study says sitting and lack of sleep should join a short list of behaviors known to increase your risk of premature death

Karen Kaplan

You already know that smoking is bad for you and that drinking too much alcohol may shorten your life. Now a new study says that spending too much time in a chair and depriving yourself of necessary sleep should join a short list of behaviors known to increase your risk of premature death.

Sedentary time and lack of sleep were damaging in their own right, but when combined with more traditional risk factors, they had a multiplier effect that made an early death far more likely.

The findings, published Tuesday in the journal PLOS Medicine, make clear that "some risk behaviors tend to cluster, particularly in certain patterns, and that the joint risk could be much higher than the sum of the individual risks," the study authors wrote.

For instance, smoking was the most dangerous single risk factor among the six studied — the small number of people for whom smoking was their only vice were 90 percent more likely to die during the course of the study than were people with practiced clean living across the board. People who reported high alcohol consumption — more than 14 alcoholic drinks per week — as their sole risk factor did not seem to be putting their lives in danger. But for those who combined heavy drinking with smoking, the risk of premature death was nearly tripled. And when lack of sleep was added to the mix, the odds of an early death were nearly five times greater — even though lack of sleep by itself had only a slight effect on mortality.

These numbers are based on the lives, and sometimes deaths, of 231,048 Australians from Sydney and rest of the state of New South Wales. They enrolled in the 45 and Up Study between 2006 and 2009, answering questions about their smoking history, eating and drinking habits, exercise routines, sedentary time and sleep duration. The study volunteers were tracked until the middle of 2014; during that time, 15,635 died.

When they joined the study, 7.2 percent of the participants were smokers, 19.1 percent were heavy drinkers, 17.2 percent had a poor diet, 22.9 percent got too little exercise, 25 percent spent more than 7 hours sitting each day and 23.1 percent got either too little or too much sleep. Nearly one-third (31.2 percent) of the volunteers did not engage in any of these risk factors, and 36.7 reported only one. However, 21.4 percent of them admitted to two of these bad habits, 8.1 percent admitted to three, 2.1 percent reported four, 0.4 percent had five and 0.04 percent engaged in all six.

Except for heavy drinking, each of the six behaviors was associated with at least a slight increased risk of death during the study period, the researchers found. Smoking was the most dangerous, followed by lack of exercise.

After accounting for factors such as age, gender, education and other demographic factors, the researchers saw a clear pattern: The more deviations a person had from a clean lifestyle, the greater his or her risk of premature death. Compared to people with no risk factors, those with just one were 27 percent more likely to die during the course of the study, and those with two had a 73 percent increased risk

of death. At the other end of the spectrum, people with five risk factors were 4.61 times more likely to die, and those with all six were 5.38 times more likely.

Some combinations were more deadly than others, the researchers found. Those who blended insufficient exercise with prolonged sitting were 2.42 times more likely to die during the study, and those who were also guilty of sleeping for too many hours were 4.23 times more likely die by the time the study ended.

"These findings suggest there is a 'synergistic effect' among risk factors," the study authors wrote.

The authors acknowledged that it was up to each volunteer to report on their smoking, sitting, sleeping and other behaviors, and some of them might have shaded the truth to impress the researchers. If so, the study results probably underestimate the true effects of the risk factors, they wrote.

The authors added that their results would be more meaningful if they tracked people's risks behaviors over time, and if they could link those behaviors to heart disease or other specific causes of death. That information was not available when the analysis was done, they wrote.

http://www.eurekalert.org/pub_releases/2015-12/tl-tlh120815.php

The Lancet: Happiness and unhappiness have no direct effect on mortality

Study has shown that happiness itself has no direct effect on mortality

A study of a million UK women, published today in The Lancet, has shown that happiness itself has no direct effect on mortality, and that the widespread but mistaken belief that unhappiness and stress directly cause ill health came from studies that had simply confused cause and effect.

Life-threatening poor health can cause unhappiness, and for this reason unhappiness is associated with increased mortality. In addition, smokers tend to be unhappier than non-smokers. However, after taking account of previous ill health, smoking, and other lifestyle and socio-economic factors, the investigators found that unhappiness itself was no longer associated with increased mortality.

The lead author, Dr Bette Liu, now at the University of New South Wales, Australia said: "Illness makes you unhappy, but unhappiness itself doesn't make you ill. We found no direct effect of unhappiness or stress on mortality, even in a ten-year study of a million women."^[1]

The investigation was conducted within the UK Million Women Study. Three years after joining the study, women were sent a questionnaire asking them to self-rate their health, happiness, stress, feelings of control, and whether they felt relaxed. Five out of six of the women said they were generally happy, but one in six said they were generally unhappy.

As in other studies, unhappiness was associated with deprivation, smoking, lack of exercise, and not living with a partner. The strongest associations, however, were that the women who were already in poor health tended to say that they were unhappy, stressed, not in control, and not relaxed.

The main analyses included 700 000 women, average age 59 years, and over the next 10 years these women were followed by electronic record linkage for mortality, during which time 30 000 of the women died.

