

http://www.eurekalert.org/pub_releases/2013-02/sfmm-rpt021113.php

Preemptive treatment of severe morning sickness decreases suffering for moms-to-be

Researchers will present data showing the effectiveness of preemptive treatment for severe morning sickness

In a study to be presented on February 14 between 1:15 p.m., and 3:30 p.m. PST, at the Society for Maternal-Fetal Medicine's annual meeting, The Pregnancy Meeting™, in San Francisco, California, researchers will present data showing the effectiveness of preemptive treatment for hyperemesis gravidarum and severe morning sickness.

Hyperemesis gravidarum is a severe form of morning sickness which affects two percent of pregnant women. HG is marked by persistent nausea and vomiting, and can begin early in the first trimester, continuing well into the second, third or even up to giving birth. Women who suffer from HG become severely dehydrated, and often end up in the hospital on IV fluids. Recurrence rate for women who had HG in their first pregnancy is 75-85 percent in subsequent pregnancies, and the condition can be fatal.

Previous treatment for HG was to administer medication (Diclectin in Canada, Bendectin in the US) at the onset of symptoms, but this course of treatment provided little, if any, relief.

Drs. Gideon Koren and Caroline Maltepe, of The Hospital for Sick Children in Toronto, ON, Canada, divided 59 women with a history of HG or severe morning sickness into two groups: one would begin taking Diclectin as soon as the pregnancy was discovered; the second group would begin treatment at the first sign of nausea. They found the group receiving treatment before the onset of symptoms, had a significant decrease in risk of severe nausea and vomiting. "This is the first time there is an answer," said Dr. Koren. "Women who have experienced hyperemesis are so traumatized by it, they are afraid of a second pregnancy."

Dr. Koren, who with Dr. Maltepe runs a severe morning sickness counseling program at The Hospital for Sick Children, says the drug used to treat HG is safe to take throughout pregnancy or even before conception.

Koren and Maltepe conducted the study at The Hospital for Sick Children, The Motherisk Program/Division of Clinical Pharmacology and Toxicology, Toronto, ON, Canada.

http://www.eurekalert.org/pub_releases/2013-02/ru-ops021113.php

1-2 punch strategy against bacteria and cancer

Combining synthetic, natural toxins could disarm cancer, drug-resistant bacteria

HOUSTON - Cancer researchers from Rice University suggest that a new man-made drug that's already proven effective at killing cancer and drug-resistant bacteria could best deliver its knockout blow when used in combination with drugs made from naturally occurring toxins.

"One of the oldest tricks in fighting is the one-two punch -- you distract your opponent with one attack and deliver a knockout blow with another," said José Onuchic of Rice's Center for Theoretical Biological Physics (CTBP). "Combinatorial drug therapies employ that strategy at a cellular level.

"A wealth of research in recent years has shown that both cancer and bacteria can mount sophisticated, coordinated defenses against almost any drug," said Onuchic, Rice's Harry C. and Olga K. Wiess Professor of Physics and Astronomy, professor of chemistry, and biochemistry and cell biology. "By combining drugs, particularly those that place stress on different parts of the cell, we expect it will be possible to knock out either cancer cells or bacteria while simultaneously inhibiting their ability to become drug-resistant."

Onuchic and CTBP colleagues Eshel Ben-Jacob and Patricia Jennings reached their conclusions after analyzing several studies on anti-microbial peptides (AMPs), corkscrew-shaped chains of amino acids that kill Gram-negative bacteria. The CTBP team's ideas appear this week in the Proceedings of the National Academy of Sciences (PNAS) as a commentary on new findings from MD Anderson Cancer Center about a promising synthetic AMP called D-KLAKLAK-2. In its new research, MD Anderson researchers found D-KLAKLAK-2, which was already known to kill cancer cells, is also an effective drug against antibiotic-resistant Gram-negative bacteria.

"AMPs are produced naturally by a number of animals to fight bacteria," said Ben-Jacob, professor of biochemistry and cell biology at Rice and the Maguy-Glass Chair in Physics of Complex Systems and professor of physics and astronomy at Tel Aviv University. "AMPs are corkscrew-shaped. They do not harm the animals' own cells, but they penetrate and shred the double-layered membranes of Gram-negative bacteria."

Gram-negative bacteria are a class of pathogens that includes drug-resistant varieties of bacteria that cause pneumonia, sepsis and other deadly diseases.

Ben-Jacob said cancer researchers have previously shown that they can tag AMPs with special "marker" molecules that allow the AMPs to penetrate and kill cancer cells. The markers allow the AMPs to be taken inside the cancer cells, something they cannot normally do. "Once inside the cancer cells, the AMPs target and damage the cell's power plant, an organelle called the mitochondria, which has a double-layered membrane that is remarkably similar to that of Gram-negative bacteria," he said.

Though research has shown that AMPs can kill cancer cells, scientists are concerned that cancer cells could develop resistance to the compounds. In part, this concern arises from the fact that AMPs are fairly common in nature and that some organisms already have genetic mutations that allow them to evade AMP attacks.

To circumvent these natural defenses, MD Anderson researchers Wadih Arap and Renata Pasqualini led an effort a few years ago to create a synthetic version of a natural corkscrew-shaped AMP called KLAKLAK-2. Like all naturally occurring AMPs, KLAKLAK-2 has a left-handed twist -- much like the threads of a screw that turn clockwise. To make the molecule more difficult for cancer cells to fight, the MD Anderson team built a right-handed, "counterclockwise" version of the molecule called D-KLAKLAK-2, with the "D" denoting right-handedness. In its most recent studies, which also appear this week in PNAS, the MD Anderson team found that D-KLAKLAK-2 is an effective killer of Gram-negative bacterial pathogens, including several types that have grown resistant to traditional antibiotics.

"Bacteria are notorious for their rapid development of drug resistance," Ben-Jacob said. "However, both bacteria and cancer have impaired ability to resist these man-made 'mirror' compounds because they cannot use the machinery they have evolved to disarm the right-handed weapons."

Onuchic said another advantage of therapies involving synthetic AMPs like D-KLAKLAK-2 is that the drugs can be administered in extremely small doses, which will reduce side effects.

The Rice team suggests maximizing the benefits of synthetic AMPs by using them in drug cocktails that act like a one-two punch for either bacteria or cancer.

Naturally occurring AMPs are chemical weapons that bacteria themselves have developed over millions of years in their never-ending war among themselves. The team reasons that combining these natural toxins with man-made mirror drugs will create the drug equivalent of a one-two punch. The combination should "confuse" bacteria and cancer and prevent them from rapidly becoming resistant to the man-made drugs.

"Nature is smarter than we are," Ben-Jacob said. "Time and again, we have seen that seemingly simple cellular foes like bacteria and cancer can learn to mount effective defenses against any new drug we create. It is time to accept them as sophisticated enemies. We should attack them in much the same way that a well-trained boxer or military commander would go after a wily opponent -- with multiple, coordinated blows of very different kinds."

Jennings is professor of chemistry and biochemistry at the University of California, San Diego. Research at CTBP is supported by the National Science Foundation and by the Cancer Prevention and Research Institute of Texas.

http://www.eurekalert.org/pub_releases/2013-02/uoc--sca021113.php

Scientists create automated 'time machine' to reconstruct ancient languages

Computer program speeds up replication of ancestral tongues

Ancient languages hold a treasure trove of information about the culture, politics and commerce of millennia past. Yet, reconstructing them to reveal clues into human history can require decades of painstaking work. Now, scientists at the University of California, Berkeley, have created an automated "time machine," of sorts, that will greatly accelerate and improve the process of reconstructing hundreds of ancestral languages.

In a compelling example of how "big data" and machine learning are beginning to make a significant impact on all facets of knowledge, researchers from UC Berkeley and the University of British Columbia have created a computer program that can rapidly reconstruct "proto-languages" – the linguistic ancestors from which all modern languages have evolved. These earliest-known languages include Proto-Indo-European, Proto-Afroasiatic and, in this case, Proto-Austronesian, which gave rise to languages spoken in Southeast Asia, parts of continental Asia, Australasia and the Pacific.

"What excites me about this system is that it takes so many of the great ideas that linguists have had about historical reconstruction, and it automates them at a new scale: more data, more words, more languages, but less time," said Dan Klein, an associate professor of computer science at UC Berkeley and co-author of the paper published online today (Feb. 11) in the journal *Proceedings of the National Academy of Sciences*.

The research team's computational model uses probabilistic reasoning – which explores logic and statistics to predict an outcome – to reconstruct more than 600 Proto-Austronesian languages from an existing database of more than 140,000 words, replicating with 85 percent accuracy what linguists had done manually. While manual reconstruction is a meticulous process that can take years, this system can perform a large-scale reconstruction in a matter of days or even hours, researchers said.

Not only will this program speed up the ability of linguists to rebuild the world's proto-languages on a large scale, boosting our understanding of ancient civilizations based on their vocabularies, but it can also provide clues to how languages might change years from now.

"Our statistical model can be used to answer scientific questions about languages over time, not only to make inferences about the past, but also to extrapolate how language might change in the future," said Tom Griffiths,

associate professor of psychology, director of UC Berkeley's Computational Cognitive Science Lab and another co-author of the paper.

The discovery advances UC Berkeley's mission to make sense of big data and to use new technology to document and maintain endangered languages as critical resources for preserving cultures and knowledge. For example, researchers plan to use the same computational model to reconstruct indigenous North American proto-languages.

Humans' earliest written records date back less than 6,000 years, long after the advent of many proto-languages. While archeologists can catch direct glimpses of ancient languages in written form, linguists typically use what is known as the "comparative method" to probe the past. This method establishes relationships between languages and identifying sounds that change with regularity over time to determine whether they share a common mother language.

"To understand how language changes -- which sounds are more likely to change and what they will become -- requires reconstructing and analyzing massive amounts of ancestral word forms, which is where automatic reconstructions play an important role," said Alexandre Bouchard-Côté, an assistant professor of statistics at the University of British Columbia and lead author of the study, which he started while a graduate student at UC Berkeley.

The UC Berkeley computational model is based on the established linguistic theory that words evolve along the branches of a family tree – much like a genealogical tree – reflecting linguistic relationships that evolve over time, with the roots and nodes representing proto-languages and the leaves representing modern languages. Using an algorithm known as the Markov chain Monte Carlo sampler, the program sorted through sets of cognates, words in different languages that share a common sound, history and origin, to calculate the odds of which set is derived from which proto-language. At each step, it stored a hypothesized reconstruction for each cognate and each ancestral language.

"Because the sound changes and reconstructions are closely linked, our system uses them to repeatedly improve each other," Klein said. "It first fixes its predicted sound changes and deduces better reconstructions of the ancient forms. It then fixes the reconstructions and re-analyzes the sound changes. These steps are repeated, and both predictions gradually improve as the underlying structure emerges over time."

<http://phys.org/news/2013-02-dogs-human-view.html>

Dogs may understand human point of view, researcher finds

Domestic dogs are much more likely to steal food when they think nobody can see them, suggesting for the first time they are capable of understanding a human's point of view.

Phys.org - Many dog owners think their pets are clever or that they understand humans but, until now, this has not been tested by science. Dr Juliane Kaminski, of the University of Portsmouth's Department of Psychology, has shown that when a human forbids a dog from taking food, dogs are four times more likely to disobey in a dark room than a lit room, suggesting they take into account what the human can or cannot see.

Dr Kaminski said: "That's incredible because it implies dogs understand the human can't see them, meaning they might understand the human perspective."

This is the first study to examine if dogs differentiate between different levels of light when they are developing strategies on whether to steal food. It is published in the journal *Animal Cognition*.

Dr Kaminski said: "Humans constantly attribute certain qualities and emotions to other living things. We know that our own dog is clever or sensitive, but that's us thinking, not them. "These results suggest humans might be right, where dogs are concerned, but we still can't be completely sure if the results mean dogs have a truly flexible understanding of the mind and others' minds. It has always been assumed only humans had this ability." The research is an incremental step in our understanding of dogs' ability to think and understand which could, in turn, be of use to those who work with dogs, including the police, the blind and those who use gun dogs, as well as those who keep them as pets.

Dr Kaminski ran a series of experiments in varied light conditions. In each test, a dog was forbidden by a human from taking the food. When the room was dark, the dogs took more food and took it more quickly than when the room was lit. The tests were complex and involved many variables to rule out that dogs were basing their decisions on simple associative rules, for example, that dark means food. There is no evidence on how well dogs can see in the dark, but the results of this research show dogs can differentiate between light and dark. Dr Kaminski said: "The results of these tests suggest that dogs are deciding it's safer to steal the food when the room is dark because they understand something of the human's perspective."

Dogs' understanding may be limited to the here and now, rather than on any higher understanding, Dr Kaminski said, and more research is needed to identify what mechanisms are controlling dogs' behaviour.

In total, 42 female and 42 male domestic dogs aged one year or older took part in the tests. They were chosen only if they were comfortable without their owners in the room, even in complete darkness, and if they were interested in food. "Some dogs are more interested in by food than others," Dr Kaminski said.

Previous studies have shown chimpanzees have a sophisticated understanding and seem to know when someone else can or can't see them and can also remember what others have seen in the past. It is not known how sophisticated dogs' understanding is in comparison. Many earlier research papers have found that, for dogs, a human's eyes are an important signal when deciding how to behave, and that they respond more willingly to attentive humans, than inattentive ones. *Provided by University of Portsmouth*

<http://www.sciencedaily.com/releases/2013/02/130211150745.htm>

Increase in Dance-Related Injuries in Children and Adolescents

An estimated 113,000 children and adolescents were treated in U.S. emergency departments for dance-related injuries.

Dance is a beautiful form of expression, but it could be physically taxing and strenuous on the human body, particularly for children and adolescents. A new study by researchers at the Center for Injury Research and Policy of The Research Institute at Nationwide Children's Hospital examined dance-related injuries among children and adolescents 3 to 19 years of age from 1991 to 2007. During the 17-year study period, an estimated 113,000 children and adolescents were treated in U.S. emergency departments for dance-related injuries.

According to the study, which is being published in the February 2013 print issue of the *Journal of Physical Activity and Health*, the annual number of dance-related injuries increased 37 percent, climbing from 6,175 injuries in 1991 to 8,477 injuries in 2007. Sprains and/or strains (52 percent) were found to be the most common types of dance-related injuries, with falls (45 percent) being the most common causes of injuries.

The study also found that 4 out of 10 injured dancers were between 15 and 19 years of age.

"We believe this could be due to adolescent dancers getting more advanced in their skills, becoming more progressed in their careers and spending more time training and practicing," said Kristin Roberts MS, MPH, lead author of the study and senior research associate at the Center for Injury Research and Policy at Nationwide Children's Hospital. "We encourage children to keep dancing and exercising. But it is important that dancers and their instructors take precautions to avoid sustaining injuries."

"Safety precautions such as staying well-hydrated, properly warming up and cooling down, concentrating on the proper technique and getting plenty of rest can help prevent dance-related injuries," said the study's senior author Lara McKenzie, PhD, principal investigator at the Center for Injury Research and Policy at Nationwide Children's and also a faculty member at The Ohio State University College of Medicine.

The Sports Medicine experts at Nationwide Children's treat the types of injuries seen in performing arts and dance athletes. Due to the increase in the number of dance-related injuries seen during the last few years, they have designed a number of services to address the needs of the young dancer.

"Adolescents are still growing into their bodies and as such often develop imbalances that can lead to injury," said Eric Leighton, ATC, an athletic trainer in Sports Medicine at Nationwide Children's. "It's critical that intervention and injury prevention be made available to them to address balance, strength and functional body control deficits as they grow. From pointe readiness screens to injury prevention programming, our team has a comprehensive approach to address the needs of these athletes."

This is the first study to use a nationally representative sample to examine dance-related injuries that were treated in U.S. emergency departments. Data for this study were obtained from the National Electronic Injury Surveillance System (NEISS), which is operated by the U.S. Consumer Product Safety Commission. The NEISS provides information on consumer product-related and sports and recreation-related injuries treated in hospital emergency departments across the country.

*Kristin J. Roberts, Nicolas G. Nelson, and Lara McKenzie. Dance-Related Injuries in Children and Adolescents Treated in US Emergency Departments in 1991–2007. *Journal of Physical Activity and Health*, 2013, 143 %u2013 150*

<http://www.sciencedaily.com/releases/2013/02/130211162223.htm>

Gene Today, Gone Tomorrow

Genes for Autism and Schizophrenia Only Active in Developing Brains

Genes linked to autism and schizophrenia are only switched on during the early stages of brain development, according to a study in mice led by researchers at the University of Oxford.

This new study adds to the evidence that autism and schizophrenia are neurodevelopmental disorders, a term describing conditions that originate during early brain development.

The researchers studied gene expression in the brains of mice throughout their development, from 15-day old embryos to adults, and their results are published recently in *Proceedings of the National Academy of Sciences*.

The study is a collaboration between researchers from the University of Oxford, King's College London and Imperial College London, and was funded by the Medical Research Council and the Wellcome Trust. The research focused on cells in the 'subplate', a region of the brain where the first neurons (nerve cells) develop. Subplate neurons are essential to brain development, and provide the earliest connections within the brain.

'The subplate provides the scaffolding required for a brain to grow, so is important to consider when studying brain development,' says Professor Zoltán Molnár, senior author of the paper from the University of Oxford, 'Looking at the pyramids in Egypt today doesn't tell us how they were actually built. Studying adult brains is like looking at the pyramids today, but by studying the developing brains we are able to see the transient scaffolding that has been used to construct it.'

The study shows that certain genes linked to autism and schizophrenia are only active in the subplate during specific stages of development. 'The majority of the autism susceptibility genes are only expressed in the subplate of the developing mouse brain,' explains Dr Anna Hoerder-Suabedissen, who led the study at the University of Oxford, 'Many can only be found at certain stages of development, making them difficult to identify at later stages using previous techniques.'

The group were able to map gene activity in full detail thanks to powerful new methods which allowed them to dissect and profile gene expression from small numbers of cells. This also enabled them to identify the different populations of subplate neurons more accurately.

Subplate neurons were first discovered in the 1970s by Professors Ivica Kostović and Pasko Rakic of Yale University. 'I am excited to see tangible genetic links supporting, even indirectly, the idea of a possible role of the transient embryonic subplate zone in the origin of disorders such as autism and schizophrenia,' says Professor Rakic, 'If this is possible to show in mice, where the subplate is relatively small, it is likely to be even more pronounced in humans, where it is much more evolved.'

'The study from Professor Molnár's group at Oxford may be the first step toward finding more such links in the future and opens the possibility of directly examining the roles of genetic variation and exposure to various environmental factors in animal models.'

