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Discovery of a new drug target could lead to novel treatment for severe autism

Penn State University scientists have discovered a novel drug target and have rescued functional deficits in human nerve cells derived from patients with Rett Syndrome, a severe form of autism-spectrum disorder.

The research, led by Gong Chen, professor of biology and the Verne M. Willaman Chair in Life Sciences at Penn State, could lead to a new treatment for Rett Syndrome and other forms of autism-spectrum disorders. A paper describing the research will be published on January 4, 2016 in the online Early Edition of the journal Proceedings of the National Academy of Sciences.

"The most exciting part of this research is that it directly uses human neurons that originated from Rett Syndrome patients as a clinically-relevant disease model to investigate the underlying mechanism," said Dr. Chen. "Therefore, the new drug target discovered in this study might have direct clinical implication in the treatment of Rett Syndrome and potentially for other autism-spectrum disorders as well."

The researchers differentiated stem cells derived from the skin cells of patients with Rett Syndrome into nerve cells that could be studied in the laboratory. These nerve cells carry a mutation in the gene MECP2, and such gene mutations are believed to be the cause of most cases of Rett Syndrome. The researchers discovered that these nerve cells lacked an important molecule, KCC2, that is critical to normal nerve cell function and brain development.

"KCC2 controls the function of the neurotransmitter GABA at a critical time during early brain development," Chen said. "Interestingly, when we put KCC2 back into Rett neurons, the GABA function returns to normal. We therefore think that increasing KCC2 function in individuals with Rett Syndrome may lead to a potential new treatment."

The researchers also showed that treating diseased nerve cells with insulin-like growth factor 1 (IGF1) elevated the level of KCC2 and corrected the function of the GABA neurotransmitter. IGF1 is a molecule that has been shown to alleviate symptoms in a mouse model of Rett Syndrome and is the subject of an ongoing phase-2 clinical trial for the treatment of the disease in humans.

"The finding that IGF1 can rescue the impaired KCC2 level in Rett neurons is important not only because it provides an explanation for the action of IGF1," said Xin Tang, a graduate student in Chen's Lab and the first-listed author of the paper, "but also because it opens the possibility of finding more small molecules that can act on KCC2 to treat Rett syndrome and other autism spectrum disorders."

In addition to Chen and Tang, the research team also includes Julie Kim, Li Zhou, Lei Zhang, and Zheng Wu at Penn State; Eric Wengert at Bucknell University; Carol Marchetto and Fred Gage at the Salk Institute for Biological Studies; and Cassiano Carromeu and Alysson Muotri at the University of California - San Diego.

The research was funded by grants from National Institutes of Health (MH083911 and AG045656) and a Stem Cell Fund from the Penn State Eberly College of Science.

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The first European farmers are traced back to Anatolia DNA from Anatolian remains indicates the importance of the role Anatolia played in spread of farming through Europe

When farming spread throughout Europe some 8,000 years ago, Anatolia functioned as a hub, spreading genes and the new ideas westward. An international study coordinated from Stockholm and based on DNA from Anatolian remains indicates the importance of the role Anatolia played, and also in attracting attention both from the east and the west.

Human material from the Anatolian site Kumtepe was used in the study. The material was heavily degraded, but yielded enough DNA for the doctorate student Ayca Omrak to address questions concerning the demography connected to the spread of farming. She conducted her work at the Archaeological Research Laboratory.

"I have never worked with a more complicated material. But it was worth every hour in the laboratory. I could use the DNA from the Kumtepe material to trace the European farmers back to Anatolia. It is also fun to have worked with this material from the site Kumtepe, as this is the precursor to Troy", says doctorate student Ayca Omrak, at the Archaeological Research Laboratory Stockholm University.

Jan Storå, associate professor in osteoarchaeology and coauthor to the study agrees with Ayca. The results confirm Anatolia's importance to Europe's cultural history. He also thinks that material from the area needs to be researched further.

"It is complicated to work with material from this region, it is hot and the DNA is degraded. But if we want to understand how the process that led from a hunter-gatherer society proceeded to a farming society, it is this material we need to exhaust", says Jan Storå, associate professor in osteoarchaeology, Stockholm University.

Anders Götherström who heads the archaeogenetic research at the Archaeological Research Laboratory agrees that this study indicates further possibilities:

"Our results stress the importance Anatolia has had on Europe's prehistory. But to fully understand how the agricultural development proceeded we need to dive deeper down into material from the Levant. Jan is right about that."

The archaeogenetic group in Stockholm is presently advancing its collaboration with colleagues in Anatolia and Iran.

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Higher monthly doses of vitamin D associated with increased risk of falls

Higher monthly doses of vitamin D were associated with no benefit on low extremity function and with an increased risk of falls in patients 70 or older in a randomized clinical trial, according to an article published online by JAMA Internal Medicine.

Lower extremity function that is impaired is a major risk factor for falls, injuries and a loss of autonomy. Vitamin D supplementation has been proposed as a possible preventive strategy to delay functional decline. However, definitive data are lacking.

Heike A. Bischoff-Ferrari, M.D., Dr.P.H., of the University Hospital Zurich, Switzerland, and coauthors conducted a one-year, randomized clinical trial that include 200 men and women 70 or older with a prior fall.

Participants were divided into three study groups: 67 people in a low-dose control group who received 24,000 IU of vitamin D3 per month; 67 people who received 60,000 IU of vitamin D3 per month; and 66 people who received 24,000 IU of vitamin D3 plus calcifediol per month. The study measured improvement in lower extremity function, achieving 25-hydroxyvitamin D levels of at least 30 ng/mL at six and 12 months, and reported falls.

The authors report:

Of the 200 participants, 58 percent were vitamin D deficient at baseline

Doses of 60,000 IU and 24,000 IU plus calcifediol were more likely to result in 25-hydroxyvitamin D levels of at least 30 ng/mL but they were associated with no benefit on lower extremity function

Of the 200 participants, 60.5 percent (121 of 200) fell during the 12-month treatment period

The 60,000 IU and 24,000 IU plus calcifediol groups had higher percentages of participants who fell (66.9 percent and 66.1 percent, respectively) compared with the 24,000 IU group (47.9 percent)

The 60,000 IU and 24,000 IU plus calcifediol groups had a higher average number of falls (1.47 and 1.24, respectively) compared with the 24,000 IU group (0.94)

"Compared with a monthly standard-of-care dose of 24,000 IU of vitamin D3, two monthly higher doses of vitamin D (60,000 IU and 24,000 IU plus calcifediol) conferred no benefit on the prevention of functional decline and increased falls in seniors 70 years and older with a prior fall event. Therefore, high monthly doses of vitamin D or a combination of calcifediol may not be warranted in seniors with

a prior fall because of a potentially deleterious effect on falls. Future research is needed to confirm our findings for daily dosing regimens," the study concludes.

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Available pre-embargo to the media at <http://media.jamanetwork.com>

Commentary: Vitamin D Supplementation, Increased Risk of Falling

"The strategy of supplementation with vitamin D to achieve serum levels of at least 30 ng/mL has not been established by RCTs [randomized clinical trials] to reduce the risk of falls and fractures. It may increase the risk of falling. Until that approach is supported by randomized trials with updated meta-analyses, it would be prudent to follow recommendations from the Institute of Medicine (IOM) that people 70 years or older have a total daily intake of 800 IU of vitamin D without routine measurement of serum 25 (OH)D levels. It is prudent to get recommended intakes of vitamin D and other vitamins from a balanced diet with foods that naturally contain what is manufactured into supplements," writes Steven R. Cummings, M.D., of the California Pacific Medical Center Research Institute, San Francisco, and coauthors.

JAMA Intern Med. Published online January 4, 2016. doi:10.1001/jamainternmed.2015.6994.

Available pre-embargo to the media at <http://media.jamanetwork.com>

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Students with influence over peers reduce school bullying by 30 percent

Curbing school bullying has been a focal point for educators, administrators, policymakers and parents, but the answer may not lie within rules set by adults, according to new research led by Princeton University.

PRINCETON, N.J.- Instead, the solution might actually be to have the students themselves, particularly those most connected to their peers, promote conflict resolution in school.

A team of researchers from Princeton, Rutgers University and Yale University engaged groups of influential students in 56 New Jersey middle schools to spread messages about the dangers of bullying and school conflict. Using messaging platforms such as Instagram, print posters and colorful wristbands, the selected students were encouraged to discuss in their own voices positive ways to handle conflict, using terms with which their peers could identify.

The research team wanted to test whether certain students, who they label "social referents" or social influencers, have an outsized influence over school climate or the social norms and behavioral patterns in their schools. Social referents are not necessarily the most popular kids school-wide, but rather students who demonstrate influence within their smaller peer group. All activities were

designed to test whether, by making their anti-conflict stance well known, these social influencers could shape their peers' behaviors and social norms.

In the course of a year, the middle schools that employed social referents saw a 30 percent reduction in student conflict reports, the researchers report in the Proceedings of the National Academy of Sciences (PNAS). Critically, the greatest drop in conflict was observed among the teams with the highest proportion of social influencers, supporting the researchers' hypothesis that these students do exert an outsized influence over school climate.

"We designed our own curriculum because current programs address problems as defined by adults, and they aren't necessarily fitted to each individual school environment," said lead author Elizabeth Levy Paluck, associate professor of psychology and public affairs at Princeton's Woodrow Wilson School of Public and International Affairs. "We think the best way to change social norms is to have these student influencers speak in their own voices. Encouraging their own messages to bubble up from the bottom using a grassroots approach can be very powerful."

Peers influencing peers is a widely accepted concept. But the question of whether certain, more influential peers have more influence on social norms governing a group is what spurred Paluck and her colleagues to design their test program, the Roots program.

This program is designed to engage the school's most influential students, only some of whom fit the typical profile of a student leader or a popular student, to spread anti-conflict messages. Using a survey measurement known as social network mapping, the researchers are able to identify students with the most connections to other students, both in person and online. These students serve as the "roots" to influence perceptions and social norms in schools.

"The real innovation here is using student social networks to choose the peers ... which can lead to a less unorthodox group of student leaders," Paluck said. "When adults choose student leaders, they typically pick the 'good' kids. But the leaders we find through social network mapping are influential among students and are not all the ones who would be selected by adults. Some of the students we find are right smack in the center of student conflicts. But the point is, these are the students whose behavior gets noticed more."

During the 2012-13 school year, Paluck and study co-authors Hana Shepherd from Rutgers University and Peter Aronow from Yale University were able to implement the study into middle schools across New Jersey. The timing was paramount. Just a year prior, Governor Chris Christie signed a bill issuing a law that required all teachers to have anti-bullying training. The bill was passed without funding.

This gave Paluck, Shepherd and Aronow a chance to offer their program as a training solution. With encouragement from the State Department of Education, they implemented the program in volunteer middle schools, as they were seeing higher rates of student conflict than high schools.

For the purposes of the experiment, half of the middle schools were randomly assigned to receive the intervention, which was training through the Roots program. The schools not selected were given the opportunity to receive free training on how to run the program at the end of the school year.

To pinpoint the most influential students, the researchers distributed a survey to the 24,191 students enrolled at all schools. The survey asked them to nominate the top 10 students at their school who they chose to spend time with, either in or outside of school, or face to face or online. Using these data, the researchers then mapped each school's social networks.

A representative sample of 22 to 30 students in the intervention schools was invited to participate in the Roots program. Only the researchers knew which students within each group were expected to be the top influencers, based on the fact that they were in the top 10 percent of students at their school nominated by their peers in the survey.

These students had some important shared traits, the researchers found. Many had an older sibling, were in dating relationships and received compliments from peers on the house in which they lived.

"This cluster of characteristics suggests that these students are hooked into more mature social patterns in their lives and at schools," Paluck said. "Earlier dating is one indicator, and an older sibling suggests they have more exposure to older students with a more mature vocabulary, perhaps making them savvier communicators. Receiving compliments on their house was a way for us to evaluate their socioeconomic background."

Once the sample of students was selected, they were invited, but not required, to attend Roots training sessions, held during convenient school hours. More than half showed up regularly. The researchers provided students with templates for campaign materials, both print and online, which the students were able to customize. They also trained students in dealing with student conflict.

"We wanted to distinguish ourselves from other school campaigns by letting students lead the messaging efforts. We even wanted the aesthetics of the program to look different," Paluck said. "So we put a lot of value into very clean sharp designs and bright colors. We gave them the templates to work with, and they controlled the messaging."

Throughout the year, the students launched several messaging campaigns. One entailed using hashtags such as "#iRespect" on Instagram, which represented

tolerance and conflict resolution. Students printed the hashtags on bright colored paper, which they signed and hung around school, highlighting which students were involved in the effort.

Another campaign used brightly colored rubber wristbands, which remain very popular among adolescents, Paluck said. These orange wristbands included the Roots program logo and came with a tag that said, "A Roots student caught you doing something great." Each Roots student received 20 wristbands and when the student saw a peer intervening in a conflict or helping another student, he or she gave them a wristband.

Among the most popular campaigns was Roots Day, a one-day festival in which students promoted Roots through posters, other multicolored and Roots-themed wristbands, and even the T-shirts they wore. There were giveaways, and students asked others to sign a petition to do something nice for someone at school.

"Roots Day made the Roots program and the Roots students enormously salient to all of the other students at each school," Paluck said. "Students loved the giveaways and were clamoring to sign the petition. It brought everyone in the school together and seemed to unify their attention and energies in a big way."

After this yearlong effort, the authors found stark statistical differences between the schools that had participated versus those that hadn't. On average, schools participating in the program saw a 30 percent reduction in disciplinary reports. Because each conflict can take up to an hour to resolve, this reduction is equivalent to hundreds of saved hours.