After allowing for any differences already present in health and lifestyle, the overall death rate among those who were unhappy was the same as the death rate among those who were generally happy. The study is so large that it rules out unhappiness being a direct cause of any material increase in overall mortality, in women. This was true for overall mortality, for cancer mortality, and for heart disease mortality, and it was true for stress as well as for unhappiness.

Co-author Professor Sir Richard Peto, of the University of Oxford, Oxford, UK said: "Many still believe that stress or unhappiness can directly cause disease, but they are simply confusing cause and effect. Of course people who are ill tend to be unhappier than those who are well, but the UK Million Women Study shows that happiness and unhappiness do not themselves have any direct effect on death rates."^[1]

Previous reports of reduced mortality being associated with happiness, with being in control, with being relaxed, or with related measures of wellbeing had not allowed properly for the strong effect of ill health on unhappiness and on stress.

In a linked Comment, Dr Philippe de Souto Barreto and Professor Yves Rolland, Institute of Ageing, University Hospital of Toulouse, France say that the study provides extremely valuable and robust information about happiness, health, and mortality. Dr de Souto Barreto and Professor Rolland also call for randomised trials to investigate the issue further: "Such studies should be powered to allow comparisons to be made across age ranges and between men and women. Cross-cultural studies could also shed light on the generalisability of interventions to promote happiness."

http://www.eurekalert.org/pub_releases/2015-12/difr-pcf121015.php

Plant compound found in spices and herbs increases brain connections

Brazilian research shows that the flavonoid apigenin has potential to treat diseases like schizophrenia, depression, Alzheimer's and Parkinson's

Brazilian researchers from D'Or Institute for Research and Education (IDOR), Federal University of Rio de Janeiro (UFRJ) and Federal University of Bahia (UFBA) have demonstrated in laboratory that apigenin, a substance found in

parsley, thyme, chamomile and red pepper, improves neuron formation and strengthens the connections between brain cells.

Previous experiments with animals had already shown that substances from the same chemical group as the apigenin, known as flavonoids, positively affect memory and learning. Many studies highlight the potential of flavonoids to preserve and enhance brain function. While the effectiveness of flavonoids for brain health is not an entirely new concept, this research is the first to show the positive effects of apigenin directly on human cells and the first to unraveling its mechanism.

The neurons treated with apigenin (right) show more formation of synapses (red) than the neurons that were not treated. Rehen et al.

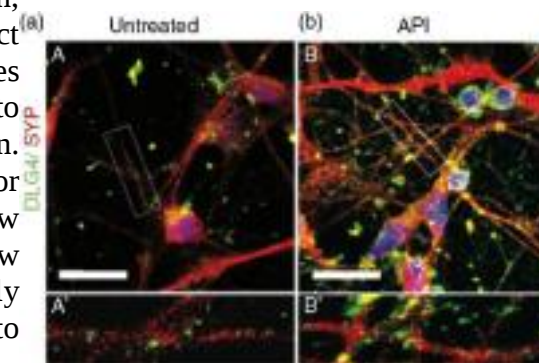
The scientists observed that just by applying apigenin to human stem cells in a dish they become neurons after 25 days - an effect they would not see without the substance. Moreover, the neurons that were formed made stronger and sophisticated connections among themselves after being treated with this natural compound.

"Strong connections between neurons are crucial for good brain function, memory consolidation and learning", says neuroscientist from IDOR and UFRJ Stevens Rehen, leader author of the paper published today at *Advances in Regenerative Biology*.

The research team conducted by Rehen demonstrated that apigenin works by binding to estrogen receptors, which affect the development, maturation, function, and plasticity of the nervous system. This group of hormones is known to delay the onset of psychiatric and neurodegenerative disorders such as schizophrenia, depression, Alzheimer's and Parkinson's disease. However, the use of estrogen-based therapies is limited by the increased risk of estrogen-dependent tumors and cardiovascular problems.

Researchers believe apigenin can be used as an alternative approach on future treatments for neurodegenerative diseases as well as in neuronal differentiation strategies in laboratory.

"We show a new path for new studies with this substance", points out Rehen. "Moreover, flavonoids are present at high amounts in some foods and we can speculate that a diet rich in flavonoids may influence the formation of neurons and the way they communicate within the brain."



The study was part of the Phd dissertation of Cleide Souza, at the Program on Morphological Sciences of UFRJ and received financial support from the Brazilian agencies FAPERJ, CNPq, CAPES, BNDES and FINEP.