Professor David Edwards, Director of the Centre for the Developing Brain at King's College London, and co-author of the paper, said: 'Using advanced techniques we have been able to define the biochemical pathways that are important during a particular phase of brain development. It has been suspected for a long time that if the development of the cortex is disrupted by genetic abnormalities or environmental stress (such as prematurity) this would have long-lasting adverse effects on brain development and could lead to problems like ADHD or autism. This study defines genes that are important in mice at this critical period and this does indeed seem to include genes known to predispose to autism and schizophrenia. It focuses attention even more firmly on early brain development as a cause of these distressing neuropsychological problems.'

Professor Hugh Perry, chair of the Medical Research Council's Neuroscience and Mental Health Board, said: 'By being able to pinpoint common genetic factors for neurological conditions such as autism and schizophrenia, scientists are able to understand an important part of the story as to why things go awry as our brains develop. The Medical Research Council's commitment to a broad portfolio of neuroscience and mental health research places us in a unique position to respond to the challenge of mental ill health and its relationship with physical health and wellbeing.'

Anna Hoerder-Suabedissen, Franziska M. Oeschger, Michelle L. Krishnan, T. Grant Belgard, Wei Zhi Wang, Sheena Lee, Caleb Webber, Enrico Petretto, A. David Edwards, and Zoltán Molnár. Expression profiling of mouse subplate reveals a dynamic gene network and disease association with autism and schizophrenia. PNAS, February 11, 2013 DOI: 10.1073/pnas.1218510110

<http://nyti.ms/15hrFiH>

Chagas Disease Costs U.S. More Than Better-Known Illnesses

Chagas disease may be obscure, but the economic burden it imposes on the world is greater than that of better-known diseases, like cervical cancer or cholera, according to a new study.

By DONALD G. McNEIL Jr.

Even in the United States, the authors said, the costs of Chagas are commensurate with those of more publicized diseases, like Lyme disease. (In the same league, perhaps, but not quite equal. In their study, published in *Lancet Infectious Diseases*, the authors calculated that Chagas cost the American economy \$900 million a year. A 1998 study estimated that Lyme disease cost \$2.5 billion.)

Chagas disease is caused by a trypanosome parasite transmitted by the bloodsucking "kissing bug," which bites victims as they sleep. Transmission is endemic in much of Latin America, from central Mexico to northern Argentina. Kissing bugs have been found in the southern United States; the bugs tend to live in substandard

housing and animal pens. The parasites cause an initial flulike illness that can be cured if it is caught. But it is often not diagnosed, and the infection may become chronic. It may be silent for decades and then emerge as long-term damage to the heart or intestines. It can be fatal.

Up to 10 million people may be infected, many of whom have emigrated from Latin America seeking jobs in the United States, Canada and Europe — especially Spain.

The authors, from the schools of public health and medicine of the University of Pittsburgh and from the Baylor College of Medicine, estimated the economic burden by trying to calculate the cost of hospitalization and care, including pacemaker implants, for those with heart damage or other organ failure. The costs vary by country, of course, with the United States being the most expensive.

The researchers then added estimates of “disability-adjusted life years,” a measure of how many years of healthy life are lost. They “cost” more when they are subtracted from the life of a working-age adult in a high-wage country than from a retiree or an infant in a poor country.

The authors estimate that the global burden of Chagas is about \$7 billion a year. By comparison, the burden of cervical cancer — a notorious killer of women, but almost only in poor countries, and usually as they age out of their working lives — is estimated at below \$5 billion.

The burden of rotavirus, a diarrheal disease that kills many babies but rarely endangers anyone over age 5, is estimated at \$2 billion. (By contrast, lung cancer’s burden is estimated at \$83 billion a year, and breast cancer’s at \$35 billion.) Many millions have been spent developing a rotavirus vaccine and on ways to fight cervical cancer in poor countries.

Knowing that Chagas is a serious economic threat could push policy makers to spend more money on developing vaccines against it, said Dr. Peter J. Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine and a co-author of the new study. Dr. Hotez is also president of the Sabin Vaccine Institute, which is doing research on Chagas vaccines.

This article has been revised to reflect the following correction: February 14, 2013 An earlier version of this article misstated the institution some of the researchers are affiliated with. It is the Baylor College of Medicine, not Baylor University.

<http://nyti.ms/XIU6m0>

Mice Fall Short as Test Subjects for Humans’ Deadly Ills

Researchers report evidence that the mouse model has been totally misleading for at least three major killers

By GINA KOLATA

For decades, mice have been the species of choice in the study of human diseases. But now, researchers report evidence that the mouse model has been totally misleading for at least three major killers — sepsis, burns and trauma. As a result, years and billions of dollars have been wasted following false leads, they say.

do raise troubling questions about diseases like the ones in the study that involve the immune system, including cancer and heart disease.

“Our article raises at least the possibility that a parallel situation may be present,” said Dr. H. Shaw Warren, a sepsis researcher at Massachusetts General Hospital and a lead author of the new study.

The paper, published Monday in Proceedings of the National Academy of Sciences, helps explain why every one of nearly 150 drugs tested at a huge expense in patients with sepsis has failed. The drug tests all were based on studies in mice. And mice, it turns out, can have something that looks like sepsis in humans, but is very different from the condition in humans.

Medical experts not associated with the study said that the findings should change the course of research worldwide for a deadly and frustrating condition. Sepsis, a potentially deadly reaction that occurs as the body tries to fight an infection, afflicts 750,000 patients a year in the United States, kills one-fourth to one-half of them, and costs the nation \$17 billion a year. It is the leading cause of death in intensive-care units.

“This is a game changer,” said Dr. Mitchell Fink, a sepsis expert at the University of California, Los Angeles, of the new study.

“It’s amazing,” said Dr. Richard Wenzel, a former chairman at the department of internal medicine at Virginia Commonwealth University and a former editor of The New England Journal of Medicine. “They are absolutely right on.”

Potentially deadly immune responses occur when a person’s immune system overreacts to what it perceives as danger signals, including toxic molecules from bacteria, viruses, fungi, or proteins released from cells damaged by trauma or burns, said Dr. Clifford S. Deutschman, who directs sepsis research at the University of Pennsylvania and was not part of the study.

The ramped-up immune system releases its own proteins in such overwhelming amounts that capillaries begin to leak. The leak becomes excessive, and serum seeps out of the tiny blood vessels. Blood pressure falls, and vital organs do not get enough blood. Despite efforts, doctors and nurses in an intensive-care unit or an

emergency room may be unable to keep up with the leaks, stop the infection or halt the tissue damage. Vital organs eventually fail.

The new study, which took 10 years and involved 39 researchers from across the country, began by studying white blood cells from hundreds of patients with severe burns, trauma or sepsis to see what genes were being used by white blood cells when responding to these danger signals.

The researchers found some interesting patterns and accumulated a large, rigorously collected data set that should help move the field forward, said Ronald W. Davis, a genomics expert at Stanford University and a lead author of the new paper. Some patterns seemed to predict who would survive and who would end up in intensive care, clinging to life and, often, dying.

The group had tried to publish its findings in several papers. One objection, Dr. Davis said, was that the researchers had not shown the same gene response had happened in mice.

“They were so used to doing mouse studies that they thought that was how you validate things,” he said. “They are so ingrained in trying to cure mice that they forget we are trying to cure humans.”

“That started us thinking,” he continued. “Is it the same in the mouse or not?”

The group decided to look, expecting to find some similarities. But when the data were analyzed, there were none at all.

“We were kind of blown away,” Dr. Davis said.

The drug failures became clear. For example, often in mice, a gene would be used, while in humans, the comparable gene would be suppressed. A drug that worked in mice by disabling that gene could make the response even more deadly in humans.

Even more surprising, Dr. Warren said, was that different conditions in mice — burns, trauma, sepsis — did not fit the same pattern. Each condition used different groups of genes. In humans, though, similar genes were used in all three conditions. That means, Dr. Warren said, that if researchers can find a drug that works for one of those conditions in people, it might work for all three.

The study’s investigators tried for more than a year to publish their paper, which showed that there was no relationship between the genetic responses of mice and those of humans. They submitted it to the publications *Science* and *Nature*, hoping to reach a wide audience. It was rejected from both.

Science and *Nature* said it was their policy not to comment on the fate of a rejected paper, or whether it had even been submitted to them. But, Ginger Pinholster of *Science* said, the journal accepts only about 7 percent of the nearly 13,000 papers submitted each year, so it is not uncommon for a paper to make the rounds.

Still, Dr. Davis said, reviewers did not point out scientific errors. Instead, he said, “the most common response was, ‘It has to be wrong. I don’t know why it is wrong, but it has to be wrong.’”

The investigators turned to *Proceedings of the National Academy of Sciences*. As a member of the academy, Dr. Davis could suggest reviewers for his paper, and he proposed researchers who he thought would give the work a fair hearing. “If they don’t like it, I want to know why,” he said. They recommended publication, and the editorial board of the journal, which independently assesses papers, agreed.

Some researchers, reading the paper now, say they are as astonished as the researchers were when they saw the data.

“When I read the paper, I was stunned by just how bad the mouse data are,” Dr. Fink said. “It’s really amazing — no correlation at all. These data are so persuasive and so robust that I think funding agencies are going to take note.” Until now, he said, “to get funding, you had to propose experiments using the mouse model.”

Yet there was always one major clue that mice might not really mimic humans in this regard: it is very hard to kill a mouse with a bacterial infection. Mice need a million times more bacteria in their blood than what would kill a person.

“Mice can eat garbage and food that is lying around and is rotten,” Dr. Davis said. “Humans can’t do that. We are too sensitive.”

Researchers said that if they could figure out why mice were so resistant, they might be able to use that discovery to find something to make people resistant.

“This is a very important paper,” said Dr. Richard Hotchkiss, a sepsis researcher at Washington University who was not involved in the study. “It argues strongly — go to the patients. Get their cells. Get their tissues whenever you can. Get cells from airways.”

“To understand sepsis, you have to go to the patients,” he said.

This article has been revised to reflect the following correction: February 11, 2013

An earlier version of this article misstated the position of Dr. Richard Wenzel. He is a former chairman of the department of internal medicine at Virginia Commonwealth University. He is not currently the chairman.

http://www.eurekalert.org/pub_releases/2013-02/wuso-ecd021213.php

Emerging cancer drugs may drive bone tumors

Investigational cancer drugs, IAP antagonists, may increase the risk of tumors spreading to bone.

Cancer drugs should kill tumors, not encourage their spread. But new evidence suggests that an otherwise promising class of drugs may actually increase the risk of tumors spreading to bone, according to researchers at Washington University School of Medicine in St. Louis.

The drugs, IAP antagonists, block survival signals that many cancer cells rely on to stay alive. Working in mice, the investigators found that targeting the same protein that makes tumors vulnerable to death also overactivates cells called osteoclasts, which are responsible for tearing down bone.

"These investigational drugs are getting broad attention right now because they seem to be very effective against primary tumors," says senior author Deborah V. Novack, MD, PhD, associate professor of medicine.

"There is also excitement because until now, these drugs have not appeared to have major side effects."

The research appears in the February issue of *Cancer Discovery*.

In light of the study, Novack urges oncologists to think about protecting bone in patients taking IAP antagonists, including patients with cancers that don't typically spread to bone. Numerous IAP antagonists are in early clinical trials against breast, lung, pancreatic, ovarian, prostate, liver, skin and blood cancers.

"For many of these cancers, doctors are not watching bone," Novack says. "Osteoporosis is not the biggest concern when treating cancer, but if they're not doing bone scans, they may miss a cancer spreading to bone."

To maintain healthy bone, osteoclasts work in tandem with cells that build new bone. But IAP antagonists overactivate osteoclasts, destroying bone that is not replaced. In mice, the researchers showed that the drug led to osteoporosis, creating an environment that encouraged tumor growth in degrading bone, even while simultaneously killing breast cancer cells elsewhere.

After showing that the problem with IAP antagonists is specific to bone, Novack and her colleagues tested long-established drugs called bisphosphonates that inhibit osteoclasts and are used to treat osteoporosis.

"We found that bisphosphonate treatment protected bone from the negative effects of these drugs," Novack says.

"While bisphosphonates are common for breast cancer patients, they're not, for example, commonly given to lung cancer patients. But since IAP antagonists are now in lung cancer trials, we're saying doctors may want to consider bisphosphonate treatment for lung cancer or other cancer patients receiving these drugs. Or at least closely monitor the bone status."

IAP antagonists are now only available to patients enrolled in phase 1 or 2 clinical trials. While these kinds of trials examine the short-term safety and effectiveness of new drugs, the researchers say they may not catch bone metastasis.

"These trials do not necessarily look for long-term effects of the drugs," says Chang Yang, MD, PhD, staff scientist and the paper's first author. "If the cancer is going to metastasize to bone, it may take six months to two years to see that outcome. This may not be seen during the clinical trial."

Numerous drug companies are developing IAP antagonists intended for many kinds of cancer, but only Genentech agreed to provide Novack and her colleagues with its drug, called BV6, to evaluate in the study. Because the investigators could not obtain other proprietary IAP antagonists, they also made two other similar drug compounds and found them to have the same detrimental effects on the bone.

And to further ensure that over-stimulated osteoclasts are the only culprit in the bone metastasis associated with these new drugs, they performed studies in mice that lack the ability to dial up the production of osteoclasts. Even when given IAP antagonists, these mice were protected from osteoporosis and osteoclast activation. Together, Novack says the studies have demonstrated that these results are unlikely to be a quirk of a particular compound.

"The osteoporosis and spread of tumors we see in bone are unintended side effects of IAP antagonists, but they're not off-target effects," she says. "They're based on the mechanism of action for the entire class of drugs."

Yang C, Davis JL, Zeng R, Vora P, Su X, Collins LI, Vangveravong S, Mach RH, Pivnicka-Worms D, Weilbaeher KN, Faccio R, Novack DV. Anticancer IAP inhibition increases bone metastasis via unexpected osteoclast activation. Cancer Discovery. February 2013.

This study was supported by the National Institutes of Health (NIH), grant number AR052705, with additional support from AR52921 and AR53628, CA100730, and the Barnes-Jewish Foundation. Histological and microCT analysis was supported in part by the Washington University Center for Musculoskeletal Research NIH/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), grant number AR057235. The Molecular Imaging Center was supported by NIH grant P50 CA94056. Genentech, Inc. provided BV6.

http://www.eurekalert.org/pub_releases/2013-02/dai-ops021213.php

Opioid prescription is on the increase

More and more opioids are being prescribed for pain relief in Germany.

This is the conclusion arrived at by Ingrid Schubert, Peter Ihle, and Rainer Sabatowski, whose study of a sample of inhabitants of the state of Hesse with health insurance from a large statutory provider is published in the latest issue of *Deutsches Ärzteblatt International* (Dtsch Arztebl Int 2013; 110(4): 45-51).

Behind this study lies the intention to improve pain treatment with opioids, particularly for patients with cancer. Prescribing too little results in inadequate alleviation of pain, while supplying too much entails the risk of addiction, especially in patients who do not have cancer.

The proportion of persons in the sample who received opioids increased between 2000 and 2010, and so did the number of daily doses per recipient. 3.7 million inhabitants of Germany received opioids in 2010, a million more than in 2000. The frequency of prescription of WHO step 3 opioids increased—most of all in noncancer patients, in spite of the lack of good evidence for this indication.

The study points to inappropriate provision: Despite the increase in opioid prescription, it cannot be concluded that cancer patients are receiving opioids in adequate amounts.

<http://www.aerzteblatt.de/pdf.asp?id=134120>

http://www.eurekalert.org/pub_releases/2013-02/uosc-scu020713.php

Stopping cold: USC scientists turn off the ability to feel cold

USC neuroscientists have isolated chills at a cellular level, identifying the sensory network of neurons in the skin that relays the sensation of cold.

David McKemy, associate professor of neurobiology in the USC Dornsife College of Letters, Arts and Sciences, and his team managed to selectively shut off the ability to sense cold in mice while still leaving them able to sense heat and touch.

In prior work, McKemy discovered a link between the experience of cold and a protein known as TRPM8 (pronounced trip-em-ate), which is a sensor of cold temperatures in neurons in the skin, as well as a receptor for menthol, the cooling component of mint. Now, in a paper appearing in the *Journal of Neuroscience* on February 13, McKemy and his co-investigators have isolated and ablated the neurons that express TRPM8, giving them the ability to test the function of these cells specifically.

Using mouse-tracking software program developed by one of McKemy's students, the researchers tested control mice and mice without TRPM8 neurons on a multi-temperature surface. The surface temperature ranged from 0 degrees to 50 degrees Celsius (32 to 122 degrees Fahrenheit), and mice were allowed to move freely among the regions.

The researchers found that mice depleted of TRPM8 neurons could not feel cold, but still responded to heat. Control mice tended to stick to an area around 30 degrees Celsius (86 degrees Fahrenheit) and avoided both colder and hotter areas. But mice without TRPM8 neurons avoided only hotter plates and not cold — even when the cold should have been painful or was potentially dangerous.

In tests of grip strength, responses to touch, or coordinated movements, such as balancing onto a rod while it rotated, there was no difference between the control mice and the mice without TRPM8-expressing neurons. By better understanding the specific ways in which we feel sensations, scientists hope to one day develop better pain treatments without knocking out all ability to feel for suffering patients.

"The problem with pain drugs now is that they typically just reduce inflammation, which is just one potential cause of pain, or they knock out all sensation, which often is not desirable," McKemy said. "One of our goals is to pave the way for medications that address the pain directly, in a way that does not leave patients completely numb."

Coauthors on the paper are Wendy Knowlton, Radhika Palkar, Erika Lippoldt, Daniel McCoy, Farhan Baluch and Jessica Chen, all of USC.

Funding for this research came from the National Institutes of Health (grants NS054069 and NS078530).

http://www.eurekalert.org/pub_releases/2013-02/jaaj-pfa020713.php

Prenatal folic acid supplementation associated with lower risk of autism

Maternal use of supplemental folic acid from 4 weeks before to 8 weeks after the start of pregnancy was associated with a lower risk of autistic disorder in children

In a study that included approximately 85,000 Norwegian children, maternal use of supplemental folic acid from 4 weeks before to 8 weeks after the start of pregnancy was associated with a lower risk of autistic disorder in children, according to a study appearing in the February 13 issue of *JAMA*.