"Our program shows that you don't need to use a blanket treatment to reduce bullying," Paluck said. "You can target specific people in a savvy way in order to spread the message. These people -- the social referents you should target -- get noticed more by their peers. Their behavior serves as a signal to what is normal and desirable in the community. And there are many ways to figure out who those people are and work with them to inspire positive change."

The paper, "Changing climates of conflict: A social network experiment in 56 schools," was published in PNAS Early Edition on Jan. 4. Funding for this project came from the WT Grant Foundation Scholars Program, the Canadian Institute for Advanced Research, Princeton Educational Research Section, Russell Sage Foundation, the National Science Foundation and the Spencer Foundation. None of the authors are affiliated with the New Jersey school system or received compensation for this research.

The following served as intervention designers and administrators: Laura Spence-Ash, David Mackenzie, Ariel Domlyn, Jennifer Dannals and Allison Bland.

The experiment was registered at the Experiments in Governance and Politics site prior to the analysis of outcome data. The research was approved by the Princeton Institutional Review Board (Case No. 4941).

http://www.eurekalert.org/pub_releases/2016-01/uonc-sna010416.php

Social networks as important as exercise and diet across the span of our lives

UNC-Chapel Hill researchers show how social relationships reduce health risk in each stage of life

Chapel Hill, N.C. - The more social ties people have at an early age, the better their health is at the beginnings and ends of their lives, according to a new study from the University of North Carolina at Chapel Hill. The study is the first to definitively link social relationships with concrete measures of physical well-being such as abdominal obesity, inflammation, and high blood pressure, all of which can lead to long-term health problems, including heart disease, stroke and cancer.

"Based on these findings, it should be as important to encourage adolescents and young adults to build broad social relationships and social skills for interacting with others as it is to eat healthy and be physically active," said Kathleen Mullan Harris, James Haar Distinguished Professor at UNC-Chapel Hill and faculty fellow at the Carolina Population Center (CPC).

The study, published today in the Proceedings of the National Academy of Sciences, builds on previous research that shows that aging adults live longer if they have more social connections. It not only provides new insights into the biological mechanisms that prolong life but also shows how social relationships reduce health risk in each stage of life.

Specifically, the team found that the sheer size of a person's social network was important for health in early and late adulthood. In adolescence, that is, social isolation increased risk of inflammation by the same amount as physical inactivity while social integration protected against abdominal obesity. In old age, social isolation was actually more harmful to health than diabetes on developing and controlling hypertension.

In middle adulthood, it wasn't the number of social connections that mattered, but what those connections provided in terms of social support or strain. "The relationship between health and the degree to which people are integrated in large social networks is strongest at the beginning and at the end of life, and not so important in middle adulthood, when the quality, not the quantity, of social relationships matters," Harris said.

Harris and her team drew on data from four nationally representative surveys of the U.S. population that, together, covered the lifespan from adolescence to old age. They evaluated three dimensions of social relationships: social integration, social support and social strain. They then studied how individual's social

relationships were associated with four markers shown to be key markers for mortality risk: blood pressure, waist circumference, body mass index and circulating levels of C-reactive protein, which is a measure of systemic inflammation.

One of the four nationally representative surveys was part of The National Longitudinal Study of Adolescent to Adult Health, or Add Health, the largest, most comprehensive data researchers use to study how social relationships, behavior, environment and biology interact to shape health in adolescence and influence well-being throughout adulthood.

"We studied the interplay between social relationships, behavioral factors and physiological dysregulation that, over time, lead to chronic diseases of aging -- cancer being a prominent example," Yang Claire Yang, a professor at UNC-Chapel Hill, CPC fellow and a member of the Lineberger Comprehensive Cancer Center. "Our analysis makes it clear that doctors, clinicians, and other health workers should redouble their efforts to help the public understand how important strong social bonds are throughout the course of all of our lives."

The National Institutes of Health and the University Cancer Research Funds at the Lineberger Cancer Center funded the study.

http://www.eurekalert.org/pub_releases/2016-01/miot-sbe010516.php

Study: Bacteria, electrons spin in similar patterns

Bacteria streaming through a lattice behave like electrons in a magnetic material

There are certain universal patterns in nature that hold true, regardless of objects' size, species, or surroundings. Take, for instance, the branching fractals seen in both tree limbs and blood vessels, or the surprisingly similar spirals in mollusks and cabbage.

Now scientists at MIT and Cambridge University have identified an unexpected shared pattern in the collective movement of bacteria and electrons: As billions of bacteria stream through a microfluidic lattice, they synchronize and swim in patterns similar to those of electrons orbiting around atomic nuclei in a magnetic material.

The researchers found that by tuning certain dimensions of the microfluidic lattice, they were able to direct billions of microbes to align and swim in the same direction, much the way electrons circulate in the same direction when they create a magnetic field. With slight changes to the lattice, groups of bacteria flowed in opposite directions, resembling electrons in a nonmagnetic material.

Surprisingly, the researchers also identified a mathematical model that applies to the motions of both bacteria and electrons. The model derives from a general lattice field theory, which is typically used to describe the quantum behavior of

electrons in magnetic and electronic materials. The researchers reduced this complex model to a much simpler, "textbook" model, which predicts that a phase transition, or a change in flow direction, should occur with certain changes to a lattice's dimensions -- a transition that the team observed in their experiments with bacteria.

"It's very surprising that we see this universality," says Jörn Dunkel, assistant professor of applied mathematics at MIT. "The really nice thing is, you have a living system here that shows all these behaviors that people think are also going on in quantum systems." Dunkel and his colleagues at Cambridge University -- Hugo Wioland, Francis Woodhouse, and Raymond Goldstein '83 -- published their results yesterday in the journal *Nature Physics*.

Guiding bacterial surfaces

Dunkel first began looking into the swimming patterns of bacteria as a postdoc with the Cambridge University group led by Goldstein. The researchers were exploring how to manipulate bacterial flow, as a way to prevent biofilms -- dense layers of microbial slime that can take over shower stalls, clog filtration systems, and cling to ship hulls.

"We were generally interested in how microbes like bacteria interact with surfaces individually and collectively, and how might surfaces guide microorganisms," Dunkel says.

In initial experiments, the researchers placed bacteria in progressively smaller pools, or wells, and observed their swimming patterns. In larger wells, the microbes tended to swim in relative disorder. In much smaller wells, measuring about 70 microns wide, thousands of bacteria began to behave in orderly way, swimming in a spiral, in the same direction within the well, for long periods of time.

Against the current

In the new study, the researchers observed bacteria flowing through an interconnected array of these small wells. Made of a transparent, rubber-like polymer, the lattice is composed of 100 wells, each measuring 70 microns and connected to its neighbors by a small channel. They injected bacteria into the array and observed the direction in which bacteria flowed within each well.

Dunkel and his colleagues found that they were able to manipulate the bacteria's flow by changing one key dimension: the diameter of the connecting channels, or what they call gap size. If the gap was too small, bacteria in one well would spiral in the opposite direction from their neighbors in the adjacent well, like the alternating circulation of electrons in a nonmagnetic material. If, however, the gap size was 8 microns or larger, the researchers observed a phase transition, in which

bacteria in every well synchronized, flowing in the same direction, like aligned electrons in a magnetic field.

Examining this phase transition more closely, the researchers found that a larger gap size allows more bacteria to flow from one well to a neighboring well. This movement of bacteria between wells creates an "edge current," or a flow of bacteria at the edges of each well, which in turn induces bacteria in the well's interior to flow against it. The overall result is that the majority of bacteria within each well flow in the same direction, opposite to the edge currents.

Modeling collective motion

To see whether the similar motions of bacteria and electrons bear out mathematically, Dunkel and his colleagues looked to lattice field theory, the model typically applied to describe the behavior of electrons in quantum systems. They reduced this more complicated model to the Ising model -- a "textbook" model used to describe the spin of electrons within a two-dimensional square lattice similar to the microfluidic lattice fabricated by the researchers.

Applying the Ising model to their physical lattice, the researchers found that the model predicted a phase transition in response to a change in one parameter, which, in this case, turned out to be gap size. Dunkel and his colleagues found that the model predictions matched their experiments in a square lattice.

The group also studied bacteria flowing through a triangular lattice -- a repeating pattern of three interconnected wells -- and found that, again, theoretical expectations matched observations. Going forward, Dunkel says he would like to explore bacterial flow in more random arrangements and environments.

"In real porous medium like soil or tissue, you don't have this very even distribution of bacteria," Dunkel says. "So how is collective motion of bacteria controlled by randomness of the medium? That's the next bigger goal."

This research was funded, in part, by an European Research Council Advanced Investigator Grant 247333 (R.G. and F. W.), EPSRC (R.G. and H.W.), an MIT Solomon Buchsbaum Fund Award and an Alfred P. Sloan Research Fellowship (J.D.).

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Twin study estimates familial risks of 23 different cancers

A large new study of twins has found that having a twin sibling diagnosed with cancer poses an excess risk for the other twin to develop any form of cancer.

Boston, MA - Among the 23 different types of cancer studied, an excess familial risk was seen for almost all of the cancers, including common cancers such as breast and prostate cancer, but also more rare cancers such as testicular cancer, head and neck cancer, melanoma, ovarian and stomach cancer.

The study, led by researchers at the Harvard T.H. Chan School of Public Health, the University of Southern Denmark, and the University of Helsinki, is the first to

provide family risk estimates for these and other rarer cancers. The study also showed, for the first time, that in twin pairs where both developed cancer, each twin often developed a different type of cancer--which suggests that, in some families, there is a shared increased risk of any type of cancer.

"Prior studies had provided familial risk and heritability estimates for the common cancers--breast, prostate, and colon--but, for rarer cancers, the studies were too small, or the follow-up time too short, to be able to pinpoint either heritability or family risk," said Lorelei Mucci, associate professor of epidemiology at Harvard Chan School and co-lead author of the study. The study will be published online January 5, 2016 in JAMA (Journal of the American Medical Association).

Familial risk of cancer is a measure of the cancer risk in an individual. The study also looked at heritability of cancer, a measure of how much of the variation in cancer risk of populations is due to genetic factors.

"Findings from this prospective study may be helpful in patient education and cancer risk counseling," said Jaakko Kaprio, from the University of Helsinki and co-senior author of the study.

The researchers looked at more than 200,000 twins, both identical and fraternal, in Denmark, Finland, Norway, and Sweden, who participated in the Nordic Twin Study of Cancer followed over an average of 32 years between 1943 and 2010. Large twin studies can help scientists assess the relative contribution of inherited factors in cancer and characterize familial cancer risk by taking into account the genetic relatedness of identical and fraternal twins.

Overall, one in three people in the study developed cancer over the course of a lifetime. Cancer was diagnosed in both twins for 3,316 of the pairs, in whom the same cancer was diagnosed among 38% of the identical twins and 26% of the fraternal twins. The researchers estimated that, when one fraternal twin was diagnosed with any cancer, the co-twin's risk of getting cancer was 37%; among identical twins, the risk jumped to 46%. One of the strongest familial risks was observed for testicular cancer. The researchers found that a man's risk of developing this disease was 12 times higher if his fraternal twin developed it, and 28 times higher if his genetically identical twin developed it.

Given the fact that fraternal twins are similar genetically to siblings who aren't twins, the finding of excess cancer risk among fraternal twin pairs can provide information about an increased cancer risk for families in which one sibling gets cancer.

The researchers also found that the heritability of cancer overall was 33%. Significant heritability was found for skin melanoma (58%), prostate cancer (57%), non-melanoma skin cancer (43%), ovarian cancer (39%), kidney cancer (38%), breast cancer (31%), and uterine cancer (27%).

"Because of this study's size and long follow-up, we can now see key genetic effects for many cancers," said Jacob Hjelmborg, from the University of Southern Denmark and co-lead author of the study.

"This study was possible given the unique databases in the four Nordic countries, and will be a future resource to solve other complex questions in cancer," said Hans-Olov Adami, adjunct professor of epidemiology at Harvard Chan School and co-senior author of the study.

Other Harvard Chan School researchers involved in the study included Rebecca Graff, David Havelick, Peter Kraft, Christina McIntosh, Elizabeth Nuttall, Kathryn Penney, Giovanni Parmigiani, and Robert Unger.

Funding for the study came from the Ellison Foundation to Harvard T.H. Chan School of Public Health and the Nordic Cancer Union.

"Familial risk and heritability of cancer among twins in Nordic countries," Lorelei A. Mucci, Jacob B. Hjelmborg, Jennifer R. Harris, Kamila Czene, David J. Havelick, Thomas Scheike, Rebecca E. Graff, Klaus Holst, Sören Möller, Robert H. Unger, Christina McIntosh, Elizabeth Nuttall, Ingunn Brandt, Kathryn L. Penney, Mikael Hartman, Peter Kraft, Giovanni Parmigiani, Kaare Christensen, Markku Koskenvuo, Niels V. Holm, Kauko Heikkilä, Eero Pukkala, Axel Skytthe, Hans-Olov Adami, Jaakko Kaprio, on behalf of the Nordic Twin Study of Cancer (NorTwinCan) collaboration. JAMA, online January 5, 2016, doi: 10.1001/jama.2015.17703.

http://www.eurekalert.org/pub_releases/2016-01/uoc--ptc010516.php

Put the cellphone away! Fragmented baby care can affect brain development

UCI study shows maternal infant-rearing link to adolescent depression

Irvine, Calif. -- Mothers, put down your smartphones when caring for your babies! That's the message from University of California, Irvine researchers, who have found that fragmented and chaotic maternal care can disrupt proper brain development, which can lead to emotional disorders later in life.

While the study was conducted with rodents, its findings imply that when mothers are nurturing their infants, numerous everyday interruptions - even those as seemingly harmless as phone calls and text messages - can have a long-lasting impact.

Dr. Tallie Z. Baram and her colleagues at UCI's Conte Center on Brain Programming in Adolescent Vulnerabilities show that consistent rhythms and patterns of maternal care seem to be crucially important for the developing brain, which needs predictable and continuous stimuli to ensure the growth of robust neuron networks. Study results appear today in *Translational Psychiatry*.