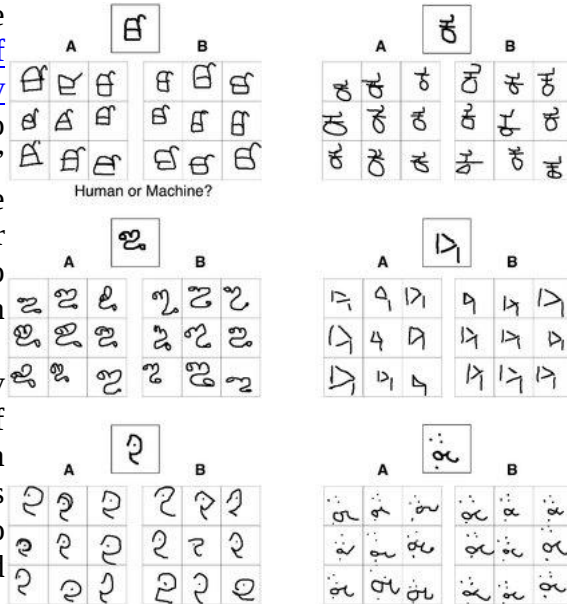
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A Learning Advance in Artificial Intelligence Rivals Human Abilities

Computer researchers reported artificial-intelligence advances on Thursday that surpassed human capabilities for a narrow set of vision-related tasks.

By [JOHN MARKOFF](#) DEC. 10, 2015

The improvements are noteworthy because so-called machine-vision systems are becoming commonplace in many aspects of life, including car-safety systems that detect pedestrians and bicyclists, as well as in video game controls, Internet search and factory robots. Researchers at the [Massachusetts Institute of Technology](#), [New York University](#) and the University of Toronto reported a new type of “one shot” machine learning on Thursday in the journal [Science](#), in which a computer vision program outperformed a group of humans in identifying handwritten characters based on a single example. The program is capable of quickly learning the characters in a range of languages and generalizing from what it has learned. The authors suggest this capability is similar to the way humans learn and understand concepts.



Humans and machines were given an image of a novel character (represented atop each grid) and then asked to copy it. Brenden Lake

The new approach, known as Bayesian Program Learning, or B.P.L., is different from current machine learning technologies known as deep neural networks. Neural networks can be trained to recognize human speech, detect objects in images or identify kinds of behavior by being exposed to large sets of examples. Although such networks are modeled after the behavior of biological neurons, they do not yet learn the way humans do — acquiring new concepts quickly. By contrast, the new software program described in the Science article is able to learn

to recognize handwritten characters after “seeing” only a few or even a single example.

The researchers compared the capabilities of their Bayesian approach and other programming models using five separate learning tasks that involved a set of characters from a research data set known as Omniglot, which includes 1,623 handwritten character sets from 50 languages. Both images and pen strokes needed to create characters were captured.

“With all the progress in machine learning, it’s amazing what you can do with lots of data and faster computers,” said Joshua B. Tenenbaum, a professor of cognitive science and computation at [M.I.T.](#) and one of the authors of the Science paper. “But when you look at children, it’s amazing what they can learn from very little data. Some comes from prior knowledge and some is built into our brain.”

Also on Thursday, organizers of an annual academic [machine vision competition](#) reported gains in lowering the error rate in software for finding and classifying objects in digital images.

“I’m constantly amazed by the rate of progress in the field,” said Alexander Berg, an assistant professor of computer science at the University of North Carolina, Chapel Hill.

The competition, known as the Imagenet Large Scale Visual Recognition Challenge, pits teams of researchers at academic, government and corporate laboratories against one another to design programs to both classify and detect objects. It was won this year by a group of researchers at the [Microsoft Research laboratory](#) in Beijing.

The [Microsoft](#) team was able to cut the number of errors in half in a task that required their program to classify objects from a set of 1,000 categories. The team also won a second competition by accurately detecting all instances of objects in 200 categories.

The contest requires the programs to examine a large number of digital images, and either label or find objects in the images. For example, they may need to distinguish between objects such as bicycles and cars, both of which might appear to have two wheels from a certain perspective.

In both the handwriting recognition task described in Science and in the visual classification and detection competition, researchers made efforts to compare their progress to human abilities. In both cases, the software advances now appear to surpass human abilities.

However, computer scientists cautioned against drawing conclusions about “thinking” machines or making direct comparisons to human intelligence.

“I would be very careful with terms like ‘superhuman performance,’ ” said Oren Etzioni, chief executive of the Allen Institute for Artificial Intelligence in Seattle.

"Of course the calculator exhibits superhuman performance, with the possible exception of Dustin Hoffman," he added, in reference to the actor's portrayal of an autistic savant with extraordinary math skills in the movie "Rain Man."

The advances reflect the intensifying focus in Silicon Valley and elsewhere on artificial intelligence.

Last month, the Toyota Motor Corporation [announced](#) a five-year, billion-dollar investment to create a research center based next to Stanford University to focus on artificial intelligence and robotics.

Also, a formerly obscure academic conference, Neural Information Processing Systems, underway this week in Montreal, has doubled in size since the previous year and has attracted a growing list of brand-name corporate sponsors, including Apple for the first time.

"There is a sellers' market right now — not enough talent to fill the demand from companies who need them," said Terrence Sejnowski, the director of the [Computational Neurobiology Laboratory](#) at the Salk Institute for Biological Studies in San Diego. "Ph.D. students are getting hired out of graduate schools for salaries that are higher than faculty members who are teaching them."

http://www.eurekalert.org/pub_releases/2015-12/ohri-cpc120715.php

Controversial prostate cancer screening can be improved by repeating abnormal tests

Ottawa study shows repeating an abnormal PSA test reduces unnecessary biopsies by 55 percent

For more than 20 years, the prostate-specific antigen (PSA) test has been used to help screen for prostate cancer, but in recent years, some task forces have called for this blood test to be abandoned because it leads to many unnecessary biopsies. Now, a new study from The Ottawa Hospital and the University of Ottawa shows that simply repeating abnormal PSA tests dramatically reduces unnecessary biopsies.