"Supplementation with folic acid around the time of conception reduces the risk of neural tube defects in children. This protective effect has led to mandatory fortification of flour with folic acid in several countries,

and it is generally recommended that women planning to become pregnant take a daily supplement of folic acid starting 1 month before conception," according to background information in the article. It has not been determined whether prenatal folic acid supplements protect against other neurodevelopmental disorders. Pal Surén, M.D., M.P.H., of the Norwegian Institute of Public Health, Oslo, and colleagues investigated the association between the use of maternal folic acid supplements before and in early pregnancy and the subsequent risk of autism spectrum disorders (ASDs) (autistic disorder, Asperger syndrome, pervasive developmental disorder-not otherwise specified [PDD-NOS]) in children. The study sample of 85,176 children was derived from the population-based, prospective Norwegian Mother and Child Cohort Study (MoBa). The children were born in 2002-2008; by the end of follow-up on March 31, 2012, the age range was 3.3 through 10.2 years (average age, 6.4 years). The exposure of primary interest was use of folic acid from 4 weeks before to 8 weeks after the start of pregnancy, defined as the first day of the last menstrual period before conception. Analyses were adjusted for maternal education level, year of birth, and parity (the number of live-born children a woman has delivered).

A total of 270 children (0.32 percent) in the study sample have been diagnosed with ASDs: 114 (0.13 percent) with autistic disorder, 56 (0.07 percent) with Asperger syndrome, and 100 (0.12 percent) with PDD-NOS. The researchers found that there was an inverse association between folic acid use and subsequent risk of autistic disorder. Autistic disorder was present in 0.10 percent (64/61,042) of children whose mothers took folic acid, compared with 0.21 percent (50/24,134) in children whose mothers did not take folic acid, representing a 39 percent lower odds of autistic disorder in children of folic acid users.

Characteristics of women who used folic acid within the exposure interval included being more likely to have college- or university-level education, to have planned the pregnancy, to be nonsmokers, to have a pre-pregnancy body mass index below 25, and to be first-time mothers.

"No association was found with Asperger syndrome or PDD-NOS, but power was limited. Similar analyses for prenatal fish oil supplements showed no such association with autistic disorder, even though fish oil use was associated with the same maternal characteristics as folic acid use," the authors write.

The researchers note that the inverse association found for folic acid use in early pregnancy was absent for folic acid use in mid pregnancy.

"Our main finding was that maternal use of folic acid supplements around the time of conception was associated with a lower risk of autistic disorder. This finding does not establish a causal relation between folic acid use and autistic disorder but provides a rationale for replicating the analyses in other study samples and further investigating genetic factors and other biological mechanisms that may explain the inverse association," the authors conclude.

(JAMA. 2013;309(6):570-577; Available pre-embargo to the media at <http://media.jamanetwork.com>)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Periconceptional Folic Acid and Risk of Autism Spectrum Disorders

"It is reassuring that the study by Surén et al found no association between folic acid supplementation and an increased risk for autistic disorder or ASDs," write Robert J. Berry, M.D., M.P.H.T.M., and colleagues at the Centers for Disease Control and Prevention, Atlanta, in an accompanying editorial.

"This should ensure that folic acid intake can continue to serve as a tool for the prevention of neural tube birth defects. The potential for a nutritional supplement to reduce the risk of autistic disorder is provocative and should be confirmed in other populations." (JAMA. 2013;309(6):611-613; Available pre-embargo to the media at <http://media.jamanetwork.com>)

Editor's Note: This editorial was supported by the Centers for Disease Control and Prevention. The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

http://www.eurekalert.org/pub_releases/2013-02/uow-ids020813.php

Isotopic data show farming arrived in Europe with migrants

For decades, archaeologists have debated how farming spread to Stone Age Europe, setting the stage for the rise of Western civilization.

MADISON – Now, new data gleaned from the teeth of prehistoric farmers and the hunter-gatherers with whom they briefly overlapped shows that agriculture was introduced to Central Europe from the Near East by colonizers who brought farming technology with them.

"One of the big questions in European archaeology has been whether farming was brought or borrowed from the Near East," says T. Douglas Price, a University of Wisconsin-Madison archaeologist who, with Cardiff University's Dusan Boric, measured strontium isotopes in the teeth of 153 humans from Neolithic burials in an area known as the Danube Gorges in modern Romania and Serbia.

The report, which appears this week (Feb. 11, 2013) in the Proceedings of the National Academy of Sciences, draws on isotopic signatures of strontium found in the tooth enamel of people who died nearly 8,000 years ago,

about 6,200 B.C. Strontium is a chemical found in rocks everywhere. It enters the body through diet at or around birth and etches an indelible signature in teeth that accurately documents the geology of an individual's birthplace.

"The evidence from the Danube Gorges shows clearly that new people came in bringing farming and replaced the earlier Mesolithic hunter-gatherers," says Price, a UW-Madison professor of anthropology and an expert on early agriculture in Europe.

The Danube Gorges slice through the Carpathian Mountains and in the Stone Age were a heavily forested setting, rich in fish and game, including huge sturgeon, catfish, red deer and wild boar. The bends and twists of the Danube in the Gorges region made it especially important as a source of fish, and thus potentially a desirable entryway to Europe for highly mobile and expanding Neolithic communities accompanied by their domesticates – wheat, barley, flax, goats and cattle.

The new research, explains Price, speaks to the question of colonization versus adoption of transformative technologies such as farming. "It is also useful because it suggests another route across the Black Sea or up the east coast of Bulgaria to the Danube for farmers moving into Europe. This contrasts with movement by sea across the Mediterranean or Aegean, which is the standard picture."

Archaeologists have long wrestled with the question of how farming spread across Europe, ushering in a host of technologies, including the use of pottery, that ultimately led to the rise of Western civilizations. Two big ideas have dominated the debate: Did the technology arrive with colonizers from Asia, notably Anatolia or modern Turkey? Or did the technology, including newly domesticated plants and animals, simply diffuse across the European landscape through networks of local foragers?

There is some evidence for the importation of early agriculture along the shores of the Mediterranean and in Central Europe, Price notes, "but elsewhere in Europe it is not clear whether it was colonists or locals adopting."

Isotopic studies of strontium and other chemicals found in the teeth and bones of Neolithic humans, however, are now helping archaeologists to better track the movement of ancient peoples across the landscape. Strontium signatures last not just a lifetime, but potentially thousands of years as tooth enamel, the densest tissue in the body, resists decomposition and contamination after death. It is now commonly used by archaeologists to determine if an individual was local or foreign to the place where their remains were discovered.

An interesting finding of the study is that 8,000 years ago, when Neolithic farmers were beginning to migrate into the Danube Gorges and overlap with Mesolithic hunter-gatherers, more women than men were identified as foreigners. A possible explanation for the variance, according to the study, is that women came to these sites from Neolithic farming communities as part of an ongoing social exchange. In the Danube Gorges, the overlap of colonizing early farmers and hunter-gatherers lasted perhaps a couple of hundred years before the forager societies were completely absorbed by the beginning of the sixth millennium B.C.

The new study was supported by the National Science Foundation.

http://www.eurekalert.org/pub_releases/2013-02/uoc--nin021113.php

Newly identified natural protein blocks HIV, other deadly viruses

Identification of a protein with broad virus-fighting properties that potentially could be used as a weapon against deadly human pathogenic viruses

A team of UCLA-led researchers has identified a protein with broad virus-fighting properties that potentially could be used as a weapon against deadly human pathogenic viruses such as HIV, Ebola, Rift Valley Fever, Nipah and others designated "priority pathogens" for national biosecurity purposes by the National Institute of Allergy and Infectious Disease.

In a study published in the January issue of the journal *Immunity*, the researchers describe the novel antiviral property of the protein, cholesterol-25-hydroxylase (CH25H), an enzyme that converts cholesterol to an oxysterol called 25-hydroxycholesterol (25HC), which can permeate a cell's wall and block a virus from getting in.

Interestingly, the CH25H enzyme is activated by interferon, an essential antiviral cell-signaling protein produced in the body, said lead author Su-Yang Liu, a student in the department of microbiology, immunology and molecular genetics at the David Geffen School of Medicine at UCLA.

"Antiviral genes have been hard to apply for therapeutic purposes because it is difficult to express genes in cells," said Liu, who performed the study with principal investigator Genhong Cheng, a professor of microbiology, immunology and molecular genetics. "CH25H, however, produces a natural, soluble oxysterol that can be synthesized and administered.

"Also, our initial studies showing that 25HC can inhibit HIV growth in vivo should prompt further study into membrane-modifying cholesterol that inhibit viruses," he added.

The discovery is particularly relevant to efforts to develop broad-spectrum antivirals against an increasing number of merging viral pathogens, Liu said.

Working with Jerome Zack, a professor of microbiology, immunology and molecular genetics and an associate director of the UCLA AIDS Institute, the researchers initially found that 25HC dramatically inhibited HIV in cell cultures. Next, they administered 25HC in mice implanted with human tissues and found that it significantly reduced their HIV load within seven days. The 25HC also reversed the T-cell depletion caused by HIV. By contrast, mice that had the CH25H gene knocked out were more susceptible to a mouse gammaherpes virus, the researchers found.

In collaboration with Dr. Benhur Lee, a professor of pathology and laboratory medicine and a member of the UCLA AIDS Institute, they discovered that 25HC inhibited HIV entry into the cell. Furthermore, in cell cultures, it was found to inhibit the growth of other deadly viruses, such as Ebola, Nipah and the Rift Valley Fever virus.

Intriguingly, CH25H expression in cells requires interferon. While interferon has been known for more than 60 years to be a critical part of the body's natural defense mechanism against viruses, the protein itself does not have any antiviral properties. Rather, it triggers the expression of many antiviral genes. While other studies have identified some antiviral genes that are activated by interferon, this research gives the first description of an interferon-induced antiviral oxysterol through the activation of the enzyme CH25H. It provides a link to how interferon can cause inhibition of viral membrane fusion, Liu said.

He noted some weaknesses in the research. For instance, 25HC is difficult to deliver in large doses, and its antiviral effect against Ebola, Nipah and other highly pathogenic viruses have yet to be tested in vivo. Also, the researchers still need to compare 25HC's antiviral effect against other HIV antivirals.

Additional study co-authors were Roghiyh Aliyari, Kelechi Chikere, Matthew D. Marsden and Olivier Pernet, of UCLA; Jennifer K. Smith, Rebecca Nusbaum and Alexander N. Frieberg, of the University of Texas–Galveston; and Guangming Li, Haitao Guo and Lishan Su, of the University of North Carolina–Chapel Hill.

The National Institutes of Health (grants R01 AI078389, AI069120, AI080432, AI095097, AI077454, AI070010 and AI028697), the Warsaw Fellowship, the UCLA Center for AIDS Research (CFAR), the UCLA AIDS Institute, the UCLA Clinical and Translational Science Institute (CTSI), and the Pacific Southwest Regional Center of Excellence (PSWRCE) for Biodefense and Emerging Infectious Diseases funded this study.

<http://www.sciencedaily.com/releases/2013/02/130212100508.htm>

Ziziphora Effective in the Battle Against Gastric Cancer, Study Suggests

Ziziphora may be effective in the treatment of the fourth most common form of the disease

A recent publication in the journal Food and Agricultural Immunology investigating the effects of aloe vera, ginger, saffron and ziziphora extracts as herbal remedies for gastric cancer suggests that the latter may be effective in the treatment of the fourth most common form of the disease.

Already applied in the treatment of various other diseases, the study now shows that this traditional Uyghur medicinal plant to have the highest cytotoxic effect on AGS cell line of those under investigation.

Professor C. J. Smith, Editor of the journal and Director of the Manchester Food Research Centre at Manchester Metropolitan University, commented "Hippocrates declared "Let your food be your medicine and let your medicine be your food." The modern world is increasingly beginning to appreciate the wisdom of this simple statement. As we have developed modern medicines over the last couple of centuries we have neglected the role which diet plays in the maintenance of good health. However, recent years have shown the importance of understanding both the role of diet and the role of the gut flora in maintaining good health."



Blue Mint Bush *Ziziphora clinopodioides*

"The understanding of the significance of the gut microflora in good health and in disease has taken major strides in the past three decades and much has been made of the importance of herbs and spices as modulators of health and as being useful in preventing various disorders including gastric ulcers and obesity. 'Cytotoxic effect of four herbal medicines on gastric cancer (AGS) cell line' is an excellent example of these developments. The authors tested four spices for their cytotoxic effect on a gastric cancer cell line and show that three of these have varying cytotoxic properties which may be of clinical relevance. This paper therefore fits in a general theme of scientific evaluations of the control and treatment of diseases by food ingredients and components which leads one readily back to the hypothesis proposed by Hippocrates."

Tooba Ghazanfari, Roya Yaraee, Jalaleddin Shams, Batoool Rahmati, Tayebbeh Radjabian, Hoda Hakimzadeh. Cytotoxic effect of four herbal medicines on gastric cancer (AGS) cell line. Food and Agricultural Immunology, 2013; 24 (1): 1 DOI: 10.1080/09540105.2011.637549

<http://www.scientificamerican.com/article.cfm?id=life-discovered-under-ice-in-antarctic-lake>

Life Discovered under Ice in Antarctic Lake

Lake Whillans, 800 meters down and on the edge of the Ross Ice Shelf in West Antarctica, harbors a host of microbes and a wetland ecosystem

By Quirin Schiermeier and Nature magazine

Antarctic borehole Drillers found a microbial ecosystem hiding under 800 meters of ice, at the end of this 50-centimeter-wide borehole in the Antarctic Ice Sheet. Image: Alberto Behar/JPL/ASU & NSF/NASA

Having just completed the tortuous 48-hour journey from the South Pole to the US west coast, John Priscu is suffering from more than his fair share of jet lag. But his tiredness can't mask the excitement in his voice. After weeks of intense field work in Antarctica, he and his team have become the first to find life in a lake trapped under the frozen continent's ice sheet.

"Lake Whillans definitely harbors life," he says. "It appears that there lies a large wetland ecosystem under Antarctica's ice sheet, with an active microbiology."

The lake in question is a 60-square-kilometer body of water that sits on the edge of the Ross Ice shelf in West Antarctica. To reach it, Priscu, a glaciologist at Montana State University in Bozeman, and his team had to drill down 800 meters of ice.

They arrived at their goal on 28 January, when their environmentally clean hot-water drill broke through to the lake's surface. What they found was a body of water just 2 meters or so deep — much shallower than the 10–25 meters seismic surveys had suggested, although Priscu notes that the lake may well have deeper spots.

The team put a camera down the borehole to make sure that the borehole was wide enough for sampling instruments to be deployed and returned safely. It was, and over the next few days, the scientists collected some 30 liters of liquid lake water and eight sediment cores from the lake's bottom, each 60 centimeters long.

What precious stuff they had retrieved soon became clear under the on-site microscope. Both water and sediment contained an array of microbes that did not need sunlight to survive. The scientists counted about 1,000 bacteria per milliliter of lake water — roughly one-tenth the abundance of microbes in the oceans. In Petri dishes, the bacteria show a "really good growth rate", says Priscu.

"These are wonderful findings, a major discovery indeed," says Martin Siebert, an Antarctic researcher at the University of Bristol, UK, who led a UK expedition to Lake Ellsworth, another subglacial body of water on the continent, in December. Unfortunately, technical difficulties halted the UK team's drilling effort.

Cool and collected

The exact nature of the life unearthed by the US team will now be established by DNA sequencing and other tests. It will take at least a month to do the basic work, says Priscu.

"What we are all dying to find out now is, of course, 'who's there' and 'what's their life style'," he says.

Researchers hope that the survival strategies of the subglacial microbes might offer clues to what the biology of extraterrestrial life might be like — Jupiter's moon Europa, for instance, is thought to host a large sub-surface ocean of water where such life might be able to exist.

As photosynthesis is impossible without sunlight, the Lake Whillans bacteria must get their energy from a different source. This could be existing organic material, or, like the 'chemotrophs' found in gold mines and near deep-sea hydrothermal vents, the bacteria might run on chemical reactions involving minerals in the Antarctic bedrock and carbon dioxide dissolved in lake water.

"We have been allowed a glimpse into Antarctica's subglacial world," Priscu says. "I'm sure our results will change the way we view that continent."

<http://www.wired.com/wiredscience/2013/02/proto-rna/>

Self-Assembling Molecules Offer Clues to Life's Possible Origin

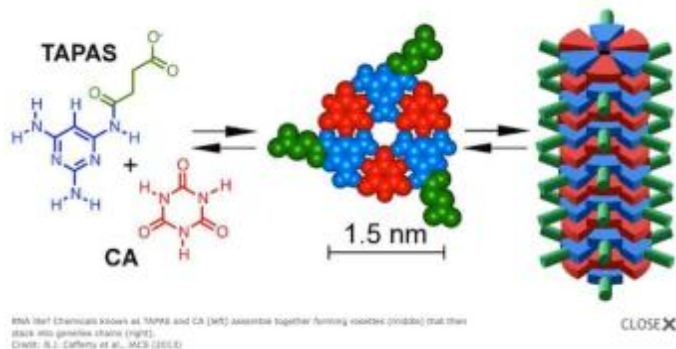
A pair of RNA-like molecules can spontaneously assemble into gene-length chains, chemists in the United States and Spain report.

By Robert F. Service, ScienceNOW

Billions of years ago, related molecules may have created a rudimentary form of genetic information that eventually led to the evolution of RNA and life itself, the researchers say. Although it's likely to be difficult, if not impossible, to prove whether similar proto-RNAs were present at the dawn of life, the researchers are working to see if the proto-RNAs can indeed faithfully encode information and evolve toward RNA.

Origin-of-life researchers have long thought that RNA, the molecular cousin of the DNA that encodes our genes, may have played a starring role in the initial evolution of life from a soup of organic molecules. RNA has a simpler structure than DNA and is a more adept chemical catalyst. So it would seem that RNA-based life might arise more readily than DNA-based life.

But there are problems with this so-called RNA World hypothesis. For starters, in water, the four chemical components of RNA — the nucleotides abbreviated A, G, C, and U — don't spontaneously assemble to create sizable molecules. So it remains a mystery how the first long gene-length chains of RNA could have taken shape in Earth's ancient oceans. This and other conundrums have led many to believe that RNA may itself be the product of early molecular evolution, and that proto-RNAs arose first and eventually gave way to RNA. "RNA is so perfect today that it has to be the product of evolution," says Nicholas Hud, a chemist at the Georgia Institute of Technology (Georgia Tech) in Atlanta.