The UCI researchers discovered that erratic maternal care of infants can increase the likelihood of risky behaviors, drug seeking and depression in adolescence and adult life. Because cellphones have become so ubiquitous and users have become

so accustomed to frequently checking and utilizing them, the findings of this study are highly relevant to today's mothers and babies ... and tomorrow's adolescents and adults.

"It is known that vulnerability to emotional disorders, such as depression, derives from interactions between our genes and the environment, especially during sensitive developmental periods," said Baram, the Danette "Dee Dee" Shepard Chair in Neurological Studies.

"Our work builds on many studies showing that maternal care is important for future emotional health. Importantly, it shows that it is not how much maternal care that influences adolescent behavior but the avoidance of fragmented and unpredictable care that is crucial. We might wish to turn off the mobile phone when caring for baby and be predictable and consistent."

The UCI team - which included Hal Stern, the Ted & Janice Smith Family Foundation Dean of Information & Computer Sciences - studied the emotional outcomes of adolescent rats reared in either calm or chaotic environments and used mathematical approaches to analyze the mothers' nurturing behaviors.

Despite the fact that quantity and typical qualities of maternal care were indistinguishable in the two environments, the patterns and rhythms of care differed drastically, which strongly influenced how the rodent pups developed. Specifically, in one environment, the mothers displayed "chopped up" and unpredictable behaviors.

During adolescence, their offspring exhibited little interest in sweet foods or peer play, two independent measures of the ability to experience pleasure. Known as anhedonia, the inability to feel happy is often a harbinger of later depression. In humans, it may also drive adolescents to seek pleasure from more extreme stimulation, such as risky driving, alcohol or drugs.

Why might disjointed maternal care generate this problem with the pleasure system? Baram said that the brain's dopamine-receptor pleasure circuits are not mature in newborns and infants and that these circuits are stimulated by predictable sequences of events, which seem to be critical for their maturation. If infants are not sufficiently exposed to such reliable patterns, their pleasure systems do not mature properly, provoking anhedonia.

With her UCI team, Baram is currently studying human mothers and their infants. Video analysis of care, sophisticated imaging technology to measure brain development, and psychological and cognitive testing are being employed to more fully understand this issue. The goal is to see whether what was discovered in rodents applies to people. If so, then strategies to limit chopped-up and unpredictable patterns of maternal care might prove helpful in preventing emotional problems in teenagers.

The work featured in *Translational Psychiatry* was supported in part by a Silvio O. Conte Center grant from the National Institute of Mental Health, which is part of the National Institutes of Health. The Conte Center funding program brings together researchers with diverse expertise to gain new knowledge and improve the diagnosis and treatment of mental health disorders.

http://www.eurekalert.org/pub_releases/2016-01/smh-sfc122115.php

Study finds cerebrovascular disease to be major determinant of psychosis in patients with Alzheimer's

About half of all patients with Alzheimer's disease develop symptoms of psychosis, such as delusions or hallucinations.

TORONTO -- But the pathological mechanisms that underlie psychotic symptoms are unclear, limiting the ability to manage and treat them. Some studies have suggested they are related to the underlying causes of Alzheimer's disease such as the protein deposits found in the brains of Alzheimer's patients, but others found no correlation.

A study published today in the *Journal of Alzheimer's Disease* found that cerebrovascular disease is a major determinant of psychosis in people with Alzheimer's disease. Cerebrovascular disease is a group of conditions that restrict the circulation of blood to the brain.

Using data from the National Alzheimer's Coordinating Centre database collected from 29 Alzheimer's disease centres in the United States between 2005 and 2012, researchers led by Dr. Corinne Fischer, a psychiatrist and researcher at St. Michael's Hospital, analyzed autopsy data from 1,073 people.

Of the 890 people who had been clinically diagnosed with Alzheimer's while they were alive, the people most likely to be psychotic were those whose autopsies showed they had more physical signs of Alzheimer's such as neuritic plaques (protein deposits) and neurofibrillary tangles (twisted fibers found inside brain cells).

But when they looked at the 728 people whose autopsies confirmed they had Alzheimer's, those with psychosis did not show increased physical evidence of Alzheimer's disease. Alzheimer's can only be confirmed through an autopsy, so some patients in the clinically diagnosed group had been misdiagnosed with Alzheimer's.

In both groups of patients, psychosis correlated significantly with Lewy bodies, abnormal protein aggregates found in nerve cells of patients with Parkinson's disease. This was not an unexpected finding since psychosis is prominent when dementia accompanies Parkinson's disease. What was entirely unexpected was the prominent role in psychosis of vascular risk factors (hypertension, diabetes, age at quitting smoking) and cerebral injuries related to small vessel disease,

About 19 per cent of people with Alzheimer's who live in the community (rather than in institutions) are thought to have delusions and 14 per cent have hallucinations. Psychotic symptoms are significant in Alzheimer's patients because they have been shown to be associated with increased burden on caregivers, increased functional decline and more rapid progression of the disease. This study received funding from the Canadian Institutes of Health Research.

http://www.eurekalert.org/pub_releases/2016-01/uoc--cdr010516.php

Cannabis-based drug reduces seizures in children with treatment-resistant epilepsy

First study to examine the safety and efficacy of cannabidiol for children

Children and young adults with severe forms of epilepsy that does not respond to standard antiepileptic drugs have fewer seizures when treated with purified cannabidiol, according to a multi-center study led by researchers from UCSF Benioff Children's Hospital San Francisco.

"Better treatment for children with uncontrolled seizures is desperately needed," said Maria Roberta Cilio, MD, PhD, senior author and director of research at the UCSF Pediatric Epilepsy Center. "It's important to get seizure control at any age, but in children, uncontrolled seizures may impact brain and neurocognitive development, which can have an extraordinary effect on quality of life and contribute to progressive cognitive impairment."

The researchers evaluated 162 children and young adults across 11 independent epilepsy centers in the U.S. All of the children were treated with Epidiolex, a purified cannabidiol that comes in a liquid form containing no tetrahydrocannabinol (THC), the psychotropic component in cannabis, over a 12-week period. The results showed a median 36.5 percent reduction in monthly motor seizures, with a median monthly frequency of motor seizures falling from 30 motor seizures a month to 15.8 over the course of the 12 week trial.

The study was published in the December 23, 2015 issue of *The Lancet Neurology*.

The patients in the trial were all between the ages of one and 30 with intractable epilepsies shown to be resistant to many if not all of the antiepileptic treatments, including drugs and a ketogenic diet. This includes children with Dravet syndrome, a rare genetic disorder that manifests in early childhood with frequent, disabling seizures often occurring daily and numbering into the hundreds, as well as profound cognitive and social deficits.

"This trial is pioneering a new treatment for children with the most severe epilepsies, for whom nothing else works," said Cilio. "This is just the first step. This open label study found that CBD both reduces the frequency of seizures and has an adequate safety profile in children and young adults. Randomized

controlled trials are the next step to characterize the true efficacy and safety profile of this promising compound."

UCSF Benioff Children's Hospital San Francisco was the first site to ever administer Epidiolex in a child with epilepsy. In April 2013, the drug was given to a patient after obtaining a special approval from the U.S. Food and Drug Administration's Investigational New Drug (IND) program, and results from that initial experience provided the framework for the current study, according to the researchers. A second patient was then enrolled at UCSF in July 2013, and in January 2014 UCSF and other centers started to enroll patients under an expanded access IND.

Produced by the biopharmaceutical company GW Pharmaceuticals, Epidiolex is considered a schedule 1 substance, meaning it has a high potential for abuse, and is closely monitored and restricted by the FDA. GW Pharmaceuticals supplied the cannabidiol for the study, but had no role in the study design, data analysis, data interpretation, writing of the study, or publication submission. The study was also funded by the Epilepsy Therapy Project of the Epilepsy Foundation, and Finding A Cure for Epilepsy and Seizures (FACES).

The other centers involved in the research included: NYU Epilepsy Center, Children's Hospital of Philadelphia, Mass General Hospital for Children, Ann and Robert H. Lurie Children's Hospital of Chicago, Miami Children's Hospital, Pediatric and Adolescent Neurodevelopmental Associates (Atlanta, GA), Texas Children's Hospital, University of Utah Medical Center and Primary Children's Hospital, Wake Forest School of Medicine and Nationwide Children's Hospital.

http://www.eurekalert.org/pub_releases/2016-01/dumc-ets123115.php

Early trial shows injectable agent illuminates cancer during surgery

New injectable agent that causes cancer cells in a tumor to fluoresce, potentially increasing a surgeon's ability to locate and remove all of a cancerous tumor

DURHAM, N.C. -- Doctors at the Duke University School of Medicine have tested a new injectable agent that causes cancer cells in a tumor to fluoresce, potentially increasing a surgeon's ability to locate and remove all of a cancerous tumor on the first attempt. The imaging technology was developed through collaboration with scientists at Duke, the Massachusetts Institute of Technology (MIT) and Lumicell Inc.

According to findings published January 6 in Science Translational Medicine, a trial at Duke University Medical Center in 15 patients undergoing surgery for soft-tissue sarcoma or breast cancer found that the injectable agent, a blue liquid called LUM015 (loom - fifteen), identified cancerous tissue in human patients without adverse effects.

Cancer surgeons currently rely on cross-sectional imaging such as MRIs and CT scans to guide them as they remove a tumor and its surrounding tissue. But in many cases some cancerous tissue around the tumor is undetected and remains in the patient, sometimes requiring a second surgery and radiation therapy.

"At the time of surgery, a pathologist can examine the tissue for cancer cells at the edge of the tumor using a microscope, but because of the size of cancer it's impossible to review the entire surface during surgery," said senior author David Kirsch, M.D., Ph.D., a professor of radiation oncology and pharmacology and cancer biology at Duke University School of Medicine. "The goal is to give surgeons a practical and quick technology that allows them to scan the tumor bed during surgery to look for any residual fluorescence."

Researchers around the globe are pursuing techniques to help surgeons better visualize cancer, some using a similar mechanism as LUM015, which is activated by enzymes. But the Duke trial described in the journal is the first protease-activated imaging agent for cancer that has been tested for safety in humans, Kirsch said.

LUM015 was developed by Lumicell, a company started by researchers at MIT and involving Kirsch. In companion experiments in mice described in the journal, LUM015 accumulated in tumors where it creates fluorescence in tumor tissue that is on average five times brighter than regular muscle. The resulting signals aren't visible to the naked eye and must be detected by a handheld imaging device with a sensitive camera, which Lumicell is also developing, Kirsch said.

In the operating room after a tumor is removed, surgeons would place the handheld imaging device on the cut surface. The device would alert them to areas with fluorescent cancer cells.

Going into surgery, the goal is always to remove 100 percent of the tumor, plus a margin of normal tissue around the edges, explained senior author Brian Brigman, M.D., Ph.D., chief of orthopedic oncology at Duke. Pathologists then analyze the margins over several days and determine whether they are clear.

"This pathologic technique to determine whether tumor remains in the patient is the best system we have currently, and has been in use for decades, but it's not as accurate as we would like," said Brigman, who is also the director of the sarcoma program at the Duke Cancer Institute. "If this technology is successful in subsequent trials, it would significantly change our treatment of sarcoma. If we can increase the cases where 100 percent of the tumor is removed, we could prevent subsequent operations and potentially cancer recurrence. Knowing where there is residual disease can also guide radiation therapy, or even reduce how much radiation a patient will receive."

Researchers at Massachusetts General Hospital are currently evaluating the safety and efficacy of LUM015 and the Lumicell imaging device in a prospective study of 50 women with breast cancer. Afterward, Kirsch said, multiple institutions would likely evaluate whether the technology can decrease the number of patients needing subsequent operations following initial breast cancer removal.

In addition to Kirsch and Brigman, study authors include Melodi Javid Whitley, Diana M. Cardona, Alexander L. Lazarides, Ivan Spasojevic, Jorge M. Ferrer, Joan Cahill, Chang-Lung Lee, Matija Snuderl, Dan G. Blazer III, E. Shelley Hwang, Rachel A. Greenup, Paul J. Mosca, Jeffrey K. Mito, Kyle C. Cuneo, Nicole A. Larrier, Erin K. O'Reilly, Richard F. Riedel, William C. Eward, David B. Strasfeld, Dai Fukumura, Rakesh K. Jain, W. David Lee, Linda G. Griffith and Mounji G. Bawendi.

Duke author Kirsch and MIT authors Griffith, Bawendi, Ferrer and W. David Lee hold interest in or are involved with Lumicell Inc., a company commercializing LUM015 and the imaging system. Duke and MIT hold a patent on the imaging device technology. More detailed conflict-of-interest information is included in the manuscript published by Science Translational Medicine.

The study was funded in part by an American Society of Clinical Oncology Advanced Clinical Research Award to Kirsch, the National Institutes of Health (NIH) (T32GM007171), a National Cancer Institute Small Business Innovation Research award to Lumicell Inc. (1U43CA165024), the NIH National Center for Advancing Translational Science (UL1TR001117), and Duke Comprehensive Cancer Center Support (5P30-CA-014236-38). Lumicell Inc. provided the imaging agents.

Video: <https://duke.app.box.com/s/4fd04fj79avba204xit6vh9rnoymwqre>

http://www.eurekalert.org/pub_releases/2016-01/qi-ipc010416.php

Insulin-producing pancreatic cells created from human skin cells

The new cells prevented the onset of diabetes in an animal model of the disease

Scientists at the Gladstone Institutes and the University of California, San Francisco (UCSF) have successfully converted human skin cells into fully-functional pancreatic cells. The new cells produced insulin in response to changes in glucose levels, and, when transplanted into mice, the cells protected the animals from developing diabetes in a mouse model of the disease.