The study is the first to examine the impact of prompt repeat PSA testing in a broad range of men being screened for prostate cancer. It was led by Drs. Rodney Breau and Luke Lavallée and colleagues, and published in the Mayo Clinic Proceedings on Dec. 10, 2015.

"A high PSA level is associated with a greater risk of prostate cancer, and PSA screening can help detect cancer at an earlier, more treatable stage," explained Dr. Breau, a prostate cancer surgeon and associate scientist in epidemiology at The Ottawa Hospital and the University of Ottawa.

"However, PSA levels can also fluctuate because of infections, physical activity and laboratory error. Because of this variation, we implemented a protocol to always repeat an abnormal test before referring a patient for a biopsy. We had a hunch that this would reduce unnecessary biopsies and our study shows that our suspicion was correct."

The research team reviewed the medical records of 1,268 men who had an abnormal (high) PSA test result and were evaluated at the Ottawa Regional Cancer Assessment Centre between 2008 and 2013. In 25 percent of these men, the second PSA test came back normal. Only 28 percent of men with conflicting test results underwent a biopsy compared to 62 percent of men who had two abnormal test results, representing a 55 percent reduction in biopsies.

In addition, only three percent of men with conflicting test results who had a biopsy were diagnosed with cancer within the year, compared to 19 percent of men who had two abnormal tests, suggesting that the second normal test is important.

"It is clear to me that any man with an abnormal PSA test should have this test repeated before a decision to biopsy," concluded Dr. Breau.

"Some doctors and patients may be worried about missing a significant cancer diagnosis if they forgo a biopsy after conflicting test results, but our study shows this is very unlikely. It is also important to remember that the PSA test is just one factor we evaluate when deciding to do a biopsy, and these decisions are always made together with the patient, and can be revisited if risk factors change."

"Our study has important implications for patients and the health-care system," said Dr. Lavallée, a prostate cancer surgeon and researcher at The Ottawa Hospital and the University of Ottawa.

"Prostate biopsies can be uncomfortable and inconvenient for patients, and in rare cases, they can lead to infections, so we only want to do these if they are really necessary. Prostate biopsies are also expensive for the health-care system."

According to the Canadian Cancer Society, approximately 24,000 Canadians will be diagnosed with prostate cancer each year and the five-year survival rate is 96 percent. A PSA test costs approximately \$30, while a prostate biopsy costs approximately \$880.

Full reference: 'Reducing the Harm of Prostate Cancer Screening by Repeating an Abnormal Prostate-Specific Antigen Test'. Mayo Clinic Proceedings. Luke T. Lavallée; Andrew Binette; Kelsey Witiuk; Sonya Cnossen; Ranjeeta Mallick; Dean Fergusson; Franco Momoli; Chris Morash; Ilias Cagiannos; and Rodney H. Breau. Dec. 10, 2015.

Funders: This study did not have dedicated funding, however, Dr. Breau is supported by a Research Chair in Urologic Oncology funded by The Ottawa Hospital Foundation.

http://www.eurekalert.org/pub_releases/2015-12/uom-sic120915.php

Safe, inexpensive chemical found to reverse symptoms of progeria in human cells

Finding could lead to treatments for rare genetic illness as well as normal aging

Progeria is a rare genetic disease that mimics the normal aging process at an accelerated rate. Symptoms typically appear within the first year of life, and individuals with the disease develop thin, wrinkled skin, fragile bones and joints, full-body hair loss and organ failure, among other complications. Most do not survive past their teen years.

New work from the University of Maryland suggests that a common, inexpensive and safe chemical called methylene blue could be used to treat progeria--and possibly the symptoms of normal aging as well. A new study shows for the first time that small doses of methylene blue can almost completely repair defects in cells afflicted with progeria, and can also repair age-related damage to healthy cells. The study was published online in the journal *Aging Cell* on December 10, 2015.

"We tried very hard to examine the effect of methylene blue on all known progeria symptoms within the cell," said Kan Cao, senior author on the study and an associate professor of cell biology and molecular genetics at UMD. "It seems that methylene blue rescues every affected structure within the cell. When we looked at the treated cells, it was hard to tell that they were progeria cells at all. It's like magic."

Progeria results from a defect in a single gene. This gene produces a protein called lamin A, which sits just inside the cell's nucleus, under the nuclear membrane. Healthy cells snip off a small piece of each new lamin A molecule--a small edit that is necessary for lamin A to work properly. Cells with progeria, however, skip this important editing step. The defective lamin A interferes with the nuclear membrane, causing the nucleus to form bulges and deformations that make normal functioning impossible.