Chemicals known as TAPAS and CA (left) assemble together forming rosettes (middle) that then stack into genelike chains (right). Image: Cafferty et al./JACS

Researchers have toyed with the idea of proto-RNA for decades and even come up with potential chemical candidates. One such set of proto-RNAs involves two chemicals called cyanuric acid (CA) and triaminopyrimidine (TAP). TAP comes from a family of compounds known as pyrimidines, as do the RNA bases C and U. CA, meanwhile, is a close pyrimidine relative. Previous research had shown that when CA and TAP were put in an organic solvent, groups of three CAs and three TAPs would spontaneously form ringlike structures called rosettes. These rosettes would then stack atop one another to form long chains. Unfortunately, in water CA and TAP clump together in large ribbons and sheets and quickly fall out of solution, making it hard to conceive of how these proto-RNAs could have stored genetic information in the earliest stages of life.

Now, however, Hud and his colleagues at Georgia Tech and the Institute for Research in Biomedicine in Barcelona, Spain, have solved this solvent problem. The researchers gave TAP a short chemical tail, transforming it into a chemical they call TAPAS, as they reported on Friday in the *Journal of the American Chemical Society*. And that one change encourages it to assemble with CA to form rosettes in water. What is more, the rosettes stack atop one another, forming long genelike chains made up of as many as 18,000 individual TAPAS and CA components — quite a stack of small plates.

"The nice thing [about the current study] is this is a demonstration of self-assembly in water," says Ramanarayanan Krishnamurthy, an origin-of-life chemist at the Scripps Research Institute in San Diego, California. "That is a step in the right direction."

The next step, Hud says, will be to see whether this two-component assembly can be made to encode information like a primitive gene and to evolve toward the structure of RNA. If so, that still won't settle the debate as to whether CA and TAPAS gave life its start. But it will suggest one plausible chemical route to life's origin. *This story provided by ScienceNOW, the daily online news service of the journal Science.*

<http://www.bbc.co.uk/news/world-latin-america-21436513>

Peru archaeologists find ancient temple in El Paraiso

Archaeologists in Peru say they have discovered a temple at the ancient site of El Paraiso, near the capital, Lima.

Entry to the rectangular structure, estimated to be up to 5,000 years old, was via a narrow passageway, they say.

At its centre, the archaeologists from Peru's Ministry of Culture found a hearth which they believe was used to burn ceremonial offerings. With 10 ruins, El Paraiso is one of the biggest archaeological sites in central Peru.

The archaeologists found the structure, measuring 6.82m by 8.04m (22ft by 26ft), in the right wing of the main pyramid.



The temple was discovered in one of the wings of the main pyramid at the ancient site of El Paraiso

'Interconnected civilisation'

They had been carrying out conservation work on the site on behalf of Peru's Ministry of Culture when they came across the remains, which had been obscured by sand and rocks. They said the temple walls were made of stone and covered in fine yellow clay which also contained some traces of red paint. The archaeologists said the find suggests that the communities in the Late Pre-ceramic Age (3500 BC to 1800 BC) were more closely connected than had been previously thought.

Peru's Deputy Minister for Culture Rafael Varon said the the temple was the first structure of its kind to be found on Peru's central coast. "It corroborates that the region around Lima was a focus for the civilisations of the Andean territory, further bolstering its religious, economic and political importance since times immemorial," Mr Varon said.

Archaeologist Marco Guillen, who led the team which made the discovery, said the hearth gave insight into the civilisation which had used the site. "The main characteristic of their religion was the use of fire, which burnt in the centre," he told the BBC's Mattia Cabitza in Lima. "The smoke allowed the priests to connect with their gods," Mr Guillen said.

The Paraiso settlement once supported a farming and fishing community numbering hundreds of people. Our correspondent says thousands of ruins are thought to remain undiscovered, making Peru a treasure-hunting destination for archaeologists and looters alike.

<http://www.sciencedaily.com/releases/2013/02/130212192030.htm>

Risk of Cardiovascular Death Doubled in Women With High Calcium Intake

High Risk Only in Those Taking Supplements as Well

High intakes of calcium (corresponding to diet and supplements) in women are associated with a higher risk of death from all causes, but cardiovascular disease in particular, compared with women with lower calcium intake, a new study suggests. Experts recommend a high calcium intake (as it plays a pivotal role in human physiology) and as such, more than 60% of middle-aged and older women in the USA now take supplements. However, recent trials have indicated a higher risk of ischemic heart disease and stroke with calcium supplements but this was not observed in another trial and few studies have examined this association.

Researchers from Uppsala University in Sweden therefore studied 61,443 Swedish women (born between 1914 and 1948) for an average of 19 years to test this association.

Data were taken from the Swedish Cause of Death Registry and data on diet were taken from the Swedish Mammography Cohort. Total calcium intake included supplemental calcium. The mean intake in the lowest quartile was 572mg/day (the equivalent of five slices of cheese) and in the highest 2137mg/day.

Information was obtained from the women on menopausal status, postmenopausal estrogen therapy, parity information, weight and height, smoking habits, leisure-time physical activity and educational level.

Results showed that during 19 years of follow-up, 11,944 women (17%) died: 3,862 of these (32%) died from cardiovascular disease, 1932 (16%) heart disease and 1100 (8%) from stroke. Highest rates of all-cause, cardiovascular and heart disease were observed among those with a dietary calcium intake higher than 1400mg/day.

In addition, researchers observed higher death rates among women with an intake below 600mg/day.

Women who had a higher dietary intake of calcium exceeding 1400mg/day and also used supplements had a higher death rate compared to those not taking supplements. Women with a high dietary calcium intake (>1400 mg/day) were more than twice as likely to die compared with women with a 600-999mg/day calcium intake. The researchers explain their findings by suggesting that diets very low or very high in calcium can override normal homeostatic control causing changes in blood levels of calcium.

The researchers conclude that high calcium is associated with "higher all-cause and cardiovascular mortality rates" and so to prevent fractures in the elderly emphasis should be placed on individuals with a low intake of calcium rather than increasing the intake of those already consuming satisfactory amounts.

http://www.eurekalert.org/pub_releases/2013-02/plos-lli020713.php

Long, low intensity exercise may have more health benefits relative to short, intense workouts

If spending equal amounts of energy, long periods of low intensity exercise may improve insulin, lipid levels more than short bursts of intense activity

Standing and walking for longer stretches improves insulin sensitivity and blood lipid levels more than an hour of intense exercise each day does, but only if the calories spent in both forms of exercise are similar. The findings are published February 13 in the open access journal PLOS ONE by Hans Savelberg and colleagues from Maastricht University, Netherlands.

The researchers recruited eighteen normal-weight 19 to 24-year-old participants for their study and asked them to follow three regimes. In the first, participants were instructed to sit for 14 hours each day and not indulge in any form of exercise; the second regime required participants to sit for 13 hours each day and exercise vigorously for 1 hour; and in the third, participants substituted six hours of sitting with four of walking and two hours standing. After each regime, the researchers tracked each participant's insulin sensitivity and blood lipid levels, both of which can help identify metabolic conditions like diabetes and obesity.

The authors found that overall, when participants followed the strictly sedentary regimen they burned over the course of the day than in the other two routines, which were roughly the same. Cholesterol and lipid levels improved slightly when participants exercised vigorously for an hour each day, but improved significantly when participants were active for longer periods at low intensity. According to the study, being active simply by standing or walking for long periods of time significantly improved insulin levels compared to both a strictly sedentary lifestyle, and one in which participants were largely sedentary except for an hour of exercise each day. The study concludes that when energy expenditure is equivalent, longer durations of low-intensity exercise may offer more benefits than shorter periods of intense activity.

Citation: Duvivier BMFM, Schaper NC, Bremers MA, van Crombrugge G, Menheere PPCA, et al. (2013) Minimal Intensity Physical Activity (Standing and Walking) of Longer Duration Improves Insulin Action and Plasma Lipids More than Shorter Periods of Moderate to Vigorous Exercise (Cycling) in Sedentary Subjects When Energy Expenditure Is Comparable. PLoS ONE 8(2): e55542. doi:10.1371/journal.pone.0055542

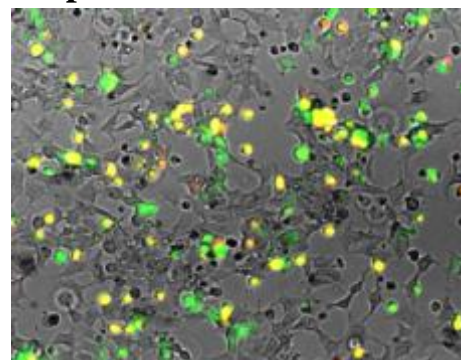
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UNC researchers discover gene that suppresses herpesviruses

Identification of a family of human genes playing a key role in the suppression and activation of herpesviruses

Chapel Hill, NC – Kaposi's sarcoma-associated herpesvirus (KSHV) and Epstein-Barr virus (EBV) hide within the worldwide human population. While dormant in the vast majority of those infected, these active herpesviruses can develop into several forms of cancer. In an effort to understand and eventually develop treatments for these viruses, researchers at the University of North Carolina have identified a family of human genes known as Tousled-like kinases (TLKs) that play a key role in the suppression and activation of these viruses.



Cells infected with the KSHV virus fluoresce yellow. The KSHV virus remains dormant in more than 95 percent of infected patients. UNC/Damania Lab

In a paper published by Cell Host and Microbe on Feb. 13, a research team led by Blossom Damania, PhD, of the Department of Microbiology and Immunology and member of the UNC Lineberger Comprehensive Cancer Center, found that suppressing the TLK enzyme causes the activation of the lytic cycle of both EBV and KSHV. During this active phase, these viruses begin to spread and replicate, and become vulnerable to anti-viral treatments. "When TLK is present, these viruses stay latent, but when it is absent, these viruses can replicate" said Dr. Damania.

Patrick Dillon, a postdoctoral fellow in Dr. Damania's lab, led the study. Other co-authors included UNC Lineberger members Drs. Dirk Dittmer, Nancy Raab-Traub and Gary Johnson.

KSHV and EBV are blood-borne viruses that remain dormant in more than 95 percent of those infected, making treatment of these viruses difficult. Both viruses are associated with a number of different lymphomas, sarcomas, and carcinomas, and many patients with suppressed immune systems are at risk for these virus-associated cancers.

"The dormant state of these viruses is what makes it so hard to treat these infections and the cancers associated with these infections," said Dr. Damania.

Researchers have known that stimuli such as stress can activate the virus from dormancy, but they do not understand the molecular basis of the viral activation cycle. With the discovery of the link between these viruses and TLKs, Dr. Damania said that researchers can begin to look for the molecular actions triggered by events like stress, and how they lead to the suppression of the TLK enzymes.

"What exactly is stress at a molecular level? We don't really understand it fully," said Dr. Damania.

With the discovery that TLKs suppresses these viruses, Dr. Damania said that the proteins can now be investigated as a possible drug target for these virus-associated cancers. In its normal function in the cell, TLKs play a role in the maintenance of the genome, repairing DNA and the assembly of the chromatin, but there is a lot more to learn about the function of the TLKs, said Dr. Damania. One avenue of her lab's future research will investigate how TLKs function in absence of the virus.

"If we prevent this protein from functioning, and we combine this with a drug that inhibits viral replication, then we could have a target to cure the cell of the virus. If the virus isn't there, the viral-associated cancers aren't present," said Dr. Damania.

This research was supported by NIH grants CA096500, CA163217, and CA019014, and the UNC Lineberger training grant NIH T32CA009156. Dr. Damania is a Leukemia & Lymphoma Foundation Scholar and a Burroughs Wellcome Investigator in Infectious Disease.

<http://bit.ly/UniCt0>

Night-vision rat becomes first animal with sixth sense

The latest bionic superhero is a rat: its brain hooked up to an infrared detector, it's become the first animal to be given a sixth sense.

Douglas Heaven, reporter

Developed by Miguel Nicolelis and colleagues at Duke University in Durham, North Carolina, the system connects a head-mounted sensor to a brain region that normally processes touch sensations from whiskers. As shown in this video, the rat's brain is tricked when infrared light is detected, giving it a new sense organ.

"Instead of seeing, the rats learned how to touch the light," says Nicolelis.

Even though the touch-processing brain area acquires a new role, the team found that it continues to process touch sensations from whiskers, somehow dividing its time between both types of signal. "The adult brain is a lot more plastic than we thought," says Nicolelis.

The finding could lead to new brain prostheses that restore sight in humans with a damaged visual cortex. By bypassing the damaged part of the brain altogether, it might be possible to wire up a video camera to a part of the brain that processes touch, letting people "touch" what the camera sees.

According to Nicolelis, it could also lead to superhero powers for humans. "It could be X-rays, radio waves, anything," he says. "Superman probably had a prosthetic device that nobody knew of."

If you enjoyed this post, watch a robot and human swap brains to learn teamwork or see a body-sharing robot that lets you experience another place.

<http://www.wired.com/wiredscience/2013/02/appendix-revolution/>

Pretty Useful: Appendix Evolved More Than 30 Times

The appendix evolved 32 times among mammals, according to a new study

By Colin Barras, ScienceNOW

The appendix may not be useless after all. The worm-shaped structure found near the junction of the small and large intestines evolved 32 times among mammals, according to a new study. The finding adds weight to the idea that the appendix helps protect our beneficial gut bacteria when a serious infection strikes.

Charles Darwin was one of the first scientists to theorize on the function of the appendix, which in his day had been identified only in humans and other great apes. He hypothesized that the distant ancestors of these animals survived on a diet of leaves, and so they required a large cecum, a portion of the gut that houses bacteria that can break down stubborn plant tissue. Later, he speculated, these ancestors shifted to a largely fruit-based diet that was easier to digest. A large cecum was no longer necessary, and it began to shrink; today our cecum is tiny. Darwin thought the appendix, which juts off of the cecum, is one of its former folds that shriveled up as the cecum shrank. Consequently, he thought it carried no function.

But some scientists have challenged the idea that the appendix serves no purpose. It's been clear for about a century that the structure contains a particular type of tissue belonging to the lymphatic system. This system carries the white blood cells that help fight infections. Within the last decade, research has shown that this lymphatic tissue encourages the growth of some kinds of beneficial gut bacteria. What's more, careful anatomical study of other mammals has revealed that species as diverse as beavers, koalas, and porcupines also have a structure jutting off of their guts in exactly the same place as our appendix—in other words, the feature is much more common among mammals than once thought.

Now, an international team of researchers that includes Heather F. Smith, an evolutionary biologist at Midwestern University in Glendale, Arizona, and William Parker, a surgeon who studies the immune system at Duke University Medical Center in Durham, North Carolina, says it has the strongest evidence yet that the appendix serves a purpose. In a new study, published online this month in *Comptes Rendus Palevol*, the researchers compiled information on the diets of 361 living mammals, including 50 species now considered to have an appendix, and plotted the data on a mammalian evolutionary tree. They found that the 50 species are scattered so widely across the tree that the structure must have evolved independently at least 32 times, and perhaps as many as 38 times.

By plotting the dietary information onto the evolutionary tree, the researchers could work out whether the appendix appears when a particular group of mammals changes its diet. In most cases, there was no sign of a dietary shift, suggesting appendix evolution doesn't necessarily proceed as Darwin thought. He may have correctly identified the origin of the ape appendix, though, which the analysis confirms did appear when our ancestors switched diets.

Randolph Nesse, an evolutionary biologist at the University of Michigan, Ann Arbor, is impressed by the new study. "I salute the authors for creating an extraordinary database," he says. "The conclusion that the appendix

has appeared 32 times is amazing. I do find their argument for the positive correlation of appendix and cecum sizes to be a convincing refutation of Darwin's hypothesis."

"I agree with the general assertion that the appendix evolved numerous times in mammals, but I think the exact count is still up for debate," adds Olaf Bininda-Emonds, an evolutionary biologist at the University of Oldenburg in Germany. There is some uncertainty over whether all 50 species considered to have an appendix really do possess one. When just the clear-cut cases are included, the appendix evolved 18 times, he says. Even that figure suggests the appendix performs a useful function, and the hunt is now on to identify what that function is. The research team may already have the answer. In 2007, Parker and his colleagues suggested that the appendix has an immunological role, acting as a "safe house" for beneficial gut bacteria. These bacteria help train the immune system and can prevent diseases by outcompeting dangerous pathogenic bacteria—but there are times when the dangerous microbes gain the upper hand and overrun the gut. The researchers reasoned that when this happens, the beneficial bacteria could retreat to the safety of the appendix, which remains unaffected. Once the immune system has beaten the infection, the beneficial bacteria emerge from the appendix to quickly recolonize the gut.

The "safe house" idea makes sense, says Indi Trehan, a pediatrician at the Institute for Public Health at Washington University in St. Louis who recently studied the importance of maintaining gut bacteria when treating people with malnutrition. "The appendix has a unique anatomical location that is out of the way," he says. "Bacteria can be kept safe there for repopulation as needed."

The safe house hypothesis is reasonable, Nesse agrees, but he points out that just 50 of the 361 mammalian species included in the analysis have an appendix. "One wonders why such a trait with such a function would not be universal," he says. That suggests it is possible we still haven't completely cracked the mystery of the appendix, he says.

<http://www.wired.com/business/2013/02/personalized-medicine>

Medicine for the Rich Is About to Get Cheap Enough for Regular People

After years of exotic and very expensive machines sequencing DNA, the genomics industry finally looks poised for its cell phone moment.

By Daniela Hernandez

Soon, the business of genetics could look a lot like the commodity-driven mobile industry, with providers selling hardware on the cheap and relying on software, apps and diagnostics to drive revenue. And, as with the app-filled smartphones we keep close to us 24/7, genomics could finally become a much more intimate part of our lives.

"With smartphones it's the data and apps where the high value has accrued over time. In the case of sequencing, it's going to be something similar," said Jorge Conde, CFO and co-founder of Knome, a genomic diagnostics company. The question, he says, then becomes whether the market looks like Apple's walled garden, Microsoft's more democratic model, or Google, where everything happens in the cloud.

In recent years, the industry has been working to solve the data storage and analysis bottlenecks resulting from an explosion of genetic data as sequencing costs have continued to drop. And they have succeeded. That means companies and institutions can finally focus on deciphering what all our genetic data actually means and how it might influence our risk for certain diseases. In other words, diagnostics is where the money is moving.

This shift is being catalyzed by a push by genomics, diagnostics and pharmaceutical giants to provide seamless services that include everything from genetic sequencing, to data analysis and interpretation, to reports medical providers can use in the clinic to make treatment decisions. The result might ultimately be the emergence of personalized medicine as the new standard of care.

"Today, most companies have a specific niche. The full integrated package is being promised but is not really being offered," says Dr. Gianrico Farrugia, the director of the Mayo Clinic Center for Individualized Medicine. With the help of medical institutions and a growing number of companies setting out to provide these services, he says, we're getting closer to that promise actually being realized.