The new study, published in Nature Communications, also presents significant advancements in cellular reprogramming technology, which will allow scientists to efficiently scale up pancreatic cell production and manufacture trillions of the target cells in a step-wise, controlled manner. This accomplishment opens the door for disease modeling and drug screening and brings personalized cell therapy a step closer for patients with diabetes.

"Our results demonstrate for the first time that human adult skin cells can be used to efficiently and rapidly generate functional pancreatic cells that behave similar to human beta cells," says Matthias Hebrok, PhD, director of the Diabetes Center at UCSF and a co-senior author on the study. "This finding opens up the

opportunity for the analysis of patient-specific pancreatic beta cell properties and the optimization of cell therapy approaches."

In the study, the scientists first used pharmaceutical and genetic molecules to reprogram skin cells into endoderm progenitor cells--early developmental cells that have already been designated to mature into one of a number of different types of organs. With this method, the cells don't have to be taken all the way back to a pluripotent stem cell state, meaning the scientists can turn them into pancreatic cells faster. The researchers have used a similar procedure previously to create heart, brain, and liver cells.

After another four molecules were added, the endoderm cells divided rapidly, allowing more than a trillion-fold expansion. Critically, the cells did not display any evidence of tumor formation, and they maintained their identity as early organ-specific cells.

The scientists then progressed these endoderm cells two more steps, first into pancreatic precursor cells, and then into fully-functional pancreatic beta cells. Most importantly, these cells protected mice from developing diabetes in a model of disease, having the critical ability to produce insulin in response to changes in glucose levels.

"This study represents the first successful creation of human insulin-producing pancreatic beta cells using a direct cellular reprogramming method," says first author Saiyong Zhu, PhD, a postdoctoral researcher at the Gladstone Institute of Cardiovascular Disease. "The final step was the most unique--and the most difficult--as molecules had not previously been identified that could take reprogrammed cells the final step to functional pancreatic cells in a dish."

Sheng Ding, PhD, a senior investigator in the Roddenberry Stem Cell Center at Gladstone and co-senior author on the study, adds, "This new cellular reprogramming and expansion paradigm is more sustainable and scalable than previous methods. Using this approach, cell production can be massively increased while maintaining quality control at multiple steps. This development ensures much greater regulation in the manufacturing process of new cells. Now we can generate virtually unlimited numbers of patient-matched insulin-producing pancreatic cells."

Holger Russ, PhD, was a co-first author on the paper from UCSF. Other Gladstone investigators include Xiajing Wang, Mingliang Zhang, Tianhua Ma, Tao Xu, and Shibing Tang. Funding was provided by the Roddenberry Foundation, National Institutes of Health, National Heart, Lung, and Blood Institute, National Eye Institute, National Institute of Child Health and Human Development, National Institute of Mental Health, California Institute of Regenerative Medicine, Prostate Cancer Foundation, and the Leona M. & Harry B. Helmsley Charitable Trust.

http://www.eurekalert.org/pub_releases/2016-01/uoe-ldq010616.php

Lab discovery gives glimpse of conditions found on other planets
Scientists have recreated an elusive form of the material that makes up much of the giant planets in our solar system, and the sun.

Experiments have given a glimpse of a previously unseen form of hydrogen that exists only at extremely high pressures - more than 3 million times that of Earth's atmosphere.

Hydrogen - which is among the most abundant elements in the Universe - is thought to be found in this high-pressure form in the interiors of Jupiter and Saturn.

Researchers around the world have been trying for years to create this form of the element, known as the metallic state, which is considered to be the holy grail of this field of physics. It is believed that this form of hydrogen makes up most of the interiors of Jupiter and Saturn.

The metallic and atomic form of hydrogen, formed at elevated pressures, was first theorised to exist 80 years ago. Scientists have tried to confirm this in lab experiments spanning the past four decades, without success.

In this latest study from a team of physicists at the University of Edinburgh, researchers used a pair of diamonds to squeeze hydrogen molecules to record pressures, while analysing their behaviour.

They found that at pressures equivalent to 3.25 million times that of Earth's atmosphere, hydrogen entered a new solid phase - named phase V - and started to show some interesting and unusual properties.

Its molecules began to separate into single atoms, while the atoms' electrons began to behave like those of a metal.

The team says that the newly found phase is only the beginning of the molecular separation and that still higher pressures are needed to create the pure atomic and metallic state predicted by theory.

The study, published in Nature, was supported by a Leadership Fellowship from the Engineering and Physical Sciences Research Council.

Professor Eugene Gregoryanz, of the University of Edinburgh's School of Physics and Astronomy, who led the research, said: "The past 30 years of the high-pressure research saw numerous claims of the creation of metallic hydrogen in the laboratory, but all these claims were later disproved.

Our study presents the first experimental evidence that hydrogen could behave as predicted, although at much higher pressures than previously thought.

The finding will help to advance the fundamental and planetary sciences."

http://www.eurekalert.org/pub_releases/2016-01/uoc-ady010616.php

Archaeological discovery yields surprising revelations about Europe's oldest city

Recent fieldwork at the ancient city of Knossos on the Greek island of Crete finds that during the early Iron Age (1100 to 600 BC), the city was rich in imports and was nearly three times larger than what was believed from earlier excavations.

The discovery suggests that not only did this spectacular site in the Greek Bronze Age (between 3500 and 1100 BC) recover from the collapse of the socio-political system around 1200 BC, but also rapidly grew and thrived as a cosmopolitan hub of the Aegean and Mediterranean regions. Antonis Kotsonas, a University of Cincinnati assistant professor of classics, will highlight his field research with the Knossos Urban Landscape Project at the 117th annual meeting of the Archaeological Institute of America and Society for Classical Studies. The meeting takes place Jan. 7-10, 2016 in San Francisco.

Kotsonas explains that Knossos, "renowned as a glorious site of the Greek Bronze Age, the leader of Crete and the seat of the palace of the mythical King Minos and the home of the enigmatic labyrinth," was the prosperous epicenter of Minoan culture. Scholars have studied the city's Bronze Age remains for more than a century, but more recent research has focused on the urban development of the city after it entered the Iron Age -- in the 11th century BC -- following the Bronze Age collapse of the Aegean palaces.

The Knossos Urban Landscape Project over the past decade has recovered a large collection of ceramics and artifacts dating back to the Iron Age. The relics were spread over an extensive area that was previously unexplored. Kotsonas says that this exploration revealed considerable growth in the size of the settlement during the early Iron Age and also growth in the quantity and quality of its imports coming from mainland Greece, Cyprus, the Near East, Egypt, Italy, Sardinia and the western Mediterranean.

"No other site in the Aegean period has such a range of imports," Kotsonas says. The imports include bronze and other metals -- jewelry and adornments, as well as pottery. He adds that the majority of the materials, recovered from tombs, provide a glimpse of the wealth in the community, because status symbols were buried with the dead during this period.

The antiquities were collected from fields covering the remains of dwellings and cemeteries. "Distinguishing between domestic and burial contexts is essential for determining the size of the settlement and understanding the demographic, socio-political and economic development of the local community," explains Kotsonas.

"Even at this early stage in detailed analysis, it appears that this was a nucleated, rather densely occupied settlement extending over the core of the Knossos valley, from at least the east slopes of the acropolis hill on the west to the Kairatos River, and from the Vlychia stream on the south until roughly midway between the Minoan palace and the Kephala hill."

Kotsonas' Jan. 9, 2016 presentation is part of a colloquium themed, "Long-Term Urban Dynamics at Knossos: The Knossos Urban Landscape Project, 2005-2015." Kotsonas serves as a consultant on the project, which is dedicated to intensively surveying the Knossos valley and documenting the development of the site from 7000 BC, to the early 20th century. The project is a research partnership between the Greek Archaeological Service and the British School at Athens. Kotsonas has served as a collaborator on the project since 2009.

Funding for the UC research was supported by the UC Department of Classics Louise Taft Semple Fund.

http://www.eurekalert.org/pub_releases/2016-01/b-sdt010416.php

Sugary drinks tax in Mexico linked with 12 percent cut in sales after one year

10% tax on sugar sweetened drinks associated with 12% reduction in sales and 4% increase in purchases of untaxed beverages one year after implementation

In Mexico, a 10% tax on sugar sweetened drinks has been associated with an overall 12% reduction in sales and a 4% increase in purchases of untaxed beverages one year after implementation, finds a study published by The BMJ this week.

The findings have important implications for policy discussions and decisions, say the researchers. Mexico has some of the highest levels of diabetes, overweight, and obesity in the world, and reducing the consumption of sugar sweetened beverages has been an important target for obesity and diabetes prevention efforts. From Jan 1, 2014, Mexico implemented an excise tax of 1 peso per litre on sugar sweetened beverages.

To evaluate the effect of this tax, researchers based in Mexico and the USA studied differences in purchases of sugary drinks before and after implementation. Using nationally representative food purchase data from over 6,200 Mexican households across 53 large cities above 50,000 inhabitants, they compared predicted volumes of taxed and untaxed beverages purchased in 2014 (post-tax period) with the estimated volumes that would have been expected without the tax, based on pretax trends.

A statistical model was used, which adjusted for several influential factors, including age and sex of household members and socioeconomic status (low,

middle, and high), and other contextual economic factors such as employment and salaries where people lived.

Purchases of taxed beverages decreased by an average of 6% in 2014 compared with expected purchases without the tax. Furthermore, these reductions became large over time, reaching a 12% decline by December 2014. In other words, during 2014 the average urban Mexican purchased 4.2 fewer litres of taxed beverages than expected without the tax.

In contrast, purchases of untaxed beverages were 4% higher than expected without the tax, mainly driven by an increase in purchases of bottled plain water. This translates to the purchase of 12.8 more litres of untaxed beverages by the average urban Mexican over 2014 than expected.

All three socioeconomic groups reduced purchases of taxed beverages, but the reduction was greatest among households of low socioeconomic status, averaging a 9% decline during 2014 and reaching a 17% decrease by December 2014 compared with pretax trends. The researchers emphasise that this is an observational study so no definitive conclusions can be drawn about cause and effect. They also point to some study weaknesses, such as incomplete data on dairy beverages and their focus on Mexican cities.

Nevertheless, they conclude that this short term change "is moderate but important" and they say continued monitoring is needed "to understand purchases longer term, potential substitutions, and health implications."

Taxes can be part of a public health strategy, but they cannot be viewed as a magic bullet in the fight against obesity, argues Franco Sassi, a senior health economist at the OECD, in an accompanying editorial.

He believes that other, complementary, policies are needed, including regulatory measures, health education around food choices, incentives for research and development in food production, and changes in the food choice environment.

"If all of the above policies were used systematically and effectively, the focus of the policy debate might shift away from taxes in the future," he concludes.

<http://bit.ly/1OlV5ox>

Sleep isn't needed to create long-term memories – just time out *NEED to remember something? Take a break.*

It seems that resting in a quiet room for 10 minutes without distractions can boost our ability to remember new information. A lot of people think the brain is a muscle that needs to be continually stimulated, but perhaps that's not the best way," says [Michaela Dewar](#) at Heriot-Watt University in Edinburgh, UK.

To store them long-term, new memories must be [consolidated](#), a process thought to happen [while we sleep](#). But at least some consolidation may occur while we're awake, says Dewar – all you need is time out.

In 2012, her team found that people who had a 10-minute rest after hearing a story remembered [10 per cent more](#) of it a week later than those who played a spot-the-difference game immediately afterwards. “We dim the lights and ask them to sit in an empty, quiet room, with no mobile phones,” says Dewar. Most volunteers said they let their minds wander during this time.

Now Dewar and her colleagues have shown that rest can also consolidate spatial memories. Volunteers who rested after exploring a virtual-reality environment were 10 per cent more accurate at orientating themselves in relation to virtual landmarks (*Hippocampus*, [doi.org/926](https://doi.org/10.1016/j.neuroscience.2016.01.012)). “People with amnesia who could not remember words from a list were able to after a few minutes’ rest”

This is good news for insomniacs, suggesting that simply resting while awake can give us some of the memory benefits of sleep. “As long as you’re reasonably relaxed, you might still be experiencing some of the memory-consolidation processes,” says [Gareth Gaskell](#) at the University of York, UK.

The effect is particularly strong in people with amnesia. In a memory test of a list of words, eight of 12 volunteers with the condition were unable to remember any of them without a break. But after resting for 9 minutes, the same volunteers could recall [between 30 and 80 per cent of the list](#).

“Most of them can’t lead a normal life because they can’t remember what they did 10 minutes ago,” says Dewar. The results suggest that people with amnesia may not have completely lost the ability to form new memories after all.

Dewar thinks that overstimulation may be what causes memory problems in amnesia. “If we try to reduce the amount of information going in, people with amnesia can form new memories,” she says.

<http://bit.ly/1Zm24U2>

Nuclear Confusion: The Data Suggest North Korea's "H-Bomb" Isn't

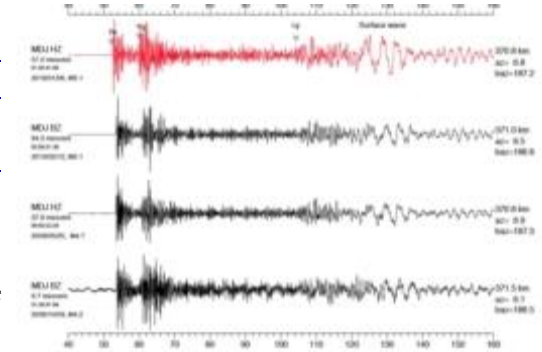
The recent underground test and subsequent earthquake are roughly the same as North Korea's previous nukes

By [Larry Greenemeier](#) on January 6, 2016

North Korea’s nuclear threats reached new heights when the country claimed to have successfully tested a [hydrogen bomb](#) underground on Tuesday night. Regional measurements confirmed a seismic event took place in North Korea, but the estimated size of the disruption cast doubt that the secretive nation had in fact detonated a thermonuclear weapon.