Cells with progeria also have misshapen and defective mitochondria, which are the small organelles that produce energy for the cell. Although previous studies suggested damage to mitochondria in progeria cells, the current study is the first to document the nature and extent of this damage in detail. Cao and her colleagues found that a majority of the mitochondria in progeria cells become swollen and fragmented, making it impossible for the defective mitochondria to function.

The team found that methylene blue reverses the damages to both the nucleus and mitochondria in progeria cells remarkably well. The precise mechanism is still unclear, but treating the cells with the chemical effectively improved every defect,

causing progeria cells to be almost indistinguishable from normal cells. Cao and her colleagues also tested methylene blue in healthy cells allowed to age normally. The normal aging process degrades mitochondria over time, causing these older mitochondria to resemble the mitochondria seen in progeria cells. Once again, methylene blue repaired these damages.

"We have repeated these experiments many times and have not seen a single one fail," said Zheng-Mei Xiong, lead author on the study and a postdoctoral associate in the UMD Department of Cell Biology and Molecular Genetics. "This is such an exciting result with so much potential, both for progeria and normal aging. Methylene blue is common and inexpensive. It is fully water soluble and non-toxic. People use it to clean fish tanks because it is so safe for the fish eggs."

Because methylene blue can repair the cell defects that ultimately lead to whole-body symptoms in progeria patients, Cao, Xiong and their colleagues believe methylene blue could be used as a treatment for the disease in the future. Similarly, methylene blue could show promise as an over-the-counter treatment for the symptoms of normal aging, perhaps as an additive to cosmetic products or nutritional supplements.

Cao and her team are moving quickly to complete the next crucial step: testing in animal models. "So far, we have done all of our work in stem cell lines. It is critical to see whether the effect extends to whole animals," Cao explained. "We also want to see if methylene blue can repair specific effects of progeria in various cell types, such as bone, skin, cardiovascular cells and others. Further down the line, other groups might begin human clinical trials. It's very exciting."

This research was supported by the National Institutes of Health's National Human Genome Research Institute (Award Nos R01HG007104 and R21AG043801). The content of this article does not necessarily reflect the views of this organization.

*The research paper, "Methylene blue alleviates nuclear and mitochondrial abnormalities in progeria," Zheng-Mei Xiong, Ji Young Choi, Kun Wang, Haoyue Zhang, Zeshan Tariq, Di Wu, Eunae Ko, Christina LaDana, Hiromi Sesaki and Kan Cao, was published online in the journal *Aging Cell* on December 10, 2015.*

http://www.eurekalert.org/pub_releases/2015-12/b-mdl120815.php

Moderate drinking linked to reduced risk of death in early stage Alzheimer's disease

Death rates lower among those totting up 2-3 daily units than among drinkers of more or fewer

Drinking 2 to 3 units of alcohol every day is linked to a reduced risk of death among people with early stage Alzheimer's disease, finds research published in the online journal *BMJ Open*. Moderate drinking has been associated with a lower risk of developing and dying from heart disease and stroke. But alcohol is known

to damage brain cells, and given that dementia is a neurodegenerative disorder, drinking might be harmful in those with the condition.

The researchers therefore wanted to find out if the same potentially positive association between alcohol and a reduced risk of cardiovascular death could be applied to 321 people with early stage Alzheimer's disease, defined as a score of 20 or less on the Mini Mental State Exam (MMSE).

The research team analysed data originally collected on 330 people with early stage dementia or Alzheimer's disease and their primary carers from across Denmark as part of the Danish Alzheimer's Intervention Study (DAISY).

DAISY set out to assess the impact of a 12 month programme of psychosocial counselling and support, and tracked progress for three years afterwards, accumulating a considerable amount of data.

This included information on how much alcohol people with early stage dementia or Alzheimer's drank every day. Around one in 10 (8%) drank no alcohol and at the other end of the scale, around one in 20 (4%) drank more than 3 units daily.

Most of the sample (71%) drank 1 or fewer units a day; 17% drank 2-3 units.

During the monitoring period, 53 (16.5%) of those with mild Alzheimer's disease died. Consumption of 2-3 units of alcohol every day was associated with a 77% lowered risk of death compared with a tally of 1 or fewer daily units. There was no significant difference in death rates among those drinking no alcohol or more than 3 units every day compared with those drinking 1 or fewer daily units.

These results held true after taking account of influential factors: gender, age, other underlying conditions, whether the individual lived alone or with their primary carer, educational attainment, smoking, quality of life, and MMSE result.

The researchers say there could be several explanations for the findings, including that people who drink moderately have a richer social network, which has been linked to improved quality, and possibly length, of life.

Another explanation may lie in the fact that the seemingly protective effect of alcohol may have been caused by reverse causality, whereby those drinking very little alcohol were in the terminal phase of their life, which would have artificially inflated the positive association. In a bid to correct for this, the researchers re-analysed the data, omitting the first year of monitoring. But this made no difference to the findings.