Right now, the market for soup-to-nuts genomics is small — less than \$50 million — but it could grow into a multi-billion dollar industry if insurance companies start paying for more kinds of genetic testing, says Andrew Kress, senior vice president of healthcare value solutions at IMS Health, a health information and technology services company. "Payers are open to just about anything if someone can demonstrate it's lowering the overall cost of care."

Other estimates suggest the market is already in the billions but agree it's far from reaching its peak. The use of genetics is on the rise at major medical centers like Stanford, Vanderbilt, Mount Sinai, and the Mayo Clinic and annual spending on genetic tests has been steadily increasing, according to a UnitedHealthcare 2012 report.

The largest healthcare players in the industry are convinced we're heading in this direction fast, and have been on a buying binge to cement their place in this new genomic order.

In 2007, Swiss pharmaceutical giant Roche acquired 454 Life Sciences to up its sequencing capabilities and last year, it attempted to takeover Illumina, which makes the world's most widely used sequencing machines. In July, Life Technologies bought Navigenics, one of the first personal genomics companies. In September, Illumina bought UK-based BlueGnome, which specializes in pre-implantation genetic screening for in vitro fertilization, and last month, the sequencing giant paid a ballpark figure of \$350 million in cash for Verinata Health, which sells a chromosomal test that scans a mom's blood for traces of her baby's DNA to detect possible birth defects.

And then, there is the most contentious of all recent deals — the bidding saga between Illumina and China's BGI to acquire Complete Genomics a Mountain View-based company that developed its own sequencers and analysis platforms? After hand wringing about national security, BGI eventually won even though its reported offer of \$118 million was lower than Illumina's. The merger is pending approval. Illumina and Complete Genomics were not available for comment. "All these guys are snatching up little companies to augment their markets," says Joel Dudley, director of biomedical informatics at Mount Sinai School of Medicine in New York. "It makes you wonder how the little guys are going to compete." And who the likely customers are.

Right now, most genetic testing happens in top-tier hospitals for conditions like cancer or rare genetic diseases and to test whether patients might have adverse reactions to certain medications. But it will likely become more mainstream as scientists and doctors learn more about the genome and genetic interpretation gets better and cheaper. Entrepreneurs are counting on it, and startups aiming to make genomic medicine as routine as having a blood test or getting an EKG are launching all the time.

Image: SV Bio

Young companies like Knome and Silicon Valley Biosystems (SV Bio) are trying to make it on their own (or perhaps to make themselves look as an attractive takeover target as possible) by providing clinical labs and doctors as close to a full service as possible, and they're teaming up with academic institutions to help them make their products mainstream. Knome's knoSYS platform, a \$125,000 countertop appliance marketed as a lab in a box, crunches sequencing data from Illumina, Life Technologies and Complete Genomics sequencers and lets geneticists run tests from a set of preloaded or self-customized panels. knoSYS then creates a report, which can help physicians make medical decisions.

SV Bio, which recently partnered with the Mayo Clinic, takes Knome's approach a step further: They provide a sequencing service using Illumina machines — a smart move since the quality of sequencing data tends to vary greatly. SV Bio uses patients' saliva or blood samples to sequence their genome and then analyzes the resulting data with algorithms they've developed in-house to produce a 3-page report tailored for physicians, many of whom may not have a strong genetics background.

The next frontier for genomic medicine — and where much of the market value may actually lie — is in using genetic testing to screen patients at risk for developing chronic diseases like diabetes, high blood pressure, obesity and Alzheimer's and to manage those patients with the medications that work best for their genetic makeup. That's still years away, but we're starting to see signs of this for certain types of cancer.

With big and small companies duking it out to make it big in this space, patients may stand to benefit. Whoever the top players in the industry end up being, they'll likely compete on price and speed, which should not only decrease the strain on patients' wallets but also on the anxiety they may feel while they await a diagnosis. Many genomic startups and even larger companies like Illumina are storing genetic data up in the Amazon cloud and making that data available through the web. Soon that data will be integrated with medical records and people will have 24/7 access to their whole genomes through mobile devices, like they do for their financial information today, says Stanford's Dr. Euan Ashley, co-founder of another genomics startup, Personalis. "That future is not so far away."

http://www.eurekalert.org/pub_releases/2013-02/ghsu-ipc021413.php

Indian plant could play key role in death of cancer cells

Scientists have identified an Indian plant that could help kill cancer cells.

AUGUSTA, Ga. — Scientists at the Georgia Regents University Cancer Center have identified an Indian plant, used for centuries to treat inflammation, fever and malaria, that could help kill cancer cells.

Cancer cells typically avoid death by hijacking molecular chaperones that guide and protect the proteins that ensure normal cellular function and then tricking them into helping mutated versions of those proteins stay alive, says Dr. Ahmed Chadli, a researcher in the Molecular Chaperone Program at the GRU Cancer Center and senior author of the study named the Journal of Biological Chemistry's Paper of the Week.

Drug development has focused on the chaperone Hsp90 (heat shock protein 90) because it plays a key role in assisting mutated proteins, making it an attractive cancer drug target. However, the clinical efficacy of Hsp90 inhibitors has been disappointing. Most current small molecules targeting Hsp90 have inadvertently resulted in the expression of proteins that protect cancer cells from programmed cell death and compromise the Hsp90 inhibitors in the clinic.

In this study, however, Chaitanya Patwardhan, a graduate student in Dr. Chadli's lab, found that gedunin, an Indian plant compound, attacks a co-chaperone, or helper protein, of Hsp90 called p23.

"This compound binds directly to p23, leading to inactivation of the Hsp90 machine—without production of anti-apoptotic proteins—thus killing cancer cells," said Dr. Chadli. "The idea here is that this will open a door for new ways of targeting Hsp90 by targeting its helper proteins, which may be used in combination with established Hsp90 inhibitors that are ongoing clinical trials. In the future, this research could have applications in drug development for hormone-dependent cancers, including breast, prostate and endometrial cancers."

"One of the major areas of scientific emphasis of the GRU Cancer Center is to develop therapeutic approaches to cancer targeting specific molecules within the cancer cell, including chaperones," said Dr. Samir N. Khleif, Director of the GRU Cancer Center. "This finding is an important piece of the puzzle, bringing us closer to our goal of helping patients with cancer."

Along with Patwardhan, the study was also authored by Dr. Abdul Fauq, Mayo Clinic College of Medicine; Laura B. Peterson and Dr. Brian S.J. Blagg, both of the University of Kansas; and Dr. Charles Miller, Tulane University School of Public Health and Tropical Medicine.

Dr. Chadli's lab is also the recipient of a National Institutes of Health R01 grant to look for new molecules targeting the Hsp90 machine.

<http://www.sciencedaily.com/releases/2013/02/130214111606.htm>

Bilingual Babies Know Their Grammar by 7 Months

Babies as young as seven months can distinguish between, and begin to learn, two languages with vastly different grammatical structures.

Babies as young as seven months can distinguish between, and begin to learn, two languages with vastly different grammatical structures, according to new research from the University of British Columbia and Université Paris Descartes. Published February 14 in the journal *Nature Communications* and presented at the 2013 Annual Meeting of the American Association for the Advancement of Science (AAAS) in Boston, the study shows that infants in bilingual environments use pitch and duration cues to discriminate between languages -- such as English and Japanese -- with opposite word orders.

In English, a function word comes before a content word (the dog, his hat, with friends, for example) and the duration of the content word is longer, while in Japanese or Hindi, the order is reversed, and the pitch of the content word higher. "By as early as seven months, babies are sensitive to these differences and use these as cues to tell the languages apart," says UBC psychologist Janet Werker, co-author of the study.

Previous research by Werker and Judit Gervain, a linguist at the Université Paris Descartes and co-author of the new study, showed that babies use frequency of words in speech to discern their significance.

"For example, in English the words 'the' and 'with' come up a lot more frequently than other words -- they're essentially learning by counting," says Gervain. "But babies growing up bilingual need more than that, so they develop new strategies that monolingual babies don't necessarily need to use."

"If you speak two languages at home, don't be afraid, it's not a zero-sum game," says Werker. "Your baby is very equipped to keep these languages separate and they do so in remarkable ways."

Judit Gervain, Janet F. Werker. Prosody cues word order in 7-month-old bilingual infants. Nature Communications, 2013; 4: 1490 DOI: 10.1038/ncomms2430

http://www.eurekalert.org/pub_releases/2013-02/sjha-rdb021413.php

Researchers discover breakthrough in ovarian cancer

Findings from University of Arizona Cancer Center at St. Joseph's

Phoenix, AZ - Researchers at The University of Arizona Cancer Center at St. Joseph's Hospital and Medical Center in Phoenix have discovered that many women with low-grade serous carcinoma of the ovary or peritoneum have seen their tumors stabilize or shrink after taking a regular dose of the compound selumetinib. The findings, published in the Feb. 14 edition of *The Lancet Oncology*, show that selumetinib targets a mutation in the MAPK pathway for patients with low-grade serous carcinoma, allowing for treatment on previously chemoresistant tumors. "This is a potentially important breakthrough for the Gynecologic Oncology Group," said John Farley, MD, a gynecologic oncologist in the Division of Gynecologic Oncology and the Department of Obstetrics and Gynecology at the Creighton University School of Medicine at St. Joseph's Hospital and Medical Center, a Dignity Health Member.

The Gynecologic Oncology Group is a non-profit international organization with the purpose of promoting excellence in the quality and integrity of clinical and basic scientific research in the field of gynecologic malignancies.

Dr. Farley is part of the University of Arizona Cancer Center at St. Joseph's and is board certified in obstetrics and gynecology with a subspecialty certification in gynecologic oncology. He is a retired decorated Army colonel who completed a residency in obstetrics and gynecology and a fellowship in gynecologic oncology at Walter Reed Army Medical Center. He is the first author on this study.

This study was initially developed in 2007, with 52 patients enrolled for the Phase II clinical trial between December 2007 and November 2009. Patients were given 50 milligrams of selumetinib orally twice daily. Of those participants, eight had a measurable decrease in tumor size, seven had partial responses and 34 patients saw their tumors stabilize. The findings suggest that inhibitors of the MAPK pathway warrant further investigation in patients with low-grade ovarian cancer.

"There just aren't very good treatments for low-grade ovarian cancer, so this discovery opens up a lot of new exciting possibilities for us," Dr. Farley said. He added that Phase III of this trial is scheduled to begin in the next few weeks, with that trial to be the "definitive test" before the treatment becomes available to the general population. *This study is registered with ClinicalTrials.gov, number NCT00551070.*

http://www.eurekalert.org/pub_releases/2013-02/ghsu-lho021413.php

Losing hope of a good night's sleep is risk factor for suicide

When people lose hope that they will ever get another good night's sleep, they become at high risk for suicide, researchers report.

AUGUSTA, Ga. – Insomnia and nightmares, which are often confused and may go hand-in-hand, are known risk factors for suicide but just how they contribute was unknown, said Dr. W. Vaughn McCall, Chair of the Medical College of Georgia Department of Psychiatry and Health Behavior at Georgia Regents University. The new study reaffirms that link and adds the element of hopelessness about sleep that is independent of other types of hopelessness, such as those regarding personal relationships and careers, said McCall, corresponding author of the study in *Journal of Clinical Sleep Medicine*, the journal of the American Academy of Sleep Medicine.

"It turns out insomnia can lead to a very specific type of hopelessness and hopelessness by itself is a powerful predictor of suicide," he said. "It's fascinating because what it tells you is we have discovered a new predictor for suicidal thinking." If the findings hold true in larger studies, they wave a red flag about suicide risk and point toward prevention that targets the negative thoughts with pharmaceuticals and psychological intervention. The finding also is a reminder to physicians that depressed patients who report increased sleep problems should be asked if they are having suicidal thoughts, McCall said.

The scientists used psychometric testing to objectively assess the mental state of 50 depressed patients age 20-80 being treated as an inpatient, outpatient or in the Emergency Department. More than half had attempted suicide and most were taking an anti-depressant. Testing enabled the researchers to filter out other suicide risks such as depression itself and hone in on the relationship between insomnia and suicide risk, asking specific questions about dysfunctional beliefs about sleep such as: Do you think you will ever sleep again?

"It was this dysfunctional thinking, all these negative thoughts about sleep that was the mediating factor that explained why insomnia was linked to suicide," said McCall, who specializes in depression and sleep disorders. He's seen insomnia patients spiral downward with increasingly negative and unrealistic thoughts about not sleeping, thinking, for example, that their immune system is being irrevocably damaged. McCall challenges such negatives from his patients and asks other doctors to consider doing the same: to disagree, strongly stating there is no scientific evidence for the thoughts but there is hope and help. "People have choices," he said.

Once insomnia has been diagnosed, some fairly rigid guidelines can help turn the exhausting and potentially deadly tide, including:

Wake up at the same time every day no matter when you go to bed

Not going to bed until you are sleepy

Eliminating caffeine, known to stay in your system up to 15 hours

Eliminating alcoholic beverages or tobacco products

Complete cardiovascular exercise at least four hours before bedtime

Allowing ample time to digest a meal before heading to bed.

The likelihood of being suicidal at least doubles with insomnia as a symptom, McCall noted.

"If you talk with depressed people, they really feel like they have failed at so many things. It goes something like, 'My marriage is a mess, I hate my job, I can't communicate with my kids, I can't even sleep.' There is a sense of failure and hopelessness that now runs from top to bottom and this is one more thing," McCall said.

Collaborators include scientists at Wake Forest University School of Medicine in North Carolina and the University of Louisville in Kentucky.

http://www.eurekalert.org/pub_releases/2013-02/hms-fam021113.php

First animal model of recent human evolution

The first animal model of recent human evolution reveals that a single mutation produced several traits common in East Asian peoples, from thicker hair to denser sweat glands, an international team of researchers reports.

The team, led by researchers from Harvard Medical School, Harvard University, the Broad Institute of MIT and Harvard, Massachusetts General Hospital, Fudan University and University College London, also modeled the spread of the gene mutation across Asia and North America, concluding that it most likely arose about 30,000 years ago in what is today central China. The findings are reported in the cover story of the Feb. 14 issue of Cell.

"This interdisciplinary approach yields unique insight into the generation of adaptive variation among modern humans," said Pardis Sabeti, associate professor in the Center for Systems Biology and Department of Organismic and Evolutionary Biology at Harvard University, and one of the paper's senior authors.

"This paper tells a story about human evolution in three parts," said Cliff Tabin, head of the HMS Department of Genetics and co-senior author. "The mouse model links multiple traits to a single mutation, the related association study finds these traits in humans, and computer models tell us where and when the mutation likely arose and spread."

Previous research in Sabeti's lab had identified the mutation as a strong candidate for positive selection. That is, evidence within the genetic code suggested the mutant gene conferred an evolutionary advantage, though what advantage was unclear.

The mutation was found in a gene for ectodysplasin receptor, or EDAR, part of a signaling pathway known to play a key role in the development of hair, sweat glands and other skin features. While human populations in Africa and Europe had one, ancestral, version of the gene, most East Asians had a derived variant, EDARV370A, which studies had linked to thicker scalp hair and an altered tooth shape in humans.

The ectodysplasin pathway is highly conserved across vertebrates — the same genes do the same thing in humans and mice and zebrafish. For that reason, and because its effects on skin, hair and scales can be observed directly, it is widely studied.

This evolutionary conservation led Yana Kamberov, one of two first authors on the paper, to reason that EDARV370A would exert similar biological effects in an animal model as in humans. The HMS research fellow in genetics developed a mouse model with the exact mutation of EDARV370A — a difference of one DNA letter from the original, or wild-type, population. That mouse manifested thicker hair, more densely branched mammary glands and an increased number of eccrine, or sweat, glands.

"This not only directly pointed us to the subset of organs and tissues that were sensitive to the mutation, but also gave us the key biological evidence that EDARV370A could have been acted on by natural selection," Kamberov said.

The findings prompted the team to look for similar traits in human populations. When co-first author Sijia Wang and the team including collaborators at Fudan examined the fingertips of Chinese volunteers at colleges and farming villages, they found that the sweat glands of Han Chinese, who carry the derived variant of the gene, were packed about 15 percent more densely than those of a control population with the ancestral variant. At the same time, Wang and the team including collaborators at University College London were working to zero in on when and where the mutation arose. Computer models suggested that the derived variant of the gene emerged in central China between 13,175 and 39,575 years ago, with a median estimate of 30,925 years. Researchers concluded the derived variant is at least 15,000 years old, predating the migration from Asia by Native Americans, who also carry the mutation.

That time span suggests that different traits could have been under selection at different times. The mutation's many effects, known as pleiotropy, only complicate the question. If changes to the sweat glands conferred an advantage in new climates — one of the theories the researchers plan to explore further — changes to hair and to mammary glands could have conferred other advantages at other times.

Not all of these advantages need be direct effects on fitness. "When Pardis started this work, I would not have predicted that a gene that makes good hair would top of a list of mutations that confer evolutionary advantage among humans," said Bruce Morgan, HMS associate professor of dermatology at Massachusetts General Hospital and co-senior author on the paper. "However, in this case 'good hair' may have a biological meaning because it is genetically linked to a physiologically adaptive trait like increased sweating capacity. A cultural

preference for a physically obvious trait like hair type could have arisen because individuals with it were more successful, and this would help increase selection on the new variant."

"That (pleiotropy) makes it harder for us to make a guess," Wang said. "If there were only one associated trait, we could say with confidence that's where the selective advantage comes from. But with many traits, we don't know which is the target of selection, and which are just hitchhiking." Wang intends to focus on that question in his new role, as a Max Planck independent research group leader in dermatogenomics at Chinese Academy of Sciences – Max Planck Partner Institute for Computational Biology in Shanghai.

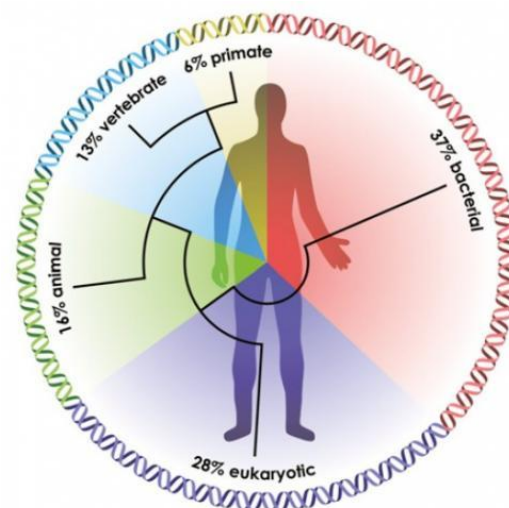
By leveraging the power of diverse fields, the team is piecing together the foundation for understanding how selected mutations like EDARV370A have impacted human diversity. But, they say, this is only the beginning. "These findings point to what mutations, when, where and how," said Daniel Lieberman, a professor of human evolutionary biology at Harvard University and a co-senior author on the study. "We still want to know why."