Such a device would be hundreds of times more powerful than the bombs Pyongyang detonated during its previous three nuclear weapon tests. The estimated size of this disruption is about the same as those from previous tests, however.

Researchers can estimate the yield of a nuclear explosion based on the amplitude of the seismic waves it creates. Data collected at a [Global Seismographic Network Station in Mudanjiang, China](#), however, suggest roughly a 3.4- to seven-kiloton blast, says [Won-Young Kim](#), a senior research scientist at Columbia University’s Lamont–Doherty Earth Observatory. (A kiloton is equal to 1,000 tons of TNT.)



Seismograms of North Korea’s four nuclear tests, with the most recent detonation on top (in red). The latest explosion generated data similar to the previous three. Researchers noted slightly larger surface waves this time around, but the reasons for this are unclear without more information about the test itself.

[Lamont–Doherty Earth Observatory](#), Columbia University

Kim calculated this yield based on the [magnitude 5.1 body waves](#) the detonation sent rippling through Earth. This was more powerful than North Korea’s [previous nuclear test](#), a 2.2- to four-kiloton blast in 2013 that set off waves equivalent to a magnitude 4.5 to 4.7 earthquake, but not nearly enough to confirm the use of a thermonuclear bomb.

Researchers have difficulty [quantifying the exact size of North Korea’s nuclear detonations](#) because the depth of the explosive device, properties of the rock surrounding the explosion and other factors influence the seismic measurements produced, Kim says.

North Korea does not publicize the depth of its tests, although the material at the test site in Punggye-ri is thought to be hard granite.

Nuclear weapons such as the bombs dropped by the U.S. on Japan to end World War II in 1945 rely on fission for their power. A thermonuclear weapon, or hydrogen bomb, uses a nuclear fission reaction to ignite a secondary hydrogen fusion reaction that makes greater use of the weapon’s atomic fuel, typically uranium or plutonium.

To provide some perspective on the difference between the two: the U.S.’s first successful H-bomb test in 1952 produced an estimated yield equivalent to more than 10 megatons (10 million tons) of TNT, about 500 times more powerful than the bomb dropped on Nagasaki just seven years earlier.

Even if North Korea’s latest test was at the high end of Kim’s estimates, 0.007 megatons of TNT is a far cry from thermonuclear.

http://www.eurekalert.org/pub_releases/2016-01/cp-ngq123015.php

Neanderthal genes gave modern humans an immunity boost, allergies

Human interbreeding with Neanderthals may have improved immunity to disease while leaving us prone to allergies

When modern humans met Neanderthals in Europe and the two species began interbreeding many thousands of years ago, the exchange left humans with gene variations that have increased the ability of those who carry them to ward off infection. This inheritance from Neanderthals may have also left some people more prone to allergies.

The discoveries reported in two independent studies in the American Journal of Human Genetics on January 7 add to evidence for an important role for interspecies relations in human evolution and specifically in the evolution of the innate immune system, which serves as the body's first line of defense against infection.

"We found that interbreeding with archaic humans--the Neanderthals and Denisovans--has influenced the genetic diversity in present-day genomes at three innate immunity genes belonging to the human Toll-like-receptor family," says Janet Kelso of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.



This world map shows the frequencies of Neanderthal-like TLR DNA in a 1000 Genomes dataset. The size of each pie is proportional to the number of individuals within a population. Dannemann et al./American Journal of Human Genetics 2016

"These, and other, innate immunity genes present higher levels of Neanderthal ancestry than the remainder of the coding genome," adds Lluís Quintana-Murci of the Institut Pasteur and the CNRS in Paris. "This highlights how important introgression events [the movement of genes across species] may have been in the evolution of the innate immunity system in humans."

Earlier studies have shown that one to six percent of modern Eurasian genomes were inherited from ancient hominins, such as Neanderthal or Denisovans. Both new studies highlight the functional importance of this inheritance on Toll-like receptor (TLR) genes--TLR1, TLR6, and TLR10. These TLR genes are expressed on the cell surface, where they detect and respond to components of bacteria, fungi, and parasites. These immune receptors are essential for eliciting inflammatory and anti-microbial responses and for activating an adaptive immune response.

Quintana-Murci and his colleagues set out to explore the evolution of the innate immune system over time. They relied on vast amounts of data available on present-day people from the 1000 Genomes Project together with the genome sequences of ancient hominins. Quintana-Murci's team focused on a list of 1,500 genes known to play a role in the innate immune system. They then examined patterns of genetic variation and evolutionary change in those regions relative to the rest of the genome at an unprecedented level of detail. Finally, they estimated the timing of the changes in innate immunity and the extent to which variation in those genes had been passed down from Neanderthals.

These investigations revealed little change over long periods of time for some innate-immunity genes, providing evidence of strong constraints. Other genes have undergone selective sweeps in which a new variant came along and quickly rose to prominence, perhaps because of a shift in the environment or as a result of a disease epidemic. Most adaptations in protein-coding genes occurred in the last 6,000 to 13,000 years, as human populations shifted from hunting and gathering to farming, they report.

But, Quintana-Murci says, the biggest surprise for them "was to find that the TLR1-6-10 cluster is among the genes presenting the highest Neanderthal ancestry in both Europeans and Asians."

Kelso and her colleagues came to the same conclusion, but they didn't set out to study the immune system. Their interest was in understanding the functional importance of genes inherited from archaic humans more broadly. They screened present-day human genomes for evidence of extended regions with high similarity to the Neanderthal and Denisovan genomes, then examined the prevalence of those regions in people from around the world. Those analyses led them to the same three TLR genes.

Two of those gene variants are most similar to the Neanderthal genome, whereas the third is most similar to the Denisovan genome, Kelso's group reports. Her team also provides evidence that these gene variants offered a selective advantage. The archaic-like variants are associated with an increase in the activity of the TLR genes and with greater reactivity to pathogens. Although this greater sensitivity

might protect against infection, it might also increase the susceptibility of modern-day people to allergies.

"What has emerged from our study as well as from other work on introgression is that interbreeding with archaic humans does indeed have functional implications for modern humans, and that the most obvious consequences have been in shaping our adaptation to our environment - improving how we resist pathogens and metabolize novel foods," Kelso says.

As surprising as it may seem, it does make a lot of sense, she adds. "Neanderthals, for example, had lived in Europe and Western Asia for around 200,000 years before the arrival of modern humans. They were likely well adapted to the local climate, foods, and pathogens. By interbreeding with these archaic humans, we modern humans gained these advantageous adaptations."

Paper 1: American Journal of Human Genetics, Deschamps et al.: "Genomic Signatures of Selective Pressures and Introgression from Archaic Hominins at Human Innate Immunity Genes" <http://dx.doi.org/10.1016/j.ajhg.2015.11.014>

This work was primarily supported by the Institut Pasteur, the Centre Nationale de la Recherche Scientifique (CNRS), and the Agence Nationale de la Recherche.

Paper 2: American Journal of Human Genetics, Dannemann et al.: "Introgression of Neanderthal- and Denisovan-like Haplotypes Contributes to Adaptive Variation in Human Toll-like Receptors" <http://dx.doi.org/10.1016/j.ajhg.2015.11.015>

Funding was provided by the Max Planck Society and the Deutsche Forschungsgemeinschaft.

http://www.eurekalert.org/pub_releases/2016-01/jhm-or010716.php

'Window of recovery' can reopen after stroke

Researchers show that stroke conditions may increase brain plasticity and recovery in some cases

Using mice whose front paws were still partly disabled after an initial induced stroke, Johns Hopkins researchers report that inducing a second stroke nearby in their brains let them "rehab" the animals to successfully grab food pellets with those paws at pre-stroke efficiency.

The findings, described online Dec. 31, 2015, in *Neurorehabilitation and Neural Repair*, show that the "window of opportunity" for recovering motor function after a stroke isn't permanently closed after brain damage from an earlier stroke and can reopen under certain conditions, in conjunction with rapid rehabilitation efforts.

The investigators strongly emphasize that their experiments do not and will never make a case for inducing strokes as a therapy in people with stroke disability. But they do suggest the mammalian brain may be far more "plastic" in such patients, and that safe and ethical ways might be found to better exploit that plasticity and reopen the recovery window for people who have never fully regained control of their motor movements.

"If we can better understand how to reopen or extend the optimal recovery period after a stroke, then we might indeed change how we treat patients for the better," says Steven Zeiler, M.D., Ph.D., assistant professor of neurology at the Johns Hopkins University School of Medicine. "Our study adds new strong and convincing evidence that there is a sensitive period following stroke where it's easiest to relearn motor movements -- a topic that is still debated among stroke researchers."

The new mouse experiments build on a previous study at Johns Hopkins, which found that the window of optimal recovery following a stroke in mice was within the first seven days, but this time period could be extended by giving mice the common antidepressant fluoxetine immediately after the stroke. The investigators suspected that the antidepressant increased the brain's response to learning. Until now, however, the researchers say, there was no evidence that once the optimal period was over -- with or without fluoxetine -- the potential for recovery could be reopened.

For the new research, which did not involve the use of the antidepressant, the researchers -- as in their first experiments -- taught mice to reach through a slit in their cage with their front paw to grasp food pellets affixed to a bar, a task that four-legged animals don't naturally perform.

See an animation of the experiment [here](#).

Once the mice became efficient at the task -- it took about 10 days of training -- the researchers measured their individual success rates. On average, they found the mice successfully grabbed pellets just over 50 percent of the time.

The researchers then induced a stroke in the motor cortex of the mice's brains, making them unable to perform the task. After waiting a week -- well beyond the known "optimal" window during which rehab training will work -- they put the mice through almost three weeks of task training, during which the mice successfully grabbed the pellets again, but only about 30 percent of the time.

For the next phase of the experiment, the scientists built on previous research and observations in mice that brain ischemia -- the cutoff or reduction of oxygen to the brain during a stroke or other insult to the cortex -- under certain conditions increased brain plasticity, the ability of the brain to compensate for injury and form new connections.

To that end, the scientists induced a second stroke in the lab mice either in the secondary motor cortex near the first stroke site or, for purposes of a control group, in the visual cortex, located far from the original site.

Instead of waiting days, the investigators began retraining these mice the next day and found that mice with the follow-up stroke in the motor cortex relearned to

grasp the food pellets just as well as they did before the first stroke, with success more than 50 percent of the time.

Mice in the control group never did any better, even with extended training, suggesting that the motor cortex may be the only part of the brain with this type of "reopening" capability for motor movements, the investigators say.

Zeiler plans to investigate other ways to reopen the window of recovery and make use of the optimal recovery window. The lead investigator of the study, John Krakauer, M.D., M.A., professor of neurology, directs the Brain, Learning, Animation and Movement Lab, which uses basic science data, like that in this study, to develop new patient therapies. Currently, the lab is investigating the importance of early and intense rehabilitation in patients to enhance brain plasticity after stroke.

According to the Centers for Disease Control and Prevention, in the U.S., stroke is the No. 1 cause of disability and costs \$34 billion each year in health care, medications and missed days of work.

Other authors on the study include Robert Hubbard, Ellen Gibson and Tony Zheng of Johns Hopkins Medicine; Kwan Ng of the University of California, Los Angeles; and Richard O'Brien of Duke University.

Funding for the study was provided by grants from the National Institute of Neurological Disorders and Stroke (grant numbers 1K08 NS085033-01, R01 NS052804-05 and R01 120 86264), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R01 HD073147), and the James S. McDonnell Foundation.

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

Genetic Flip Helped Organisms Go From One Cell to Many

It took a single mutation to flip an enzyme into a vital protein connector

Carl Zimmer

Narwhals and newts, eagles and eagle rays — the diversity of animal forms never ceases to amaze. At the root of this spectacular diversity is the fact that all animals are made up of many cells — in our case, [about 37 trillion of them](#). As an animal develops from a fertilized egg, its cells may diversify into a seemingly limitless range of types and tissues, from tusks to feathers to brains.

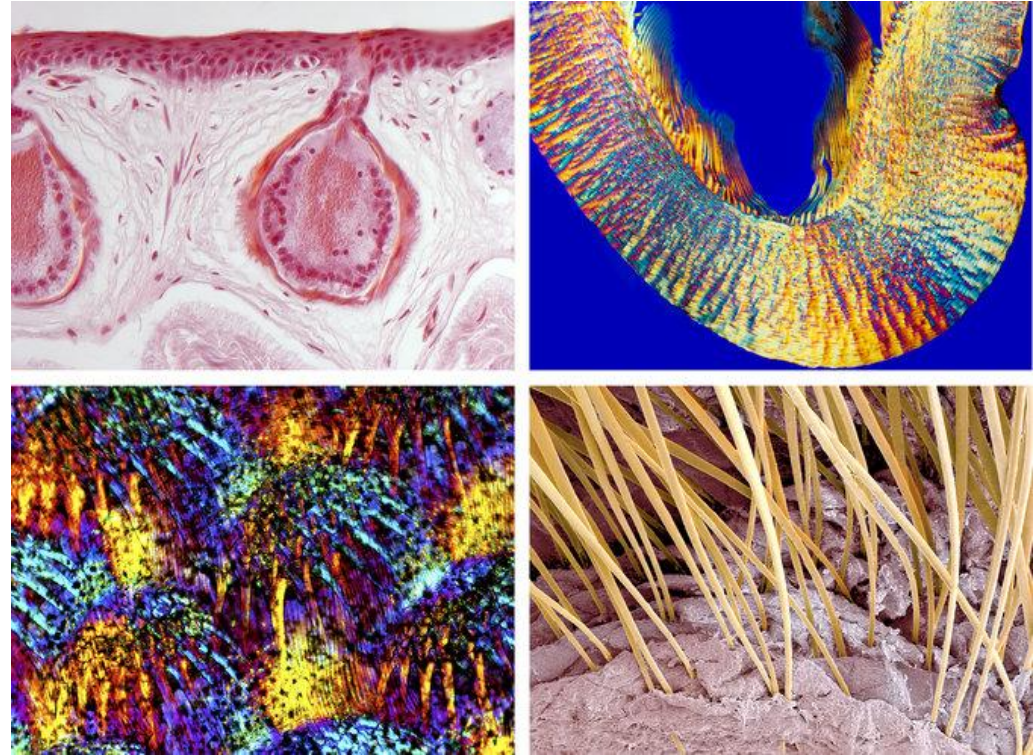
The transition from our single-celled ancestors to the first multicellular animals [occurred about 800 million years ago](#), but scientists aren't sure how it happened. In a study published in the [journal eLife](#), a team of researchers tackles this mystery in a new way.