"The results of our study point towards a potential, positive association of moderate alcohol consumption on mortality in patients with Alzheimer's disease. However, we cannot solely, on the basis of this study, either encourage or advise against moderate alcohol consumption in [these] patients," they caution. They suggest that further research looking at the impact of alcohol on cognitive decline

and disease progression in patients with mild Alzheimer's disease would be particularly informative.

<http://bit.ly/1I2XBxR>

Road map of awareness could help us rouse unconscious people

The road map of conscious awareness has been deciphered.

Now that we know which brain pathways control whether someone is awake or unconscious, we may be able to rouse people from a vegetative or minimally conscious state.

In 2007, researchers used deep brain stimulation to wake a man from a minimally conscious state. It was quite remarkable, says [Jin Lee](#) at Stanford University in California. The 38-year-old had suffered a severe brain injury in a street mugging six years earlier. Before his treatment he was unable to communicate and had no voluntary control over his limbs. When doctors stimulated his thalamus – a central hub that sends signals all around the brain – his speech and movement gradually returned.

However, attempts to [treat other people in a similar way have failed](#). The problem lies with the crudeness of the technique. "Deep brain stimulation is done without much knowledge of how it actually alters the circuits in the brain," says Lin.

The technique involves attaching electrodes to the brain and using them to stimulate the tissue beneath. Unfortunately, the electrodes can also stimulate unintended areas, which means it is hard to work out exactly what is happening in people's brains.

Black box

"There are a lot of fibres and different cells in the thalamus and working out what was going on in the brain was very difficult," says Lin. "So we wanted to figure it out." Lin and her team used a tool called optogenetics to stimulate specific groups of cells in the thalamus of mice. This meant inserting light responsive genes into cells so that they can be activated with light. This enabled the researchers to stimulate the brain in a similar way to deep brain stimulation while having complete control over what was going on.

They found that activating excitatory cells in the thalamus with a frequency of 10 hertz made the mice lose consciousness; stimulating them with 40 to 100 hertz woke them up again.

This was puzzling – how could stimulation of the same cells lead to such dramatic differences in arousal? To find out, the team used fMRI to look at what was happening elsewhere in the brain. They discovered that high frequency stimulation caused widespread activation of the cortex, which in turn, roused the mice. Low frequency stimulation damped down this activation, making the animals unconscious.

On/off switch

An area called the zona incerta, which connects the cortex and the thalamus, seemed to act as gatekeeper. The zona incerta contains inhibitory cells that suppress the cortex, but only when they receive stimulation from the thalamus at 10 hertz. Higher frequency stimulations deactivated the zona incerta, depressing the inhibitory cells and opening the way for activation of the cortex so the mouse could wake up.

Lin says that if the thalamus is not communicating with different parts of the brain, or is firing at the wrong frequency, then you would lose consciousness. “It’s pretty incredible, this one node has this active switching capability in how it turns on and off awareness,” she says.

Now that the team know which pathways need to be switched on and how to do it, they are planning on trying it on people with traumatic brain injuries.

[Anil Seth](#), co-director of the Sackler Centre for Consciousness Science in Brighton, UK, says the work certainly has the potential to help design better treatments for people in a vegetative or minimally conscious state.

Unwise assumption

“This is a very important paper,” says [Mohamad Koubeissi](#) at the George Washington University School of Medicine and Health Sciences in Washington DC. Koubeissi recently [switched off awareness](#) in a woman undergoing treatment for epilepsy by stimulating her claustrum – an area of the brain that communicates with the thalamus. He says Lin’s team have done unique work and the results need to be considered by anyone doing brain stimulation. “Whatever therapeutic response we are trying to test, it is important to assess the response of activating that structure across many frequencies.”

Classical deep brain stimulation often uses high frequency stimulation because it works for certain conditions, he says. Researchers tend to extrapolate from that and tend to favour high frequencies over low frequencies when designing new treatments. “Now we know better.”

Journal reference: *eLife*, DOI: [10.7554/eLife.09215](https://doi.org/10.7554/eLife.09215)

<http://nyti.ms/1J6griJ>

Giving Directions? Start With a Landmark

There are many ways to give directions, but some formats are more effective than others, according to a new study.

By SINDYA N. BHANOO DEC. 11, 2015

The report, which appears in *Frontiers in Psychology*, finds that order matters: Identifying a hidden person in a picture is generally easier [when a landmark is mentioned first](#). The study was done in two parts. In the first, the researchers asked volunteers to focus on a human figure hidden in a cluttered image taken

from a “Where’s Waldo?” children’s book. The volunteers then had to describe how to find that figure quickly. Most began by describing a prominent feature in the background of the image, providing directions to the figure from there.

“Almost always, people were likely to use a landmark as part of their directions,” said [Micha Elsner](#), a linguist at Ohio State University and one of the study’s authors. “And if the landmark was larger than the target object, they were more likely to put it first.” Only when the target was comparatively easy to find did the volunteers mention it first, Dr. Elsner said.

In the second part of the study, the researchers asked 31 participants to listen to directions about the location of human figures on a “Where’s Waldo?” page.

Generally, when participants heard a highly visible landmark mentioned first and the target second, they needed less time to find the object or figure than those who heard the description in the reverse order.