<http://phys.org/news/2013-02-bacterial-world-impacting-previously-thought.html>

We are living in a bacterial world, and it's impacting us more than previously thought
A team of scientists from universities around the world has shown that microorganisms have a much larger impact on the entire biosphere than scientists typically recognize

Phys.org - Throughout her career, the famous biologist Lynn Margulis (1938-2011) argued that the world of microorganisms has a much larger impact on the entire biosphere—the world of all living things—than scientists typically recognize. Now a team of scientists from universities around the world has collected and compiled the results of hundreds of studies, most from within the past decade, on animal-bacterial interactions, and have shown that Margulis was right. The combined results suggest that the evidence supporting Margulis' view has reached a tipping point, demanding that scientists reexamine some of the fundamental features of life through the lens of the complex, codependent relationships among bacteria and other very different life forms.

The project to review the current research on animal-bacterial interactions began when some scientists recognized the importance of [bacteria](#) in their own fields of study. For Michael Hadfield, Professor of Biology at the University of Hawaii at Manoa, the recognition grew over many years while studying the metamorphosis of [marine animals](#). He found that certain bacteria influence marine larvae to settle to particular places on the [sea floor](#), where they transform into juveniles and live out the rest of their lives.



The percentage of the human genome that arose at a series of stages in evolution. 37% of human genes originated in bacteria. Credit: Originally by T. Domazet-Lošo and D. Tautz ©2008 Mol Biol Evol.

"Once we determined that specific biofilm bacteria provide an essential and unique ligand to stimulate the larvae of one globally distributed [marine worm](#), our research naturally progressed to a study of the portion of the [bacterial genome](#) responsible for the signaling, and to other species, where we found the same genes involved," Hadfield told *Phys.org*. "Coming from different perspectives on the study of animal-bacterial interactions, and recognizing many more, Margaret McFall-Ngai [Professor of Medical Microbiology and Immunology at the University of Wisconsin, Madison] and I discussed the current situation extensively and then decided to attempt to draw together a significant number of experts on various approaches to the study of bacterial-animal interactions to draft a paper such as the one you have in hand. We proposed a 'catalysis meeting' on the subject to the National Science Foundation's National Evolutionary Synthesis Center (NESCent), which was funded, and the project took off."

Bacteria surround us

In many respects, it's easy to see the prominent role that bacteria play in the world. Bacteria were one of the first life forms to appear on Earth, about 3.8 billion years ago, and they will most likely survive long after humans are gone. In the current tree of life, they occupy one of the three main branches (the other two are Archaea and Eucarya, with animals belonging to the latter). Although bacteria are extremely diverse and live nearly everywhere on Earth, from the bottom of the ocean to the inside of our intestines, they have a few things in common. They are similar in size (a few micrometers), they are usually made of either a single cell or a few cells, and their cells don't have nuclei.

Although scientists have known for many years that animals serve as a host for bacteria, which live especially in the gut/intestines, in the mouth, and on the skin, recent research has uncovered just how numerous these

microbes are. Studies have shown that humans have about 10 times more bacterial cells in our bodies than we have human cells. (However, the total bacteria weigh less than half a pound because bacterial cells are much smaller than human cells.)

While some of these bacteria simply live side-by-side with animals, not interacting much, some of them interact a lot. We often associate bacteria with disease-causing "germs" or pathogens, and bacteria are responsible for many diseases, such as tuberculosis, bubonic plague, and MRSA infections. But bacteria do many good things, too, and the recent research underlines the fact that animal life would not be the same without them.

"The true number of bacterial species in the world is staggeringly huge, including bacteria now found circling the Earth in the most upper layers of our atmosphere and in the rocks deep below the sea floor," Hadfield said.

"Then add all of those from all of the possible environments you can think of, from cesspools to hot springs, and all over on and in virtually every living organism. Therefore, the proportion of all bacterial species that is pathogenic to plants and animals is surely small. I suspect that the proportion that is beneficial/necessary to plants and animals is likewise small relative to the total number of bacteria present in the universe, and surely most bacteria, in this perspective, are 'neutral.' However, I am also convinced that the number of beneficial microbes, even very necessary microbes, is much, much greater than the number of pathogens."

Animal origins and coevolution

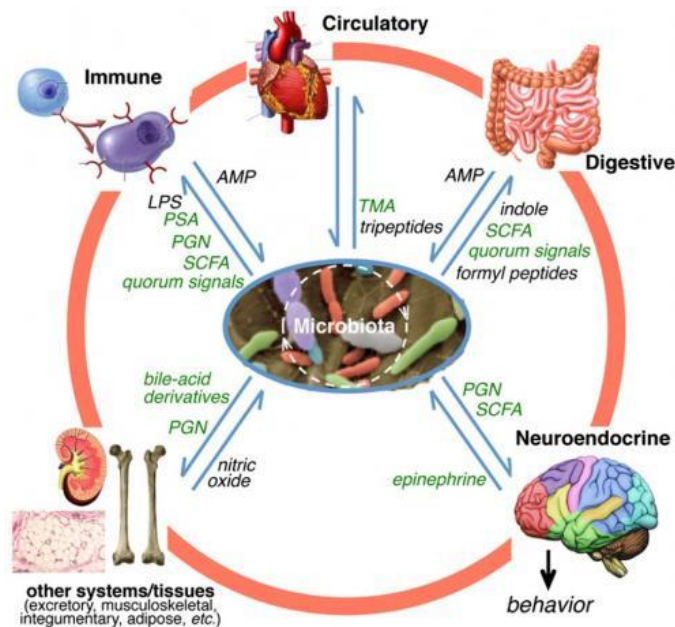
From our humble beginnings, bacteria may have played an important role by assisting in the origins of multicellular organisms (about 1-2 billion years ago) and in the origins of animals (about 700 million years ago). Researchers have recently discovered that one of the closest living relatives of multicellular animals, a single-celled choanoflagellate, responds to signals from one of its prey bacterium. These signals cause dividing choanoflagellate cells to retain connections, leading to the formation of well-coordinated colonies that may have become multicellular organisms. However, such questions of origin have been subjects of intense debate, and scientists have many hypotheses about how these life forms emerged. A bacterial role in these processes does not exclude other perspectives but adds an additional consideration.

Bacteria in an animal's microbiota, such as those in the gut, in the mouth, and on the skin, communicate among themselves and exchange signals with the animal's organ systems. Some of the chemical signals are noted in this illustration. Credit: Margaret McFall-Ngai, et al. ©2013 PNAS

After helping get animals started, bacteria also played an important role in helping them along their evolutionary path. While animal development is traditionally thought to be directed primarily by the animal's own genome in response to environmental factors, recent research has shown that animal development may be better thought of as an orchestration among the animal, the environment, and the coevolution of numerous microbial species. One example of this coevolution may have occurred when mammals evolved endothermy, or the ability to maintain a constant temperature of approximately 40 °C (100 °F) by metabolic means. This is also the temperature at which mammals' bacterial partners work at optimum efficiency, providing energy for the mammals and reducing their food requirement. This finding suggests that bacteria's preferred temperature may have placed a selection pressure on the evolution of genes associated with endothermy.

Bacterial signaling

Evidence for a deep-rooted alliance between animals and bacteria also emerges in both groups' genomes. Researchers estimate that about 37% of the 23,000 human genes have homologs with bacteria and Archaea, i.e., they are related to genes found in bacteria and Archaea that were derived from a common ancestor. Many of these homologous genes enable signaling between animals and bacteria, which suggests that they have been able to communicate and influence each other's development. One example is Hadfield and his group's discovery that bacterial signaling plays an essential role in inducing metamorphosis in some marine invertebrate larvae, where the bacteria produce cues associated with particular environmental factors. Other studies have found that bacterial signaling influences normal brain development in mammals, affects reproductive behavior in both vertebrates and invertebrates, and activates the immune system in tsetse flies. The olfactory chemicals



that attract some animals (including humans) to their prospective mates are also produced by the animals' resident bacteria.

Bacterial signaling is not only essential for development, it also helps animals maintain homeostasis, keeping us healthy and happy. As research has shown, bacteria in the gut can communicate with the brain through the central nervous system. Studies have found that mice without certain bacteria have defects in brain regions that control anxiety and depression-like behavior. Bacterial signaling also plays an essential role in guarding an animal's immune system. Disturbing these bacterial signaling pathways can lead to diseases such as diabetes, inflammatory bowel disease, and infections. Studies also suggest that many of the pathogens that cause disease in animals have "hijacked" these bacterial communication channels that originally evolved to maintain a balance between the animal and hundreds of beneficial bacterial species.

Signaling also appears in the larger arena of ecosystems. For example, bacteria in flower nectar can change the chemical properties of the nectar, influencing the way pollinators interact with plants. Human infants who are born vaginally have different gut bacteria than those delivered by Caesarean section, which may have long-lasting effects. And bacteria feeding on dead animals can repel animal scavengers—organisms 10,000 times their size—by producing noxious odors that signal the scavengers to stay away.

In the gut

In the earliest animals, gut bacteria played an important role in nutrition by helping animals digest their food, and may have influenced the development of other nearby organ systems, such as the respiratory and urogenital systems. Likewise, animal evolution likely drove the evolution of the bacteria, sometimes into highly specialized niches. For example, 90% of the bacterial species in termite guts are not found anywhere else. Such specialization also means that the extinction of every animal species results in the extinction of an unknown number of bacterial lineages that have evolved along with it.

Scientists have also discovered that bacteria in the human gut adapts to changing diets. For example, most Americans have a gut microbiome that is optimized for digesting a high-fat, high-protein diet, while people in rural Amazonas, Venezuela, have gut microbes better suited for breaking down complex carbohydrates. Some people in Japan even have a gut bacterium that can digest seaweed. Researchers think the gut microbiome adapts in two ways: by adding or removing certain bacteria species, and by transferring the desired genes from one bacterium to another through horizontal gene transfer. Both host and bacteria benefit from this kind of symbiotic relationship, which researchers think is much more widespread than previously thought.

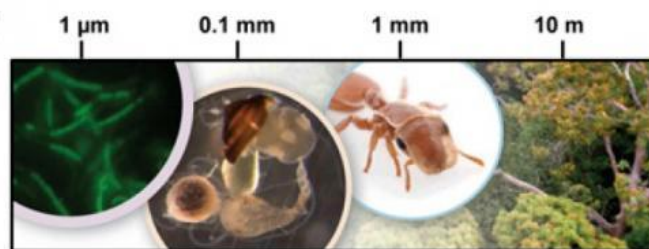
The big picture

Altogether, the recent studies have shown that animals and bacteria have histories that are deeply intertwined, and depend on each other for their own health and well-being as well as that of their environments. Although the researchers focused exclusively on animal-bacteria interactions, they expect that similar trends of codependency and symbiosis are universal among and between other groups, such as Archaea, fungi, plants, and animals. Once considered an exception, such intermingling is now becoming recognized as the rule—just as Margulis predicted many decades ago. Due to these symbiotic relationships, the scientists here propose that the very definitions of an organism, an environment, a population, and a genome have become blurred and should be reviewed. It may be, for instance, that animals are better viewed as host-microbe ecosystems than as individuals.

An insect (1 mm) living in a forest canopy (10 m) illustrates the effects animal-bacterial interactions across multiple scales. Bacteria (1 micrometer) residing in the animal's gut (0.1 mm) are essential to the insect's nutrition, and insects often make up a majority of the animal biomass in forest canopies. Credit: Margaret McFall-Ngai, et al. ©2013 PNAS

In addition, the scientists predict that the recent findings on animal-bacteria interactions will likely require biologists to significantly alter their view of the fundamental nature of the entire biosphere. Along these lines, large-scale research projects such as the Human Microbiome Project and the Earth Microbiome Project are already underway to investigate the wide range of bacteria in the individual and global systems, and to see what happens when the bacteria are disturbed.

In the end, the scientists hope that the results will promote more cross-disciplinary collaboration among scientists and engineers from different fields to explore the new microbial frontier. They argue that these discoveries should revolutionize the way that biology is taught from the high school level on up, by focusing more on the relationships between bacteria, their animal partners, and all other life forms.



"It is hard to summarize a single 'most important conclusion,' other than the admonition to biologists studying animals, from behavior to physiology and ecology to molecular biology, that no matter what process you think you are studying, you must look for and consider a major role for bacteria," Hadfield said. "In many cases, this may require partnerships across traditional boundaries of research, meaning that zoologists must collaborate with microbiologists to advance their research, that molecular biologists must collaborate with whole-organism biologists, etc. We want badly for the message in 'Animals in a bacterial world,' to be a call for the necessary disappearance of the old boundaries between life science departments (e.g., Depts of Zoology, Botany, Microbiology, etc.) in universities, and societies (e.g., the American Society for Microbiology, etc.). We also want the message disseminated in college and university classes from introductory biology to advanced courses in the various topic areas of our paper."

The results will profoundly change the way that the scientists of this collaboration continue with their own areas of research, Hadfield said.

"Each of the authors of our paper conducts basic research in one or more areas of animal-bacterial interactions discussed in the paper, and each will continue to focus on her/his own speciality, I'm sure," he said. "However, I'm also certain that the interactions developed during the composition and writing of the paper (starting with our NESCent meeting in October 2011, when most of us met for the first time) will impact our own research and cause us to establish new collaborations with other laboratories. That has already occurred for me; I have a new collaboration with Dianne Newman's group at CalTech, an outstanding group of bacteriologists who are helping us do a much more in-depth investigation of the bacterial gene-products responsible for larval development."

More information: Margaret McFall-Ngai, et al. "Animals in a bacterial world, a new imperative for the life sciences." *PNAS Early Edition*. DOI: [10.1073/pnas.1218525110](https://doi.org/10.1073/pnas.1218525110)

<http://phys.org/news/2013-02-health-effects-fukushima-japan.html>

No health effects from Fukushima: Japan researcher

A Japanese government-backed researcher said Friday no health effects from radiation released by the stricken Fukushima nuclear plant have been seen in people living nearby.

The pronouncement by Kazuo Sakai of Japan's National Institute of Radiological Sciences is the latest by authorities seeking to quell fears over the long-term effects of the disaster.

But it was dismissed by campaign group Greenpeace who said the government should not seek to play down health worries. "Since the accident in Fukushima, no health effects from radiation have been observed, although we have heard reports some people fell ill due to stress from living as evacuees and due to worries and fears about radiation," Sakai said.

"We know from epidemiological surveys among atomic-bomb victims in Hiroshima and Nagasaki that if exposure to radiation surpasses 100 millisieverts, the risk of cancer will gradually rise.

"To put it the other way round, we can't say risk of cancer will rise if you are exposed to radiation lower than 100 millisieverts," he said, adding that most people measured had radiation exposure of 20 millisieverts or less. Sakai said radiation is not at "the level we have to worry about its health effect," for people in Fukushima, taking into account exposure from the atmosphere and ingestion from food.

His comments came as the Fukushima prefectural government panel said this week three people who were 18 or younger when the nuclear crisis erupted in March 2011 have been diagnosed with thyroid cancer.

Radioactive iodine released in nuclear accidents tends to accumulate in thyroid glands, particularly in young people. In the 1986 Chernobyl disaster, a noticeable increase in thyroid cancer cases was detected among children in the affected area.

Referring to the thyroid cancers reported in Fukushima, Sakai said "there is no clear link between the cancers and exposure to radiation, as empirical knowledge says it takes several years before thyroid cancer is detected after exposure to radiation." "It is important, however, to monitor these cases," he added, noting that comparison with the pre-accident situation and other regions was necessary.

Kazue Suzuki, nuclear campaigner at Greenpeace, who is not a scientist, said Japan should not try to play down the potential dangers. "Japan should pour more energy into prevention of diseases including thyroid cancer than talking down the risk of low-level radiation."

"Even if there is no comparative epidemiological data, the government should err on the side of caution and carry out more frequent health checks among residents not only in Fukushima but in other prefectures," she said. A massive undersea earthquake in March 2011 sent a huge tsunami crashing into Japan's northeast, crushing whole communities and sending nuclear reactors on the coast into meltdown.

Around 19,000 people were killed by the natural disaster, but no one is officially recorded as having died as a direct result of the radiation that spewed from the crippled units in the following months.

<http://phys.org/news/2013-02-metallic-behavior-material-heralds-electronic.html>

The observation of truly metallic behavior in an organic material heralds a new generation of electronic devices

Organic materials can also exhibit metallic behavior

When we think about metals, objects like copper wires and sheets of iron spring to mind. However, organic materials—those based, as all living matter, on carbon and oxygen atoms—can also exhibit metallic behavior. Some organic compounds have been established as good electric conductors, but these systems can be full-fledged metals as Reizo Kato of the RIKEN Advanced Science Institute, Wako, and co-workers in Japan and China have shown. They found unambiguous signatures in an organic compound which establish that the material behaves at low temperatures precisely like most metals.

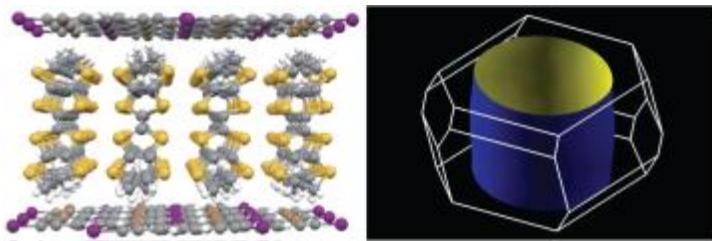


Figure 1: The crystal structure of the organic metal (BEDT-TTF)3Br(pBIB) in real space (left) and a rendering of the 'wave-number space' (right), representing the space where conducting electrons exist. Credit: 2012 Nature Publishing Group (left); Reizo Kato, RIKEN Condensed Molecular Materials Laboratory (right)

The interest in 'organic metals' is fuelled by the prospect of technological applications reaching from stretchable electronics to bio-integrated devices. However, almost 40 years after the first discovery of organic metals, a number of fundamental aspects remain to be explored in these materials. In particular, until now it has never been shown that organic metals behave according to the so-called Fermi-liquid theory—the model that describes the behavior of most metals at low temperatures.