The researchers resurrected ancient molecules that once helped single-celled organisms thrive, then recreated the mutations that helped them build multicellular bodies.

The authors of the new study focused on a single molecule called GK-PID, which animals depend on for growing different kinds of tissues. Without GK-PID, cells

don't develop into coherent structures, instead growing into a disorganized mess and sometimes even turning cancerous.

GK-PID's job, scientists have found, is to link proteins so cells can divide properly. "I think of it as a molecular carabiner," said Joseph W. Thornton, an evolutionary biologist at the University of Chicago and a co-author of the new study.



Clockwise from top left: microscopic views of glands in frog skin, a sheep's hoof, a tamarin's skin and fish scales. Science Source

When a cell divides, it first has to make an extra copy of its chromosomes, and then each set of chromosomes must be moved into the two new cells.

GK-PID latches onto proteins that drag the chromosomes, then attaches to anchor proteins on the inner wall of the cell membrane.

Once those proteins are joined by GK-PID, the dragging proteins pull the chromosomes in the correct directions.

Bad things happen if the chromosomes head the wrong way. Skin cells, for example, form a stack of horizontal layers. New cells need to grow in the same direction so skin can continue to act as a barrier.

If GK-PID doesn't ensure that the chromosomes move horizontally, the cells end up in a jumble, like bricks randomly set at different angles.

Previous studies have offered clues to how this important molecule might have evolved in the ancestors of animals.

All animals (ourselves included) carry a gene sequence that's very similar to the one producing GK-PID. But that gene encodes a different molecule with a different job: an enzyme that helps build DNA. The enzyme can be found even in other organisms, like fungi to bacteria.

Dr. Thornton and his colleagues wondered whether that enzyme and its cousin GK-PID shared some kind of evolutionary history.

First, they made a careful study of the different forms of GK-PID and the DNA-building enzyme in about 200 species. Then they worked out how the genes for these molecules must have mutated over the millenniums.

That analysis allowed the scientists to figure out the DNA sequence for GK-PID in the single-celled ancestors of animals — a gene that hasn't been seen in hundreds of millions of years. Then Dr. Thornton and his colleagues did something even more amazing: They recreated those ancient molecules to see how they once functioned.

The ancestral version of GK-PID wasn't a carabiner, the scientists found. Instead, it behaved like a DNA-building enzyme.

That finding suggests that in the ancestors of animals, the gene for the enzyme was accidentally duplicated. Later on, mutations in one copy of the gene turned it into a carabiner.

But how many mutations did it take to transform the molecule? That's the most remarkable part of the new study. The scientists altered the gene for the ancestral enzyme with the earliest mutations that evolved in it. They found it took a single mutation to flip GK-PID from an enzyme to a carabiner. "Genetically, it was much easier than we thought possible," Dr. Thornton said. "You don't need some elaborate series of thousands of mutations in just the right order."

The evolution of a molecular carabiner did not by itself give rise to the animal kingdom, of course. Other adaptations were needed to grow multicellular bodies. Dr. Thornton said that it might be possible to resurrect other ancestral molecules to figure out how those adaptations evolved, as well.

And if GK-PID is any guide, Dr. Thornton said, their evolution may have been surprisingly simple. A single mutation might have been enough to switch a molecule from one job to another.

Antonis Rokas, an evolutionary biologist at Vanderbilt University who was not involved in the study, agreed. "One of evolution's most striking major innovations may be the end-product of a series of many minor innovations," he said.

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

The Atomic Age Ushered In the Anthropocene, Scientists Say

Geoscientists have concluded that the Age of Humans officially began at the start of the nuclear age.

By [Ker Than](#)

Humans are living in a new geologic epoch, one that is largely of their own making, scientists say.

In a new study, published in this week's issue of the journal *Science*, an international team of geoscientists concluded that the impact of human activity on the Earth is so widespread and persistent that it warrants formal recognition with the creation of a new geologic time unit, which they propose to call the Anthropocene epoch.



A mushroom cloud rises in the sky during an atomic weapons test in the 1950s. Roger Ressmeyer/CORBIS

"We're saying that humans are a geological process," says study coauthor Colin Waters, a geologist with the British Geological Survey in the U.K. "We are the dominant geologic force shaping the planet. It's not so much river or ice or wind anymore. It's humans."

The term "Anthropocene"—from *anthropo*, for "man", and *cene*, for "new"—has been slowly gaining popularity as an environmental buzzword to describe humanity's planet-scale influence since 2000, when it was popularized by the atmospheric chemist and Nobel laureate Paul Crutzen.

In recent years, however, there has been a growing movement amongst scientists to formally adopt the term as part of the official nomenclature of geology. Those who advocate this action argue that the current epoch dominated by humanity is markedly different from the Holocene epoch of the past 12,000 years, the time during which human societies developed and flourished.

The new study is not the first to propose a formal establishment of an Anthropocene epoch—Simon Lewis and Mark Maslin of the University of College London [made a similar recommendation](#) last year— but it is one of the most comprehensive to date. In it, Waters and his colleagues sought to answer whether human actions have left measurable signals in the geological strata, and whether those signals are markedly different from those of Holocene. The answer to both questions, the scientists say, is overwhelmingly yes.

The researchers conducted a review of the published scientific literature and found evidence for numerous ways that humans have changed the Earth to produce signals in ice and rock layers that will still be detectable millions of years from now. Among them: a preponderance of unique human products such as concrete, aluminum and plastics; elevated atmospheric levels of the greenhouse gases carbon dioxide and methane; higher levels of nitrogen and phosphorus in the soil from fertilizers and pesticides; and radionuclide fallout from above-ground nuclear weapons testing in the 20th century.

Humans have also indelibly shaped the biological realm by raising a few domesticated animals and cultivated crops to prominence while pushing other species toward extinction. “I think these changes will be really obvious in the fossil record,” says Scott Wing, the curator of fossil plants at the Smithsonian National Museum of Natural History. “Imagine the abundance of beef and chicken bones and corn cobs in sediments from now versus sediments deposited 300 years ago,” says Wing, who was not involved in the study.

Humans have also facilitated the mixing of species to a degree unprecedented in the history of the Earth, says Waters, who is also the secretary of the [Anthropocene Working Group](#), an organization within the International Union of Geological Sciences.

“If we find a plant that’s nice to look at, within years we’ve transported it across the globe,” Waters says. “That is creating pollen signatures in sediments that are very confusing. Normally, you have to wait for two continents to collide until you get that kind of transfer of species, but we’re doing it in a very short period of time.”

As far as epochs go, the Anthropocene is a young one: Waters and his team argue that it only began around 1950 C.E., at the start of the nuclear age and the mid-20th century acceleration of population growth, industrialization, and mineral and energy use. In this, the group differs from Lewis and Maslin, who suggested the Anthropocene’s “golden spike”—the line between it and the Holocene—be set at either 1610 or 1964. The year 1610 is when the collision of the New and Old Worlds a century earlier was first felt globally, and the year 1964 is discernable in rock layers by its high proportion of radioactive isotopes—a legacy of nuclear weapons tests.

“The Holocene was an abrupt event as far as geologists are concerned. And yet, we’re seeing changes that are even more rapid than that,” Waters says.

The Smithsonian’s Wing says he agrees that humans have changed the Earth sufficiently to create a distinct stratigraphic and geochemical signal. “I don’t think there is any doubt about it,” he says. “Not only is the signal distinct and large, it will persist for a geologically long amount of time, so it will be recognizable

hundreds of thousands or millions of years into the future, should there be anyone then to look at the record.”

Interestingly, unlike the notion of climate change, for which scientific consensus was established long before public acceptance became widespread, Waters says members of the general public appear to be more willing to accept the idea of an Anthropocene epoch than some scientists. “Geologists and stratigraphers”—scientists who study the layers of the Earth—“are used to looking at rocks that are millions of years old, so many of them have a hard time appreciating that such a small interval of time can be a geologic epoch,” Waters says.

Both Waters and Wing say that in addition to being scientifically important, formally recognizing the Anthropocene epoch could have a powerful impact on the public perception of how humanity is changing the planet.

“There’s no doubt that when 7 billion people put their minds to doing something, they can have a big impact. We’re seeing that now,” Waters says. “But it also means that we can reverse some of those impacts if we wish, if we are aware of what we’re doing. We can modify our progress.”

Wing agrees. “I think the Anthropocene is a really important mechanism for getting people of all sorts to think about their legacy,” he says. “We humans are playing a game that affects the whole globe for an unimaginably long time into the future. We should be thinking about our long-term legacy, and the Anthropocene puts a name on it.”

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

Does Icy Pluto Have a Hidden Ocean? New Horizons Offers New Clues

Data from the NASA probe are helping to build a solid case for a liquid ocean inside the tiny, distant world

By [Ker Than](#)

When NASA's New Horizons spacecraft [reached Pluto last July](#), it gave scientists their [first detailed look](#) at one of the most mysterious objects in the solar system. In addition to wonders like soaring mountains, [ice volcanoes](#) and a giant heart-shaped basin, images beamed back by the probe revealed a surface marred by a network of fissures and a notably spherical shape.



These cracks hint at subsurface seas. NASA/JHUAPL/SwRI

For some scientists, those last two discoveries are hints that something even wilder may be hidden inside the tiny world, because they are the first direct clues that Pluto could host a subsurface ocean beneath its thick, icy crust. If confirmed, an ocean on Pluto would have profound implications, because it would increase the likelihood that other icy bodies could host liquid water—and possibly life.

"The fact that even cold, distant Pluto could have a subsurface ocean means that there are potential habitats even in apparently unpromising locations," says [Francis Nimmo](#), a New Horizons scientist based at the University of California, Santa Cruz.

Aside from Earth, no bodies in the solar system have large amounts of liquid water on their surfaces. That's a bummer for astrobiologists, as most scientists believe that water is a necessary ingredient for life to arise.

Still, space probes have been collecting evidence for decades that icy moons around Jupiter and Saturn hold vast oceans beneath their crusts. [Saturn's moon Enceladus](#) spews geysers that are tantalizingly rich with water and carbon, while [Jupiter's Europa](#) is covered in fractures and ridges that hint at a subsurface ocean melting through the ice. These worlds are currently considered some of the best places to look for life elsewhere in the solar system.

Pluto is similarly icy, but the difference is that those moons have more obvious sources of heat to keep internal water liquid: the gravitational kneading they receive as they swing around their massive parent planets. Pluto has no massive companion and orbits between 3 and 5 billion miles from the sun, so astronomers mostly thought it must be too cold for a modern ocean.

Some theoretical models suggested that radioactive decay in Pluto's rocky interior could heat things up enough to create a subsurface ocean at some point in its history, maybe even enough heat that waters persist today, but there was no real evidence, says Nimmo—until now.

Speaking at a recent meeting of the [American Geophysical Union](#) (AGU) in San Francisco, Nimmo outlined two key clues from New Horizons. Neither one alone is a slam dunk, he says, but together, they're suggestive.

First, New Horizons revealed the presence of extensional tectonics, faults and fissures across the face of Pluto that could indicate the surface has undergone expansion in the recent past.

"An easy way of doing that is if you have an ocean that's starting to refreeze," Nimmo says, because water expands in volume as it changes from a liquid to a solid. "As the liquid water freezes back into ice, the outer surface of Pluto has to move outward, and you get expansion."

The second piece of evidence has to do with Pluto's shape, in particular, the notable lack of a bulge around its equator like the one found on Earth, its moon and other rounded celestial bodies.

As spherical bodies spin, the rotational forces push material toward the equator, flattening them out somewhat. The moon's equatorial bulge is even greater than it should be given its current rotation rate, and scientists think that's because it was spinning faster earlier in its history, when lunar rock was more ductile. By contrast, although Pluto is spinning faster than our moon, it has no bulge at all.

"The moon is recording an ancient spin state," Nimmo says. "Pluto shows no evidence of that. There are different ways of destroying a fossil bulge, and one of them is to have an ocean." That's because water has more freedom of motion than ice, so a global liquid layer sloshing around inside would help counteract the spinning forces, reducing such a bulge.

So far, the New Horizons team is making a pretty solid case for an ocean on Pluto, says [Amy Barr Mlinar](#), an expert in the formation and evolution of solid planetary bodies at the Planetary Science Institute in Tucson, Arizona.

"It's based on a basic planetary-science type of analysis. It doesn't require a lot of fancy modeling where there are 45 different input parameters that can be messed up," says Barr Mlinar.

But not everyone is convinced just yet, even other members of the New Horizons team. Pluto's surface cracks could be explained by other internal changes in the ice's temperature or structure, says [Bill McKinnon](#), a planetary scientist at Washington University in St. Louis.

"Likewise, the collapse of a fossil bulge is consistent with an ocean on Pluto," McKinnon says. "But an ocean is not required. Nor does it mean the ocean, even if it did exist, has to exist today. The collapse of the fossil bulge could have occurred billions of years ago."