<http://nyti.ms/1Rjxqpo>

Fewer Young People Are Drinking and Driving, Study Says
Far fewer young Americans are drinking and driving than they once did, according to a new survey, even as vehicle accidents remain their No. 1 killer.

By MIKE McPHATE DEC. 11, 2015

Comparing data from 2002 and 2014, government researchers discovered a 59 percent drop in drinking and driving among 16- to 20-year-olds. For adults between 21 and 25, the decline was 38 percent.

“It’s very encouraging,” said Dr. Alejandro Azofeifa, an author of the study published Thursday in the *Morbidity and Mortality Weekly Report* from the Centers for Disease Control and Prevention.

Dr. Azofeifa offered three likely explanations: an overall drop in drinking among young people, aggressive law enforcement steps like roadside testing and “a lot of prevention efforts” at schools across the country.

Even with the declines, the numbers suggest there still were a lot of dangerous young motorists on the road last year. Nearly one in five people between the ages of 21 and 25 acknowledged drinking and driving. Among 16- to 20-year olds, they were far fewer, about one in 15.

The study relied on data from more than 380,000 respondents to the federal government’s annual National Survey on Drug Use and Health. Young people were asked during in-person interviews to report their use of alcohol and other drugs over the past 12 months.

As the study notes, vehicle accidents are the leading cause of death among young people. In 2013, more than 2,000 people between the ages of 16 and 19 were killed on American roads — or about six a day, according to the C.D.C.

J. T. Griffin, a lobbyist with Mothers Against Drunk Driving, welcomed the latest findings, attributing at least part of the improvement to education efforts. "We are encouraged by the news," he said, "but there are still too many people dying of drunk driving every year."

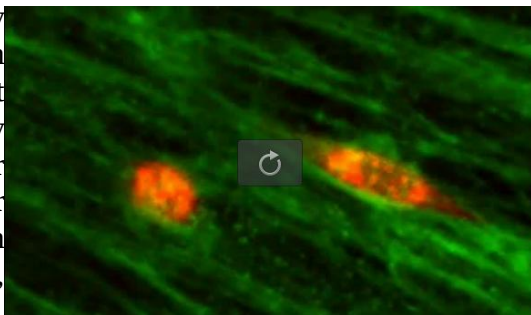
http://www.eurekalert.org/pub_releases/2015-12/asfc-ccc120715.php

Cancer cell collaborators smooth the way for cancer cells to metastasize

At ASCB 2015: Cancer cell collaborators unmasked

At ASCB 2015, Vanderbilt researchers show how metastasizing tumors use non-cancerous fibroblasts to make a migration highway through surrounding extracellular matrix.

To get moving, metastasizing cancer needs to enlist non-cancerous collaborators. Suspicions about where these secret cancer allies might be lurking have long been directed at the fibroblasts, the cells that secrete and organize the extracellular matrix (ECM), the ground on which surrounding cells can get a grip. Increasing evidence suggests that fibroblasts near growing tumors are actively assisting cancer cells in spreading locally and metastasizing elsewhere. But exactly how these cancer-associated fibroblasts (CAFs) provide aid to the cancer enemy was not known until a recent discovery by Begum Erdogan and colleagues in Donna Webb's lab at Vanderbilt University--CAFs clear a highway through the ECM for migrating cancer cells. The researchers will present their work at ASCB 2015 in San Diego on Sunday, December 13 and Tuesday, December 15.



Red labeled JHU12 head and neck carcinoma cells are migrating on CAF-derived extracellular matrix (green). Images were taken every 10 minutes for 3 hours using a confocal microscope. Begum Erdogan & Donna Webb, Vanderbilt University

The roadway that CAFs arrange is made of parallel fibers of fibronectin (Fn), a major protein in the ECM mix secreted by all fibroblasts. The Vanderbilt researchers observed CAFs rearranging Fn into parallel bundles instead of the dense mesh that normal tissue fibroblasts (NAFs) make. Taking cancer cells grown from prostate as well as head and neck tumors, the researchers plated them on ECM from CAFs and NAFs. The cancer cells on the CAF matrix were better at moving in a single direction.

But why? CAFs rearrange the matrix into a road because they get a better grip on Fn fibers, the researchers discovered. Using traction force microscopy, they were

able to measure the difference. CAFs were stronger than NAFs because they were better at delivering force from the motor protein, myosin II, through connectors called integrins to Fn fibers. CAFs had higher levels of a Fn-binding integrin plus a switched-on GTPase called Rac, which is critical to cell movement. Inhibiting myosin-II activity with a drug deprived CAFs of their super traction powers and the ECM reverted to its normal disorder. These results solve a longstanding puzzle about cancer metastasis and point to the matrix as a possible target for drugs to stop cancer in its tracks.