Kato and his colleagues have filled this gap. The team observed the signatures of a Fermi liquid in a compound known as (BEDT-TTF)3Br(pBIB) (Fig. 1, left). "In general, organic conductors are fragile and vulnerable to light irradiation," says Kato. "But over a period of more than ten years our team has made methodological advances—in particular in the area of photoelectron spectroscopy—that allowed us to reduce the disruptive factors." The team's know-how enabled them to successfully conduct a series of experiments in which they showed that at low temperatures the electrons in (BEDT-TTF)3Br(pBIB) indeed behave in the same characteristic manner as they do in a conventional metal (Fig. 1, right).

These findings call for revisiting a number of earlier experiments that indicated that the electrons in organic materials behave differently from a Fermi liquid. But most importantly, the work of Kato and his colleagues provides a sound foundation for understanding organic metals, which in turn should pave the way toward practical applications. "This project will provide important information for understanding electronic processes and designing organic materials," says Kato. Among the organic metals, the (BEDT-TTF)3Br(pBIB) system and related compounds are particularly interesting as they are characterized by an architecture in which two-dimensional conducting layers are separated by insulating supramolecular networks. Such network structures may serve as the building blocks for functional molecular materials, including computing and memory elements for electronic devices.

More information: Kiss, T., et al. Quasiparticles and Fermi liquid behaviour in an organic metal. Nature Communications 3, 1089 (2012). www.nature.com/ncomms/journal/v3/n9/full/ncomms2079.html

<http://www.scientificamerican.com/article.cfm?id=proteins-behind-mad-cow-disease-also-help-brain-develop>

Proteins Behind Mad-Cow Disease Also Help Brain to Develop

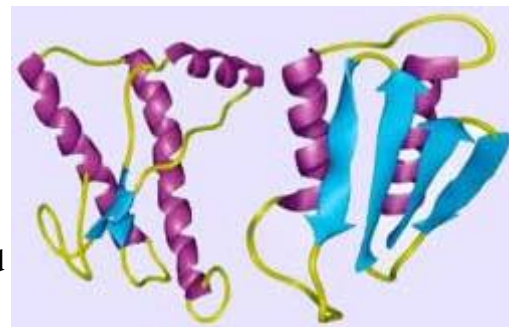
When not misfolded, prions lend a hand in formation neuronal connections

By Mo Costandi and Nature magazine | Friday, February 15, 2013

Prions are best known as the infectious agents that cause 'mad cow' disease and the human versions of it, such as variant Creutzfeldt–Jakob Disease. But the proteins also have at least one known useful function, in the cells that insulate nerves, and are suspected to have more. Now researchers have provided the first direct evidence that the proteins play an important role in neurons themselves.

The team reports in the Journal of Neuroscience that prions are involved in developmental plasticity, the process by which the structure and function of neurons in the growing brain is shaped by experience.

Prion proteins cause pathologies such as hamster scrapie when they misfold (right) — but the same protein has benign functions when folded correctly (left). Image: N. Engl. J. Med. 344, 1516-1526 (2001)



Prions come in two main forms: the normal version and the misfolded, infectious version. The normal version, known as cellular prion protein (or PrPC), is present in every cell of the body and helps to maintain the myelin sheath in the cells that protect the nerves.

But the molecule is abundant in neurons themselves, especially during development. Because it is tethered to the membrane, it is widely assumed to be involved in signaling between nerve cells, but little direct evidence has been found for this.

Neurobiologist Enrico Cherubini of the International School for Advanced Studies in Trieste, Italy, and his colleagues therefore decided to look at the effects of electrical stimulation on slices of tissue from the hippocampus of healthy 3–7-day-old mice and of animals genetically engineered to lack the gene that encodes the prion protein. They used electrodes to stimulate individual cells at the same time as the networks of young neurons showed bursts of spontaneous electrical activity, or to simultaneously stimulate pairs of cells that are connected to each other.

In the tissue from healthy animals, both procedures strengthened the links between neurons, a phenomenon known as long-term potentiation. In mice without the prion gene, however, the stimulation had the opposite effect. In these animals, the procedure induced long-term depression, or a weakening of neuronal connections.

Ups and downs

Further experiments revealed that the potentiation in mice with cellular prion protein was caused by activation of an enzyme called protein kinase A. In the absence of cellular prion protein, however, activation of a related enzyme, called protein lipase C, caused a long-term lowering of the neuron's activity.

“This shows that [the cellular prion protein] controls the direction of plasticity in the developing hippocampus,” says Cherubini, adding that he and his colleagues now want to identify the molecules that transfer the prion signal from the membrane into the cell.

Long-term potentiation in the hippocampus is thought to be crucial for learning and memory, but the importance of prions is still unknown, and Cherubini would like to investigate how the proteins are involved in behavior. He also speculates that prions have a similar role in other parts of the developing brain, such as the visual cortex, and in adults.

“The function of cellular prion protein is quite mysterious, but this convincingly demonstrates that it has a crucial role in strengthening synaptic connections within developing neural networks,” says R. Douglas Fields, chief of the Neural Development and Plasticity Section at the National Institute for Child Health and Development in Bethesda, Maryland.

http://www.eurekalert.org/pub_releases/2013-02/nu-nyc021113.php

Not your conventional nucleic acids

Spherical nucleic acids have novel properties that are perfect for biomedical applications

Northwestern University's Chad A. Mirkin, a world-renowned leader in nanotechnology research and its application, has invented and developed a powerful material that could revolutionize biomedicine: spherical nucleic acids (SNAs).

Mirkin will discuss SNAs and their applications in therapeutics and diagnostics in a talk titled "Nanostructures in Biology and Medicine" at the American Association for the Advancement of Science (AAAS) annual meeting in Boston. His presentation is part of the symposium "Convergence of Physical, Engineering, and Life Sciences: Next Innovation Economy" to be held from 1:30 to 4:30 p.m. Friday, Feb. 15.

Potential applications include using SNAs to carry nucleic acid-based therapeutics to the brain for the treatment of glioblastoma, the most aggressive form of brain cancer, as well as other neurological disorders such as Alzheimer's and Parkinson's diseases. Mirkin is aggressively pursuing treatments for such diseases with Alexander H. Stegh, an assistant professor of neurology at Northwestern's Feinberg School of Medicine.

"These structures are really quite spectacular and incredibly functional," Mirkin said. "People don't typically think about DNA in spherical form, but this novel arrangement of nucleic acids imparts interesting chemical and physical properties that are very different from conventional nucleic acids."

Spherical nucleic acids consist of densely packed, highly oriented nucleic acids arranged on the surface of a nanoparticle, typically gold or silver. The tiny non-toxic balls, each roughly 15 nanometers in diameter, can do things the familiar but more cumbersome double helix can't do:

SNAs can naturally enter cells and effect gene knockdown, making SNAs a superior tool for treating genetic diseases using gene regulation technology.

SNAs can easily cross formidable barriers in the human body, including the blood-brain barrier and the layers that make up skin.

SNAs don't elicit an immune response, and they resist degradation, resulting in longer lifetimes in the body.

"The field of medicine needs new constructs and strategies for treating disease," Mirkin said. "Many of the ways we treat disease are based on old methods and materials. Nanotechnology offers the ability to rapidly create new structures with properties that are very different from conventional forms of matter."

Mirkin is the George B. Rathmann Professor of Chemistry in the Weinberg College of Arts and Sciences and professor of medicine, chemical and biological engineering, biomedical engineering and materials science and engineering. He is director of Northwestern's International Institute for Nanotechnology (IIN).

Last year, Mirkin and Amy S. Paller, M.D., chair of dermatology and professor of pediatrics at Feinberg, were the first to demonstrate the use of commercial moisturizers to deliver gene regulation technology for skin cancer therapy. The drug, consisting of SNAs, penetrated the skin's layers and selectively targeted disease-causing genes while sparing normal genes.

"We now can go after a whole new set of diseases," Mirkin said. "Thanks to the Human Genome Project and all of the genomics research over the last two decades, we have an enormous number of known targets. And we can use the same tool for each, the spherical nucleic acid. We simply change the sequence to match the target gene. That's the power of gene regulation technology."

A member of President Obama's Council of Advisors on Science and Technology, Mirkin is known for invention and development of biological and chemical diagnostic systems based upon nanomaterials. He is the inventor and chief developer of Dip-Pen Nanolithography, a groundbreaking nanoscale fabrication and analytical tool, and is the founder of four Chicago-based companies: AuraSense, AuraSense Therapeutics, Nanosphere and NanoInk.

The National Cancer Institute through the Northwestern University Cancer Center for Nanotechnology Excellence supported the research.

http://www.eurekalert.org/pub_releases/2013-02/ip-nhc021513.php

Novel herbal compound offers potential to prevent and treat Alzheimer's disease

Findings published in Restorative Neurology and Neuroscience

Amsterdam, NL - Administration of the active compound tetrahydroxystilbene glucoside (TSG) derived from the Chinese herbal medicine Polygonum multiflorum Thunb, reversed both overexpression of α -synuclein, a small protein found in the brain, and its accumulation using a mouse model of Alzheimer's disease. These results, which may shed light on the neuropathology of AD and open up new avenues of treatment, are available in the current issue of Restorative Neurology and Neuroscience.

Aberrant accumulation of α -synuclein can form insoluble aggregates that have been implicated in several neurodegenerative diseases, including Parkinson's disease, dementia with Lewy bodies, and Alzheimer's disease (AD). Researchers have now found that overexpression of α -synuclein increases with age and have demonstrated that α -synuclein aggregates in the hippocampus of older mice compared to normal controls.

"Our results raise the possibility that TSG might be a novel compound for the treatment of AD and dementia with Lewy body," says co-lead investigator Lan Zhang, MD, PhD, Associate Professor, Key Laboratory for Neurodegenerative Diseases of Ministry of Education, Department of Pharmacology of Xuanwu Hospital of Capital Medical University in Beijing.

The study used an animal model of AD: APPV717I transgenic (Tg) mice with the London mutation. In previous work, the authors showed that these mice show cognitive impairments beginning at 4 months of age and develop amyloid plaques in the brain that are evident by 10 months.

In one series of experiments, 4 month old Tg mice were divided into 3 groups and received daily intragastric administration of distilled water (controls), low dose TSG (120 μ mol/kg/d), or high dose TSG (240 μ mol/kg/d). A fourth group consisted of age-matched non-Tg controls. The mice were treated until 10 months of age. In a second series of experiments, 10-month-old mice were divided into similar control and TSG-treated groups and were treated for 6 months.

The authors used a variety of techniques to hone in on what was happening in the brains of the Tg mice compared to age-matched controls: cDNA microarray analysis, reverse transcription PCR, western blotting, and immunochemistry. They found that α -synuclein messenger RNA (mRNA) and protein expression levels increase in a time-dependent manner in the hippocampus of Tg mice between ages 4 and 16 months and α -synuclein aggregation was noticeable at 16 months. Age-related increases in α -synuclein were also seen in the control mice but to a lesser degree.

"We suggest that, besides increased A β (beta-amyloid) and amyloid plaques, overexpression and aggregation of α -synuclein in the hippocampus might partially account for cognitive impairment in this Tg mouse model of AD," comments co-lead investigator Lin Li, MD, PhD, Professor and Director, Department of Pharmacology, Xuanwu Hospital of Capital Medical University in Beijing. She adds that " α -synuclein overexpression occurs even in the early phase of AD and may accelerate A β production and deposition, which further facilitates α -synuclein overexpression and accumulation."

Analysis of the TSG-treated groups showed that TSG-treatment from the age of 4 to 10 months significantly downregulated α -synuclein mRNA and protein overexpression in the hippocampus of the Tg mice, and the effect was stronger at the higher dose. This suggests that TSG may have a role in preventing the neurotoxic effects of α -synuclein on synaptic function and cell activity. In addition, the finding that Tg reduced α -synuclein overexpression in older animals (>10 months) may indicate that it has therapeutic potential even after neuropathologic changes have occurred.

In previous work, the authors found that TSG acts as a "cognitive enhancer" to improve learning and memory in both APP transgenic mice and aged rats. The authors emphasize that while it is not completely clear how TSG works, their findings open up a new area of research. "The role of α -synuclein, especially in the early phase of AD, and its interaction with A β should be considered when developing new therapeutic strategies to target AD pathogenesis," says Dr. Zhang.

http://www.eurekalert.org/pub_releases/2013-02/ps-eh021413.php

Evolution helped turn hairless skin into a canvas for self-expression

Hairless skin first evolved in humans as a way to keep cool -- and then turned into a canvas to help them look cool, according to a Penn State anthropologist.

Matthew Swayne

UNIVERSITY PARK, Pa. -- About 1.5 to 2 million years ago, early humans, who were regularly on the move as hunters and scavengers, evolved into nearly hairless creatures to more efficiently sweat away excess body heat, said Nina Jablonski, Distinguished Professor of Anthropology. Later, humans began to decorate skin to increase attractiveness to the opposite sex and to express, among other things, group identity.

"We can make a visual impact and present a completely different impression than we can with regular, undecorated skin," said Jablonski, who reports on her research today (Feb.

16) at the annual meeting of the American Association for the Advancement of Science in Boston.

Over the millennia, people turned their skin into canvases of self-expression in different ways, including permanent methods, such as tattooing and branding, as well as temporary ones, including cosmetics and body painting, according to the researcher.

Jablonski said both males and females use forms of skin decoration to become more attractive to the opposite sex. Women, for example, may use makeup to increase the size of their eyes, a cue that is considered attractive in most cultures. Males in some cultures also use skin decoration as a way to bring out facial features to appeal to women, or to look more menacing and warrior-like.

"We can paint a great design on our bodies and use those designs to send all sorts of messages or express group memberships," said Jablonski.

While parents may still fret that their children are choosing tattoo designs frivolously, Jablonski said people have traditionally put considerable time and thought into the tattoos.

"Usually it is something with deep meaning," Jablonski said.

"When I talk to people about their tattoos they, tell me they've spent months or years choosing a design that is incredibly meaningful and salient to them." Prior to the evolution of mostly naked skin, humans were furry creatures, not unlike chimpanzees are now, Jablonski said.

Skin decoration would not be possible if humans were still covered with fur.

Studying skin is difficult because it can be preserved only for a few thousand years, unlike bones and fossils, which last millions of years.

Jablonski said that she and other researchers based their estimate on when humans evolved hairless skin on the study of the fossil record and an examination of the molecular history of genes that code proteins that help produce skin pigmentation.

"We find a lot of evidence of when humans began to lose hair based on molecular genetics," said Jablonski.

Humans are the only primates that are essentially hairless, although aquatic mammals, like whales and dolphins, have no hair.

Prior to the idea that humans evolved hairlessness as a mechanism to cope with body heat, some researchers believed that hairlessness resulted from evolution from a common aquatic ancestor, Jablonski said.

However, the theory, often referred to as the aquatic ape theory, does not match the genetic, fossil and environmental evidence, she said.

While it is difficult to exactly say when humans began to decorate their skin, Jablonski said that some of the earliest preserved skin shows signs of tattooing.

http://www.eurekalert.org/pub_releases/2013-02/su-gns021413.php

Going negative: Stanford scientists explore new technologies that remove atmospheric CO₂

Solving climate change may require developing carbon-negative tech to remove CO₂ from the atmosphere

Mark Shwartz, Precourt Institute for Energy, Stanford University.

In his Feb. 12 State of the Union address, President Obama singled out climate change as a top priority for his second administration. "We can choose to believe that Superstorm Sandy, and the most severe drought in decades, and the worst wildfires some states have ever seen were all just a freak coincidence," he said. "Or we can choose to believe in the overwhelming judgment of science – and act before it's too late."

Four years ago, the president addressed rising global temperatures by pledging a 17 percent cut in carbon dioxide (CO₂) and other greenhouse gas emissions in the United States by 2020, and an 80 percent cut by 2050. The administration has taken a number of steps to meet those goals, such as investing billions of dollars in wind, solar and other carbon-neutral energy technologies.

But reducing CO₂ emissions may not be enough to curb global warming, according to scientists at Stanford University. The solution, they say, could also require developing carbon-negative technologies that remove large amounts of CO₂ from the atmosphere. Their findings are summarized in a report by Stanford's Global Climate and Energy Project (GCEP).

"To achieve the targeted cuts, we would need a scenario where, by the middle of the century, the global economy is transitioning from net positive to net negative CO₂ emissions," said report co-author Chris Field, a professor of biology and of environmental Earth system science at Stanford. "We need to start thinking about how to implement a negative-emissions energy strategy on a global scale."

In the GCEP report, Field and lead author Jennifer Milne describe a suite of emerging carbon-negative solutions to global warming – from bioenergy technologies to ocean sequestration. Many of the examples cited were initially presented at a negative carbon emissions workshop hosted by GCEP in 2012.

BECCS

"Net negative emissions can be achieved when more greenhouse gases are sequestered than are released into the atmosphere," explained Milne, an energy assessment analyst at GCEP. "One of the most promising net-negative technologies is BECCS, or bioenergy with carbon capture and storage."

A typical BECCS system converts woody biomass, grass and other vegetation into electricity, chemical products or fuels, such as ethanol. CO₂ emissions released during the process are captured and stored. The technology can be used in power plants, paper mills, ethanol processors and other manufacturing facilities. As a carbon-negative technology, BECCS takes advantage of the innate ability of trees, grasses and other plants to absorb atmospheric CO₂ for photosynthesis. In nature, the CO₂ is eventually released back into the atmosphere as the plant decays. But when vegetation is processed at a BECCS facility, the CO₂ emissions are captured and prevented from re-entering the environment. The result is a net-negative reduction in atmospheric CO₂.

The GCEP report identified 16 BECCS projects at various stages of development around the world. The first project was launched in 2009 by the Department of Energy at a corn ethanol production facility in Decatur, Ill., operated by the Archer Daniel Midlands Company. Each day, about 1,000 metric tons of CO₂ emitted during ethanol fermentation are captured and stored in a sandstone formation some 7,000 feet underground. The goal of the project is to sequester 1 million metric tons of CO₂ a year – the equivalent of removing 200,000 automobiles from the road.

Approximately 60 percent of global CO₂ emissions come from power plants and other industries fueled by coal, natural gas and oil. Capturing and sequestering those emissions could play a significant role in curbing global warming. To make the process carbon negative, researchers have proposed a BECCS co-fired power plant that runs on a mixture of fossil fuel (such as coal) and vegetation (wood, grass or straw, for example). A percentage of the CO₂ emissions would come from burnt vegetation. Therefore, capturing and storing those emissions would be a net-negative process.