New Horizons performed a single flyby of Pluto. For more concrete proof of Pluto's ocean, "we would need to go back with an orbiter mission, maybe later in this century," McKinnon says.

If future tests do confirm the presence of an ocean on Pluto, McKinnon thinks there could be even more hidden seas waiting to be discovered in the fringes of the solar system. Pluto is part of the Kuiper belt, a ring of similar bodies that could also be generating internal heat from radioactive decay.

"Other large Kuiper belt objects are similarly or even more rock-rich, so these worlds could also have oceans," he says.

Such distant oceans would be very different from what we're accustomed to on Earth, notes [Nadine Barlow](#), an astronomer at Northern Arizona University.

Besides being locked beneath dozens of feet of ice, a Plutonian ocean would almost certainly have a different composition than Earth's seas.

"We have to remember that the ices out at Pluto not only include water ice but also carbon dioxide and methane ices," says Barlow. Compared to our seas, Pluto's potential ocean would also likely be especially briny, rich in dissolved salts and ammonia that would help reduce its freezing point and keep it in a liquid state.

Those extra ingredients would make Pluto's seawater unappealing to astronauts, but it's still possible some forms of extreme life could call such an ocean home.

And while New Horizons has already sped away from Pluto towards its [next Kuiper belt target](#), NASA's planned mission to the Jovian moon Europa might be a crucial testing ground for studying subsurface oceans on icy bodies and determining their feasibility for hosting life.

That means the Europa mission and any future treks to explore Pluto will need to take precautions so as not to contaminate any potentially life-supporting environments with terrestrial organisms, says Barlow.

Barr Mlinar agrees: "We may have to think of clever ways to explore the chemistry of Pluto's ocean from the surface," she says. "We have to learn more about the geology of these bodies and how material from the ocean can be expressed on the surface."

<http://www.medscape.com/viewarticle/856669>

Three Must-Read Emergency Medicine Articles of 201

The past year has again been a fantastic year for the emergency medicine (EM) literature.

Amal Mattu, MD

Introduction

Some new concepts for life-saving treatments have emerged and been espoused, whereas other long-held beliefs have been torn down. Many new guidelines were published, and old guidelines were updated. Original research has continued to flourish. The overall quality of the EM literature continues to excel.

As in recent years, I present here a few of my favorite articles of the past calendar year.

Narrowing my selections was difficult, and I chose to avoid topics that I've covered in prior [Viewpoints](#) (eg, resuscitation updates, chest pain workup) or in the 2014 end-of-the-year review (eg, updates in sepsis, acute coronary syndrome [ACS] management).

I'll make the usual disclaimer that these are not necessarily the best articles from a methodological standpoint, but they are practice-changing and focus on high-risk conditions where lives are at stake.

In particular, these are articles that I would strongly suggest that all emergency physicians should read, beyond my simple summaries, for the sake of the background knowledge they will impart.

In the limited space here, I cannot possibly do them full justice. They are excellent, and worth your time to read!

Cardiac Arrest: A Treatment Algorithm for Emergent Invasive Cardiac Procedures in the Resuscitated Comatose Patient

Rab T, Kern KB, Tamis-Holland JE, et al; Interventional Council, American College of Cardiology J Am Coll Cardiol. 2015;66:62-73

In 2013, the American College of Cardiology and the American Heart Association published their joint update of the guidelines for management of ST-segment elevation myocardial infarction (STEMI).^[1] In that document, they assigned a class I recommendation for patients who have postarrest ST-segment elevation (STE) to be taken immediately for cardiac catheterization and potential percutaneous coronary intervention (PCI).

The publication of that new guideline made it much easier to send postarrest patients with STE for cardiac catheterization, but patients who did not manifest STE on the ECG after resuscitation were still a quandary. However, this past summer, the Interventional Council of the American College of Cardiology published a review of the literature and a proposed algorithm for how resuscitated postarrest patients that remain comatose and manifest a STEMI or non-STE-ACS pattern on the ECG should be treated.

The recommendations are as follows:

- ***Patients with out-of-hospital cardiac arrest who have achieved return of spontaneous circulation but remain comatose should receive an immediate ECG. Targeted temperature management should be initiated. The guidelines do not specify whether the goal temperature should be 33°C or 36°C [91.4 or 96.8F].***
- ***Patients who manifest STE should be referred for urgent cardiac catheterization and possible PCI. Negative prognostic factors should be taken into account ("unfavorable resuscitation features," discussed further below), but the default clearly appears to be activation to the catheterization laboratory.***
- ***If the patient does not manifest STE, the recommendation is to consult with interventional cardiology and intensive care services and discuss the best course of action. In the absence of multiple unfavorable resuscitation features, strong consideration should be given to proceeding with urgent cardiac catheterization and possible PCI.***
- ***Patients with multiple unfavorable resuscitation features are less likely to benefit from urgent cardiac catheterization and are best managed initially with standard resuscitation of their hemodynamic, metabolic, and other underlying conditions (eg, sepsis). The Table shows unfavorable resuscitation features.***

Table. Unfavorable Resuscitation Features

Unwitnessed arrests	pH < 7.2
Initial rhythm nonventricular fibrillation	Lactate level > 7
No bystander CPR	Age > 85 yr
> 30 min to ROSC	End-stage renal disease
Ongoing CPR	Noncardiac causes (eg, sepsis, trauma)

CPR = cardiopulmonary resuscitation; ROSC = return of spontaneous circulation

The authors provide a nice review of the literature that justifies their recommendations. As a whole, this is an outstanding review and well worth the read.

After discussions between representatives from our medical center's EM department and division of cardiology, our own University of Maryland Network of hospitals has adopted this protocol. I suggest that other EM groups should meet with their cardiology colleagues as well in order to discuss plans for how to care for these patients, and consider adopting a similar protocol.

Evaluation of Patients With Suspected Acute Pulmonary Embolism: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians

Raja AS, Greenberg JO, Qaseem A, Denberg TD, Fitterman N, Schuur JD; Clinical Guidelines Committee of the American College of Physicians *Ann Intern Med.* 2015;163:701-711

The diagnosis of pulmonary embolism (PE) is definitely one of the great challenges in acute care medicine. I can't think of any condition that is so frequently worked up with negative results and yet is also so often underdiagnosed, with catastrophic results and resulting litigation. In addition, we in EM are often chastised for overordering D-dimer levels and CT pulmonary angiograms (CTPAs), yet we continue to practice in this way for lack of an acceptable standard method of working up patients. However, there may finally be some good news that will decrease workups, misdiagnoses, and litigation.

In November 2015, the American College of Physicians' Clinical Guidelines Committee published a set of recommendations for best practice with regard to working up PE. The document was evidence-based, straightforward, and clinically relevant. The document essentially serves as a guideline recommendation from a major national organization, which provides strong medicolegal protection when following the recommendations.

There were six pieces of "Best Practice Advice" from the Committee, which I have listed below.

• **Best Practice Advice 1: Clinicians should initiate their evaluation of patients with possible PE by using validated clinical prediction rules (eg, Wells or revised Geneva scores) to estimate the pretest probability of PE as low, intermediate, or high risk.**

• **Best Practice Advice 2: Clinicians should not obtain D-dimer measurements or imaging studies in patients with a low pretest probability of PE and who meet all of the pulmonary embolism rule-out criteria (PERC). If the patient with low pretest probability is PERC-negative, PE is considered ruled out and the workup is completed. If the patient is PERC-positive, a D-dimer value may then be obtained.**

• **Best Practice Advice 3: A high-sensitivity D-dimer test (enzyme-linked immunosorbent assay) should be obtained as the initial diagnostic test in patients who (1) have a low pretest probability for PE but are PERC-positive, or (2) have an intermediate pretest probability of PE. If the D-dimer value is within normal limits, imaging is deferred and the workup for PE is completed. D-dimer testing should not be performed for patients with high pretest probability for PE (see Best Practice Advice 6, below).**

• **Best Practice Advice 4: Clinicians should use an age-adjusted D-dimer threshold (top normal level = age × 10 ng/mL rather than a generic 500 ng/mL cutoff) for patients older than 50 years to determine whether imaging is necessary.**

• **Best Practice Advice 5: Clinicians should not obtain imaging studies in patients with D-dimer levels below the cutoffs noted above.**

• **Best Practice Advice 6: Clinicians should obtain imaging with CTPA in (1) patients with high pretest probabilities for PE, or (2) patients with elevated D-dimer levels based on the evaluations noted above. Clinicians should reserve ventilation/perfusion scans for patients with contraindications to CTPA or when CTPA is not available.**

The authors add a recommendation to obtain lower-extremity ultrasound before CTPA in patients who have lower-extremity symptoms or in pregnant patients during the first trimester.

This set of recommendations, when taken as a whole, is certain to reduce testing, especially imaging and radiation exposure for many patients. The guidelines are a quick read and are chock-full of useful clinical information; they are a must-read for anyone who has an interest in the topic or who desires some of the background information behind these Best Practice Advice statements.

In-flight Medical Emergencies During Commercial Travel

Nable JV, Tupe CL, Gehle BD, Brady WJ *N Engl J Med.* 2015;373:939-945

My final selection for must-read articles of 2015 is a fantastic review of the all-too-common and uncomfortable scenario of in-flight emergencies. Physicians in general do plenty of traveling, whether for conferences or vacation, and the majority of us have heard those words over the airline speakers, "If there's a doctor on board, please ring your call bell." Ugh! Though I'm sure we all feel the moral imperative to step forward and help, we also feel the discomfort of being outside our usual comfort zone of the emergency department.

The authors of this article are clearly able to relate to our sense of discomfort and provide some very simple and reasonable recommendations. They begin by discussing legal issues and Good Samaritan protection, which usually depends on

the state or country in which the plane lands. Fortunately, physicians are typically held to a gross negligence standard. However, be wary of requesting or accepting any form of remuneration for your services!

The authors discuss the typical contents of an airline medical kit, which usually contains an automatic external defibrillator, gloves, stethoscope, blood pressure cuff, IV needle and small amount of IV fluid, and some very basic resuscitation medications that might get you through one round of advanced cardiac life support.

They also discuss flight path diversion in medical emergencies and remind us that the airline captain makes the final decision on diversion, not you.

The authors then discuss basic responses to a potpourri of specific conditions, including cardiac arrest, ACS, stroke, altered mental status, syncope, trauma, dyspnea, acute infections, and psychiatric emergencies.

Discussions of each of these are beyond the scope of this summary, but the write-ups in the article are simple, practical, and brief.

The good news is that life-threatening emergencies on-board are actually quite rare, but like most emergency physicians, I truly believe that you only avoid disasters if you are prepared to deal with them—so read this article.

With that, I conclude this year's summary and recommendations for the must-read articles of 2015. I look forward to reading your comments, critiques, and especially your own recommendations for your favorite emergency medicine articles of 2015. Best wishes in 2016!

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http://www.eurekalert.org/pub_releases/201601/nurmq010816.php

Researchers' metallic glue may stick it to soldering and welding Northeastern's Hanchen Huang and colleagues, experts in nanotechnology, have developed a glue that binds metal to metal to glass to younameit, sets at room temperature, and requires little pressure to seal

Perhaps no startup was launched for a more intriguing reason than that of Northeastern's Hanchen Huang. From the company website:

"MesoGlue was founded by Huang and two of his PhD students: They had a dream of a better way of sticking things together."

Those "things" are everything from a computer's central processing unit and a printed circuit board to the glass and metal filament in a light bulb. The "way" of attaching them is, astonishingly, a glue made out of metal that sets at room temperature and requires very little pressure to seal. "It's like welding or soldering but without the heat," says Huang, who is professor and chair in the Department of Mechanical and Industrial Engineering.

In a new paper, published in the January issue of *Advanced Materials & Processes*, Huang and colleagues, including Northeastern doctoral student Paul Elliott, describe their latest advances in the glue's development. Our curiosity was piqued: Soldering with no heat? We asked Huang to elaborate.

On new developments in the composition of the metallic glue:

"Both 'metal' and 'glue' are familiar terms to most people, but their combination is new and made possible by unique properties of metallic nanorods - infinitesimally small rods with metal cores that we have coated with the element indium on one side and gallium on the other.

These coated rods are arranged along a substrate like angled teeth on a comb: There is a bottom 'comb' and a top 'comb.' We then interlace the 'teeth.' When indium and galium touch each other, they form a liquid. The metal core of the rods acts to turn that liquid into a solid.

The resulting glue provides the strength and thermal/?electrical conductance of a metal bond. We recently received a new provisional patent for this development through Northeastern University."

On the special properties of the metallic glue:

"The standard polymer glue does not function at high temperatures or high pressures, but the metallic glue does. The standard glue is not a great conductor of heat and/?or electricity, but the metallic glue is. Furthermore, the standard glue is not very resistant to air or gas leaks, but the metallic glue is.

"Hot' processes like soldering and welding can result in metallic connections that are similar to those produced with the metallic glue, but they cost much more. In addition, the high temperature necessary for these processes has deleterious effects on neighboring components, such as junctions in semiconductor devices. Such effects can speed up failure and not only increase cost but also prove dangerous to users."

What are some applications of the technology?

"The metallic glue has multiple applications, many of them in the electronics industry. As a heat conductor, it may replace the thermal grease currently being used, and as an electrical conductor, it may replace today's solders. Particular products include solar cells, pipe fittings, and components for computers and mobile devices."

http://www.eurekalert.org/pub_releases/2016-01/si-sfk010516.php

Scientists find key driver for treatment of deadly brain cancer

Scientists at the Salk Institute have discovered how a protein helps glioblastoma proliferates so quickly and how to turn off this engine of tumor growth

LA JOLLA--Glioblastoma multiforme is a particularly deadly cancer. A person diagnosed with this type of brain tumor typically survives 15 months, if given the best care. The late Senator Ted Kennedy succumbed to this disease in just over a year.