Cancer-associated fibroblasts promote directional migration of cancer cells via parallel organization of the fibronectin matrix

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http://www.eurekalert.org/pub_releases/2015-12/jhu-rtc121015.php

Research traces cause of organ dysfunction in Down syndrome Johns Hopkins scientists find overload of one gene hinders peripheral nervous system

While most Down syndrome research has focused on the brain, a new report by Johns Hopkins University biologists uncovers how the disorder hampers a separate part of the nervous system that plays a key role in health and longevity. The paper, to be published Dec. 14 in the journal *Nature Communications*, traces complex biochemical signals leading to peripheral nervous system dysfunction found in people with Down syndrome.

Down syndrome is a genetic condition characterized by impaired physical and cognitive development. The peripheral nervous system has no known role in intellectual ability, but it does regulate organ function including heartbeat, blood pressure and blood glucose. Peripheral nervous system impairment could contribute to heart disease, diabetes and immune disorders that are associated with Down syndrome.

One of the most common genetic disorders, Down syndrome is caused by the appearance of a third copy of chromosome 21. It appears in one of nearly every 700 babies born in the United States; roughly 400,000 Americans are estimated to have the disorder. Scientists studying the condition have mostly concentrated on the central nervous system, but Rejji Kuruvilla, an associate professor in the Johns Hopkins University Department of Biology, said that leaves out a lot.

"There's been a whole aspect of the nervous system that has been ignored in Down syndrome, and perhaps in other neurological disorders" said Kuruvilla, the

co-author of the Nature Communications paper who runs the lab where the research was conducted. The lead author among eight collaborators is Ami Patel, who has since moved to Northwestern University after earning her doctorate in biology at Johns Hopkins.

While the connection between Down syndrome - one of the most common genetic conditions - and peripheral nervous system disease has been known for some time, the phenomenon has not been understood at the molecular and cellular level. Kuruvilla's lab pursued the question by examining both mice engineered to approximate a human Down syndrome genetic profile and human organ tissues from Down syndrome infants.

In the mice and in human pancreatic and spleen tissue, the scientists found stunted peripheral nerve growth early in life. The question was why.

The research focused on nerve growth factor, or NGF, a protein identified in the 1950s - the two scientists who made the discovery later won a Nobel Prize - that regulates peripheral nervous system development.

Kuruvilla's lab group - which has been studying the peripheral nervous system for years - found that abundance of a particular gene product in Down syndrome puts a brake on NGF's actions in fostering nerve development.

The culprit emerged as a gene, RCAN1, which in Down syndrome appears in three times the number that would be found in normal chromosomes. This gene regulates a protein, calcineurin, that enables NGF to stimulate nerve growth and also support neuron survival. In a mouse model, tripling RCAN1 alone caused the loss of neurons and nerve growth; reducing the extra dose of RCAN1 improved survival of neurons and nerve development.

In other words, too much RCAN1 results in not enough calcineurin activity. Insufficient calcineurin activity leads to impeded NGF functions and, thus, impaired peripheral nervous system development. Kuruvilla said the finding raises other questions that her lab plans to pursue. One is how RCAN1 affects neurons in a portion of the brain called the basal forebrain, which also responds to NGF. That brain area deteriorates in Alzheimer's disease patients.

And there is the question of possible treatments, given the array of medical conditions including cardiovascular problems and hypertension associated with peripheral nervous system dysfunction in individuals with Down syndrome. "When you think about therapeutic interventions that could affect life quality, it's important to not ignore this important aspect of the nervous system," Kuruvilla said.

This research was supported by National Institutes of Health grant NS073751 and by NIH training grant T32GM007231.

<http://www.bbc.com/news/business-35090087>

Australia pulls Nurofen products over 'misleading claims' **An Australian court has ordered products in the Nurofen pain relief range off the shelves, saying the UK-based manufacturer misled consumers.**

The court said products marketed to treat specific pains, such as migraines, were identical to one another. Research also found the products were sold for almost double the price of Nurofen's standard product.

Manufacturer Reckitt Benckiser said the case related only to Australia. It said the ruling would not be applicable in other countries, including the UK. Reckitt Benckiser said it would comply with the Australian court order and that it "did not set out to mislead consumers".



The products affected by the court order include Nurofen Back Pain, Nurofen Period Pain, Nurofen Migraine Pain and Nurofen Tension Headache Reuters

The products affected by the order include Nurofen Back Pain, Nurofen Period Pain, Nurofen Migraine Pain and Nurofen Tension Headache.

The watchdog said the court had found each product "was formulated to treat a particular type of pain; and solely or specifically treated a particular type of pain" - but that each product contained the same active ingredient, ibuprofen lysine 342mg. However the products were found to be "no more effective at treating the type of pain described on its packaging than any of the other Nurofen specific pain products."

Australia's consumer watchdog brought the matter to court earlier this year.

The Federal Court of Australia said the products must be taken off Australian shelves within three months.

The retail price for each of the pain-specific products was also found to be "significantly higher than that of other comparable analgesic products which also act as general pain relievers," the Australian Competition and Consumer Commission (ACC) said.

Reckitt Benckiser is a British-based consumer goods manufacturer and makes products including Nurofen, Dettol and Harpic, among others. It has been ordered to publish correction notices in newspapers and on its website and to pay the ACC's court costs.

This story has been amended to clarify that the products in question were different from the standard Nurofen product.