But scientists at the Salk Institute have discovered a key to how these tumor cells proliferate so quickly --and ways to turn this engine of tumor growth into a target for cancer treatment.

"This is a disease for which there has been practically no improvement in treatment outcome for years," said Inder Verma, professor in the Salk Institute's Laboratory of Genetics and senior author of the paper published January 8, 2016 in the journal *Science Advances*. "It is clear that even if a surgeon removes 99.99 percent of a glioblastoma multiforme tumor, what is left behind will come back and grow into more tumor."

To study how glioblastoma multiforme spreads, Verma's team focused on a transcription factor called nuclear factor kB (or NF-kB). A transcription factor is a protein that binds to DNA and controls the fate of gene expression for a particular set of genes. Several known factors can trigger NF-kB activity in a cell, including ultraviolet and ionizing radiation, immune proteins (cytokines) and DNA damage.

In the case of glioblastoma multiforme, Verma and colleagues ran a battery of tests to show how overzealous NF-kB activity pushed the cancer cells to proliferate, and how stopping NF-kB slowed cancer growth and increased survival.

"Our experiments confirmed that NF-kB is required for the cancer cell to proliferate," says Dinorah Friedmann-Morvinski, first author of the paper and currently a researcher in the department of biochemistry and molecular biology at Tel Aviv University in Israel. "But now we have finally found a way to ameliorate the tumor to increase lifespan."

Verma's team started with a mouse model of glioblastoma multiforme and used genetic tools to manipulate cells into shutting down NF-kB activity in two ways. The team ramped up the presence of a protein called Ikbam, which inhibits NF-kB activity. They also eliminated an enzyme that increases NF-kB activity. With less NF-kB activity, tumor growth slowed and mice lived significantly longer than mice whose NF-kB activity was left alone. But while these genetic experiments demonstrated the role of NF-kB in glioblastoma multiforme, they aren't a feasible treatment in humans.

"So we asked how could we manipulate the system using pharmacology rather than genetics," says Verma.

Scientists have long suspected that one reason why glioblastoma multiforme comes back so quickly after surgery is the so-called tumor microenvironment. In other words, a tumor changes the environment of its surroundings (nearby tissues) to make it easier for cancer cells to thrive, Verma explains.

Instead of using genetic tools, Verma and colleagues sought to treat the brain tumors in a way that also changed the tumor microenvironment. The scientists fed mice a peptide (called NBD) that is known to block NF-kB activity when NF-kB is triggered by cytokines (proteins produced by the immune system). The NBD peptide easily travels across the central nervous system, and can successfully penetrate glioblastoma tumor cells. Treating mice with the NBD peptide doubled their typical survival time compared to mice that didn't get the NBD peptide.

"We could increase survival time from one month without treatment to three months with treatment," says Verma. "That's a profound increase in life expectancy, especially considering a mouse only lives for two years." Yet, while the NBD peptide kept the tumors at bay, the peptide treatment eventually causes toxicity, most likely in the liver. So researchers explored another tactic to slow NF-kB activity.

Curbing NF-kB activity can be tricky because NF-kB has many important roles: it helps regulate cell survival, inflammation and immunity among many other functions in the cell.

"The ultimate goal is to block NF-kB, but because it turns on many genes--at least 100--our aim became finding the handful of genes that directly affect tumor growth," says Verma. "Then we can be more selective in treatment."

Salk scientists tracked which genes were influenced by NF-kB and found one, Timp1, which has been previously implicated in lung cancer. Targeting the Timp1 gene in treatment also slowed tumor growth and increased survival time in mice by a few months.

"In the future we want to focus on ways to reduce the toxicity of anti-NF-kB drugs," said Friedmann-Morvinski. "We may do this by specifically targeting these drugs to the tumor, or by identifying downstream targets of the NF-kB pathway, like Timp1, that also prolong survival." Further experiments may identify treatments that target NF-kB activity in a safe, but effective way.

Other authors on the paper included Rajesh Narasimamurthy, Yifeng Xia, Chad Myskiw and Yasushi Soda of the Salk Institute for Biological Studies.

The work was funded by the National Institutes of Health, the H.N. and Frances C. Berger Foundation, and the Leona M. and Harry B. Helmsley Charitable Trust.

<http://bit.ly/1SJ4pmU>

Rebooted Kepler Spacecraft Hauls in the Planets

Fresh worlds found by K2 mission push beyond original discoveries

By Alexandra Witze, Nature magazine on January 8, 2016

In the second phase of its life as a planet hunter, NASA's Kepler spacecraft is raking in exoplanet discoveries that are surprisingly different from those found during its first iteration.

Between 2009 and 2013, Kepler became the most successful planet-hunting machine ever, discovering at least 1,030 planets and more than 4,600 possible others in a single patch of sky. When a mechanical failure stripped the spacecraft of its ability to point precisely among the stars, engineers reinvented it in 2014 as the K2 mission, which looks at different parts of the cosmos for shorter periods of time.

In its first year of observing, K2 has netted more than 100 confirmed exoplanets, says astronomer Ian Crossfield at the University of Arizona in Tucson. They include a surprising number of systems in which more than one planet orbits the same star. The K2 planets are also orbiting hotter stars than are many of the Kepler discoveries.

"This is really showing the power and potential of K2," says Crossfield. "These are things we never found with four years of Kepler data." He and other scientists reported the findings this week at a meeting of the American Astronomical Society in Kissimmee, Florida.

The original Kepler mission was designed to answer a specific question: what fraction of Sun-like stars have Earth-size planets around them? Unbound by those constraints—even if not as good at pointing itself—K2 has been able to explore wider questions of planetary origin and evolution. "Now we get to look at a much bigger variety," says Steve Howell, the mission's project scientist at NASA's Ames Research Center in Moffett Field, California.

And because K2 looks at stars that are generally brighter and closer to Earth than Kepler did, the exoplanets that the mission finds are likely to be the best studied for the foreseeable future. This is because they are near enough to allow astronomers to explore them with other telescopes on Earth and in space.

Unexpected bounty

In the past year, K2 has uncovered not just planets—such as three super-Earths around a single star—but also surprises such as the disintegrating remains of a planet swirling around a white dwarf star. It has even probed exploding stars—because K2 stares constantly at a patch of the sky, it is able to catch a supernova as it brightens instead of later in its explosion, as other telescopes typically do.

Among the K2 planets confirmed so far, 58 are singletons, 28 come from systems with at least two planets and 14 are triples, Crossfield says. In addition, K2 has unearthed more than 200 candidate planets, says Andrew Vanderburg, an astronomer at the Harvard Smithsonian Center for Astrophysics in Cambridge, Massachusetts.

K2 observes a larger fraction of the cool stars known as M dwarfs—the most common type of star in the Galaxy—than Kepler did. But surprisingly, fewer of the K2 planets are orbiting M dwarf stars. A higher percentage of them, at least so far, circle stars that are hotter and more like the Sun, says Courtney Dressing, an astronomer at the California Institute of Technology (Caltech) in Pasadena.

K2 will begin a new type of planet-hunting on April 7. Normally the spacecraft searches for a temporary dimming of a star caused when a planet crosses in front of it.

For just under three months, however, it will look for the temporary brightening of cosmic objects, such as a galaxy, caused when a planet bends light as it crosses the line of sight between it and the observer. The team expects to catch between 85 and 120 of these 'microlensing' planets during the campaign.

The survey will involve other telescopes and be the first automated search to be done simultaneously from the ground and in space, says Calen Henderson, an astronomer at NASA's Jet Propulsion Laboratory in Pasadena, California.

That means much more work ahead for mission scientists. "Kepler was one field and it ruined your summer," says Caltech astronomer David Ciardi. "K2 is ruining our whole year."

<http://www.bbc.com/news/health-35254508>

How to deal with a medical emergency on the Space Station

A major medical emergency has never occurred on the International Space Station - but what would happen if it did? And what lessons could be learnt for treating similar emergencies on Earth?

By Philippa Roxby Health reporter, BBC News

When Tim Peake blasted into orbit in December, he knew that the 40 hours of medical training he'd received would prepare him for most health problems during his six-month stay on the International Space Station.

In addition to life-saving skills, he had been taught how to stitch a wound, give an injection and even extract a tooth.

According to Nasa, this training would prepare him and his crew members for the most common medical problems faced on the ISS - like motion sickness, headaches, back pain, skin conditions, burns and dental emergencies.

But faced with a far more serious medical emergency - what would they do?

Limited options

The medical kit on the ISS is basic. It contains a first aid kit, a large book of medical conditions and some useful medical equipment including a defibrillator, a portable ultrasound, a device for looking deep into the eye and two litres of saline. Although their lightweight ultrasound device can generate very clear pictures of the inside of the human body, and relay them to a medical team back on Earth for help with diagnosis, there would be no means of fixing the underlying problem on the ISS. Dr David Green, senior lecturer in aerospace physiology at Kings College London, says a better option would be to return the patient to Earth in the Soyuz spacecraft docked to the ISS, a journey of around three-and-a-half hours. But that's far from straightforward.

"They have limited resources on the ISS but there are no life support facilities on Soyuz either. If it's a good flight back they could experience a g-force of 4g-5g on re-entry into Earth's atmosphere. That's pretty unpleasant for a healthy individual, never mind someone who's critically ill."

The health and fitness of all astronauts is very closely monitored in the months before launch by a flight surgeon who looks after them and their family before, during and after their six-month stay on the ISS.

In a control centre on the ground, a team is constantly monitoring the astronauts, collecting data on everything from the exercise they are doing to what they are eating. As a result, Dr Green says, the risk of an astronaut developing a serious illness and needing intensive care is very small, but it is still around 1% to 2% per person per year. So it is likely to happen sooner or later.

Look to the skies

The challenges of coping with serious medical emergencies are not just confined to the ISS. Dr Fred Papali, who works in critical care medicine at the University of Maryland, US, and has spent time working in emergency wards in hospitals in Haiti and south Sudan, says there are lessons to be learnt for many remote, rural regions on Earth. He sees parallels between the isolation of the ISS and some rural areas in low-income countries, where health care services are lacking.

"In many parts of the world, basic emergency and acute medical facilities just don't exist. It's challenging because the doctors there don't have experience or training... and patients are often clinging on to life with their pinky."

He has witnessed how hospitals with no running water and no electricity saved lives using ultrasound to make quick diagnoses in medical emergencies.

"It's a simple and revolutionary technology which can look more deeply," he says. Dr Papali also says that the use of telemedicine - the remote treatment of patients by a doctor using an electronic video or audio link, which is so vital in space - should be more widespread in the developing world.

When an internet connection is all that is needed in a remote location to dial up an experienced doctor to ask for advice or to access information, "very cheap interventions can make a difference between life and death".

It is no real surprise that aerospace technology can benefit communities in disaster zones, in high-altitude areas, and in remote and isolated villages on terra firma.

Their needs are very similar. Medical devices in space must be small, light, robust, smart and low in power consumption. The same is true in remote regions.

So Nasa and the European Space Agency have made it their business to share the benefits of any innovations in aerospace technology with the wider medical and science community.

Training people to use the technology correctly is important too. Just as Tim Peake has been trained to use medical equipment and act like a space paramedic, similar training can be given to people in areas where there are shortages of doctors and healthcare workers, for example in sub-Saharan Africa.

To boldly go...

As manned space missions are planned to the Moon, Mars and beyond, the need to improve emergency medical care in space increases even more.

Making a qualified doctor part of the crew might help with the problem of dealing with medical emergencies thousands of miles from home. It worked for the crew of the Starship Enterprise in Star Trek. But would carrying out emergency surgery in space be realistic?

At present, operations would be impractical in micro gravity because blood and fluids would leak out of the patient's body (which is three-quarters water), float around, infect other astronauts and contaminate the spacecraft.

Scientists in the US have been testing the idea of placing a transparent dome over a wound and then filling it with fluid, such as saline solution, to stem the blood flow. It could stop the bleeding or give a surgeon time to seal the wound.

Nasa is also planning to turn robots into space surgeons. The Robonaut 2 is already on board the ISS and the aim is that it performs basic medical functions which can be remotely controlled from Earth. Eventually the hope is that it could be programmed to carry out complicated surgery - but this is still some way off.

On long-duration space missions there would be a need for smarter medical devices, medications with a much longer shelf life and more extensive medical training. It's a long way to Mars, and with a time delay of about 20 minutes each way when communicating with Earth, speedy medical advice won't be possible.

Space medicine experts have their work cut out - but you wouldn't bet against them coming up with an innovative solution which could benefit everyone.

<http://s.nikkei.com/1K8sn3U>

Japan's Nichi-Iko to sell brand-new drugs in US

Japan's Nichi-Iko Pharmaceutical seeks to crack the U.S. market with brand-new drugs -- not the generic drugs the company is known for -- as the domestic market is expected to stop growing in the long run.

TOKYO - The Japanese market for generics is expanding as the government strives to increase the share of these drugs in prescriptions to more than 80% by fiscal 2020. But concerns are strong that drug prices will eventually fall and the market will contract, prompting some generics makers to look overseas.

Nichi-Iko, the largest generic-drug company in Japan, plans to apply next year for approval from the U.S. Food and Drug Administration to manufacture one brand-new drug. It hopes to gain approval in 2018 and generate annual sales of 3 billion yen (\$25.2 million).

The company believes it will be able to develop drugs more efficiently in the U.S., where finding institutions carrying out clinical trials is relatively easy. It also hopes that brand-new drugs will bring it higher profit margins than generics.

Nichi-Iko is also preparing U.S. sales of biosimilars.

Sawai Pharmaceutical, the No. 2 generics player in Japan, is also eyeing the U.S. market. Unlike Nichi-Iko, Sawai will release generics there. It has applied for FDA approval for its generic version of the Livalo lipid-lowering agent and expects to start selling it as early as March 2018.