Estimates show that by 2050, BECCS technologies could sequester 10 billion metric tons of industrial CO₂ emissions annually worldwide. But according to the GCEP report, major technical and economic hurdles must be overcome, such as the relative inefficiency of biomass fuels and the high cost of carbon capture and storage (CCS).

Financial incentives are needed to encourage private sector investment in CCS and BECCS, said Olivia Ricci of the University of Orléans in France. "To meet ambitious climate targets, a cost-effective policy would be to implement a carbon tax and to recycle the revenues to subsidize captured emissions from biomass," Ricci said. A carbon tax would put a price on CO₂ emissions and increase the competitiveness of CCS, while an emission

subsidy would encourage BECCS deployment, she added. "We're going to be burning fossil fuels for many years to come," said Field, who also serves as director of the Carnegie Institution Department of Global Ecology at Stanford. "BECCS is one of the only proven technologies that uses fossil fuels and actually removes CO₂ from the atmosphere."

Biochar

Field and Milne also assessed the pros and cons of biochar – a carbon-negative technology based on the same principal as BECCS. Biochar is a plant byproduct similar to charcoal that can be made from lumber waste, dried corn stalks and other plant residues. Heating vegetation slowly without oxygen – a process called pyrolysis – produces carbon-rich chunks of biochar that can be placed in the soil as fertilizer. Like BECCS, the goal is to permanently lock carbon underground instead of letting CO₂ re-enter the atmosphere as the plant decomposes.

One advantage of biochar is its simplicity, the authors said. Implementing biochar technology on a global scale could result in the sequestration of billions of metric tons of carbon a year, they added.

However, long-term sequestration "would require high biochar stability," they wrote. "Estimates of biochar half-life vary greatly from 10 years to more than 100 years. The type of feedstock also contributes to stability, with wood being more stable than grasses and manure."

In addition to long-term stability, questions have been raised about the impact of biochar on soil conservation, biodiversity and water use. As an example, the authors pointed to research showing that negative effects on soil fertility can occur if the pH of the biochar and the soil are not well matched.

According to the authors, biochar systems can be net negative if the biochar is made from waste biomass, sustainably harvested crop residues or crops grown on abandoned land that has not reverted to forest. On the other hand, biochar production that relies on forest ecosystems may result in a net increase in greenhouse gas emissions, they cautioned.

Net-negative farming

Even large agricultural systems can be net negative. The GCEP report cited research by Jose Moreira of the University of Sao Paulo. Using computer models, Moreira found that from 1975 to 2007, ethanol production from sugar cane in Brazil resulted in a net-negative capture of 1.5 metric tons of CO₂ per cubic meter of ethanol produced. "In this model, the system took 18 years to recoup carbon emissions, with most reductions coming from soil replenishment from root growth and replacement of gasoline with ethanol," the GCEP authors wrote. However, questions remain about the long-term effects of ethanol combustion on climate.

The report also explored the possibility of sequestering carbon in the ocean, with a particular focus on the problem of ocean acidification, which is destroying coral reefs around the world. Ocean acidification results from the increased uptake of atmospheric CO₂, which causes seawater to become more acidic. The authors cited research by David Keith of Harvard University suggesting that magnesium carbonate and other minerals could be added to the ocean to reduce acidity and sequester atmospheric CO₂ absorbed in seawater. Although the potential for CO₂ sequestration in the ocean is large, "the associated risks to the marine environment need to be adequately assessed," the authors concluded.

Keith has also launched a startup company called Carbon Engineering that's developing industrial-scale machines – "artificial trees" – that are designed to capture CO₂ directly from the air. Unlike BECCS and biochar systems, which produce electricity or fuels, mechanical "trees" do not generate power and, in fact, require natural gas to operate. Following the 2012 negative-emissions workshop, GCEP issued an international request for proposals to develop net-negative carbon emissions technologies. The awardees will be announced later this year. Up to to \$6 million could be awarded.

GCEP is an industry partnership based at Stanford that addresses the challenge of global climate change by supporting innovative research on energy technologies that significantly lower greenhouse gas emissions. Funding for the report was provided by ExxonMobil, GE, Schlumberger, Toyota and DuPont.

Related information: GCEP Negative Emissions Report http://gcep.stanford.edu/events/workshops_negemissions2012.html

<http://www.bbc.co.uk/news/science-environment-21487016>

Scans reveal intricate brain wiring

Scientists are set to release the first batch of data from a project designed to create the first map of the human brain.

Pallab Ghosh By Pallab Ghosh Science correspondent, BBC News, Boston

The project could help shed light on why some people are naturally scientific, musical or artistic. Some of the first images were shown at the American Association for the Advancement of Science meeting in Boston. I found out how researchers are developing new brain imaging techniques for the project by having my own brain scanned.

Scientists at Massachusetts General Hospital are pushing brain imaging to its limit using a purpose built scanner. It is one of the most powerful scanners in the world.

The scanner's magnets need 22MW of electricity - enough to power a nuclear submarine.

The researchers invited me to have my brain scanned. I was asked if I wanted "the 10-minute job or the 45-minute 'full monty'" which would give one of the most detailed scans of the brain ever carried out. Only 50 such scans have ever been done. I went for the full monty.

It was a pleasant experience enclosed in the scanner's vast twin magnets. Powerful and rapidly changing magnetic fields were looking to see tiny particles of water travelling along the larger nerve fibres.

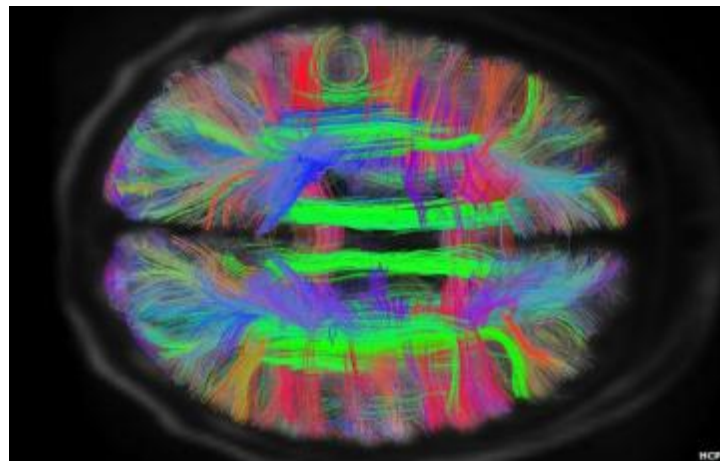
By following the droplets, the scientists in the adjoining cubicle are able to trace the major connections within my brain.

Arcs of understanding

The result was a 3D computer image that revealed the important pathways of my brain in vivid colour. One of the lead researchers, Professor Van Wedeen, gave me a guided tour of the inside of my head.

He showed me the connection that helped me to see and another one that helped me understand speech. There were twin arcs that processed my emotions and a bundle that connected the left and right sides of my brain.

Prof Wedeen used visualisation software that enabled him to fly around and through these pathways - even to zoom in to see intricate details.



The brain pathways as seen from above. Here, the two green paths near centre are the cingulum bundles, and the two C-shaped green paths closer to the sides are major pathways of language, the arcuate bundles. These paths connect the frontal lobes, where facial movements are controlled, with the temporal lobes below, where sounds are processed, hearing interpreted, and utterances planned.

He and his team hope to learn how the human mind works and what happens when it goes wrong

"We have all these mental health problems and our method for understanding them has really not changed for over a hundred years," he said.

"We don't have imaging methods as we do for the heart to tell what's really going on. Wouldn't it be fantastic if we could get in there and see these things and give people advice concerning what their risks are and how we could help them overcome those problems?"

The brain imaging technology is being developed for a US-led effort to map the human brain called the Human Connectome Project.

And just as with the Human Genome Project before it, the data will be publicly released to scientists as the scans are processed, with the first tranche of data from between 80 and a 100 people to be released in a few weeks' time.

The HCP is a five-year project funded by the National Institutes of Health. The aim the \$40m programme is to map the entire human neural wiring system by scanning the brains of 1,200 Americans.

Researchers will also collect genetic and behavioural data from the subjects in order to build up a complete picture of the factors that influence the human psyche.

The brain's wiring diagram is not like that of an electronic device which is fixed. It is thought that changes occur after each experience, and so each person's brain map is different - an ever changing record of who we are and what we have done.

The HCP will be able to test the hypothesis that minds differ as connectomes differ, according to Dr Tim Behrens of Oxford University, UK. "We're likely to learn a lot about human behaviour," he told BBC News.

"Some of the connections between different parts of the brain might be different for people with different characters and abilities, so for example there's one connection we already know about in people who like taking risks and (a different one) for people who like playing it safe.

"So we'll be able to tell the type of people who like skydiving and who would rather watch TV from their brain scans. "It will be an amazing resource for the neuroscience community to help them in their work to understand how the brain works," he said.

Prof Steve Petersen, who works with the HCP at Washington University in St Louis, wants to identify the different parts of the brain involved with our ability to think about scientific problems, to concentrate and to hold information in our memory.

"The romance to me is that we are getting to our humanity," he said.

<http://phys.org/news/2013-02-jupiter-europa-moon-likeliest-life.html>

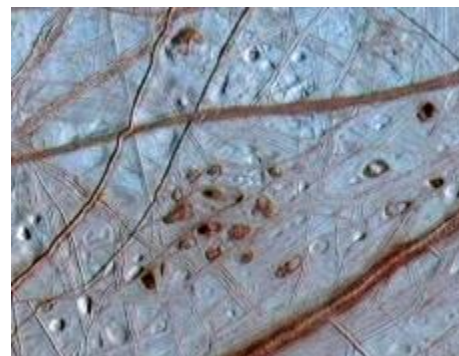
Jupiter's Europa moon 'likeliest to have life'

US astronomers believe that Europa is much more promising than Mars, which is currently the focus of the US government's attention.

US astronomers looking for life in the solar system believe that Europa, one of the moons of Jupiter, which has an ocean, is much more promising than desert-covered Mars, which is currently the focus of the US government's attention.

"Europa is the most likely place in our solar system beyond Earth to possess life," said Robert Pappalardo, a planetary scientist at NASA's Jet Propulsion Laboratory (JPL) in Pasadena, California.

"And it is the place we should be exploring now that we have a concept mission we think is the right one to get there for an affordable cost," he continued.



A NASA photo shows reddish spots and shallow pits peppering the surface of Jupiter's moon Europa in this view combining information from images from NASA's Galileo spacecraft 31 May, 1998. US astronomers looking for life in the solar system believe that Europa, which has an ocean, is much more promising than desert-covered Mars, which is currently the focus of the US government's attention.

"Europa is the most promising in terms of habitability because of its relatively thin ice shelf and an ocean ...

And we know there are oxidants on the surface of Europa."

At the request of NASA, a proposed mission to explore Europa was revised to significantly reduce the cost, the scientist told the media on the sidelines of an annual conference of the American Association for the Advancement of Science (AAAS) underway here.

As a result of this review, the JPL and the Applied Physics Laboratory at Johns Hopkins University in Maryland developed a new exploration project named Clipper with a total cost of two billion dollars minus the launch.

Following the successful example of Cassini, a probe that explored Titan, a moon of Saturn, a spacecraft would orbit Jupiter and conduct numerous close flybys of Europa.

"That way we can get effectively global coverage of Europa by doing many many flybys," Pappalardo argued.

"And that can do outstanding science—not quite as good as an orbiter, but not that bad—for half the cost, which is two billions dollars over the life of the mission excluding the launch."

If the plan is approved, Clipper could be launched by 2021 and take three to six years to reach Europa. By comparison, it takes six months to reach Mars.

But NASA already announced at the end of 2012 that there will be no funds for the Clipper mission in the current atmosphere of budgetary cuts, he said.

However, the space agency announced in December that it was sending to Mars in 2020 a new robot similar to Curiosity, a project that cost an estimated \$2.5 billion.

Curiosity, which arrived on the Red Planet in August 2012, is trying to find out whether life was possible on Mars in the past.

Under the current plans of robotic exploration, after the arrival of the probe Juno to Jupiter's orbit in 2016 and its planned crash a year later, the United States will no longer have probes in the distant reaches of the solar system.

NASA could, however, participate in a mission to Jupiter by the European Space Agency (ESA) called "Jupiter Icy Moon Explorer," during which a spacecraft is expected to arrive to its destination around 2030.

Noting that Mars consumed most attention in the course of NASA's exploration of the solar system, Pappalardo said the agency should not ignore planets that have a high scientific priority.

In his view, life could have existed on Mars several billion years ago, but Europa could have life today.

"If Europa is the best place in the solar system after Earth to host life, Encelade (a Saturn Moon) is right up there as well," said Amanda Hendrix, a senior scientist at the Planetary Science Institute in Tucson, Arizona.

"It has at least a subsurface sea, if not an ocean, and there is geological activity.

"It has heat at the south pole and is ejecting water particles in a geyser and other components in the south pole plume.

Europa was closely observed for the first time by the twin Voyager probes in 1979 and then, in more detail, by Galileo in the 1990s.

http://www.eurekalert.org/pub_releases/2013-02/dnnl-smf021213.php

Synthetic molecule first electricity-making catalyst to use iron to split hydrogen gas

Fast and efficient biologically inspired catalyst could someday make fuel cells cheaper

RICHLAND, Wash. -- To make fuel cells more economical, engineers want a fast and efficient iron-based molecule that splits hydrogen gas to make electricity. Online Feb. 17 at Nature Chemistry, researchers report such a catalyst. It is the first iron-based catalyst that converts hydrogen directly to electricity. The result moves chemists and engineers one step closer to widely affordable fuel cells.

"A drawback with today's fuel cells is that the platinum they use is more than a thousand times more expensive than iron," said chemist R. Morris Bullock, who leads the research at the Department of Energy's Pacific Northwest National Laboratory.

His team at the Center for Molecular Electrocatalysis has been developing catalysts that use cheaper metals such as nickel and iron. The one they report here can split hydrogen as fast as two molecules per second with an efficiency approaching those of commercial catalysts. The center is one of 46 Energy Frontier Research Centers established by the DOE Office of Science across the nation in 2009 to accelerate basic research in energy.

Fuel cells generate electricity out of a chemical fuel, usually hydrogen. The bond within a hydrogen molecule stores electricity, where two electrons connect two hydrogen atoms like a barbell.

Fuel cells use a platinum catalyst -- essentially a chunk of metal -- to crack a hydrogen molecule open like an egg: The electron whites run out and form a current that is electricity. Because platinum's chemical nature gives it the ability to do this, chemists can't simply replace the expensive metal with the cheaper iron or nickel.

However, a molecule that exists in nature called a hydrogenase (high-dra-jin-ace) uses iron to split hydrogen. Bullock and his PNNL colleagues, chemists Tianbiao "Leo" Liu and Dan DuBois, have taken inspiration for their iron-wielding catalyst from a hydrogenase. First Liu created several potential molecules for the team to test. Then, with the best-working molecule up to that point, they determined and tweaked the shape and the internal electronic forces to make additional improvements.

One of the tricks they needed the catalyst to do was to split hydrogen atoms into all of their parts. If a hydrogen atom is an egg, the positively charged proton that serves as the nucleus of the atom would be the yolk. And the electron, which orbits around the proton in a cloud, would be the white. The catalyst moves both the proton-yolks and electron-whites around in a controlled series of steps, sending the protons in one direction and the electrons to an electrode, where the electricity can be used to power things.

To do this, they need to split hydrogen molecules unevenly in an early step of the process. One hydrogen molecule is made up of two protons and two electrons, but the team needed the catalyst to tug away one proton first and send it away, where it is caught by a kind of molecule called a proton acceptor. In a real fuel cell, the acceptor would be oxygen. Once the first proton with its electron-wooing force is gone, the electrode easily plucks off the first electron. Then another proton and electron are similarly removed, with both of the electrons being shuttled off to the electrode.

The team determined the shape and size of the catalyst and also tested different proton acceptors. With the iron in the middle, arms hanging like pendants around the edges draw out the protons. The best acceptors stole these drawn-off protons away quickly.

With their design down, the team measured how fast the catalyst split molecular hydrogen. It peaked at about two molecules per second, thousands of times faster than the closest, non-electricity making iron-based competitor. In addition, they determined its overpotential, which is a measure of how efficient the catalyst is. Coming in at 160 to 220 millivolts, the catalyst revealed itself to be similar in efficiency to most commercially available catalysts. Now the team is figuring out the slow steps so they can make them faster, as well as determining the best conditions under which this catalyst performs.

This work was supported by the Department of Energy, Office of Science.

Reference: Tianbiao Liu, Daniel L. DuBois and R. Morris Bullock. An iron complex with pendent amines as a molecular electrocatalyst for oxidation of hydrogen, Nature Chemistry, Month Day, 2013, doi:10.1038/NCHEM.1571.

<http://www.sciencedaily.com/releases/2013/02/130217083905.htm?>

Copper Can Protect Against Alzheimer's Disease

Unequivocal evidence that copper only protects against beta amyloid forming beta sheets and is highly unlikely to be directly involved in formation of senile plaques

Researchers in The Birchall Centre at Keele University, Staffordshire, UK, have provided unequivocal evidence that under conditions which are approximately similar to those found in the brain, copper can only protect against beta amyloid forming beta sheets and as such it is highly unlikely that copper is directly involved in the formation of senile plaques in Alzheimer's disease.

The research, published by Nature's online journal Scientific Reports, may also imply that lower levels of copper in the brain may promote the mechanisms whereby beta amyloid is deposited as senile plaques in Alzheimer's disease.

This research addressed the on-going question as to whether copper in the brain contributes to the formation of the senile plaques in Alzheimer's disease. While previous research at Keele's Birchall Centre pointed towards copper being potentially protective in preventing the protein beta amyloid from aggregating as beta sheets and forming senile plaques it had remained a controversial issue for some.

Matthew Mold, Larissa Ouro-Gnao, Beata M Wieckowski, Christopher Exley. Copper prevents amyloid- β 1-42 from forming amyloid fibrils under near-physiological conditions in vitro. Scientific Reports, 2013; 3 DOI: 10.1038/srep01256

<http://nbcnews.to/XIIBWD>

Meteor warning system in the works — but not ready yet

NASA-backed effort to build observatories in Hawaii that can scan the entire visible sky twice a night

By Suzanne Choney

There aren't yet any advance warning systems that could give Earthlings a heads-up before an untracked space rock hits. But a telescope project in Hawaii aims to change that, and potentially provide a chance for those in threatened areas to evacuate. A meteor alert might have made a difference to Russia's Chelyabinsk region on Friday.

"There are excellent ongoing surveys for asteroids that are capable of seeing such a rock with one to two days' warning, but they do not cover the whole sky each night, so there's a good chance that any given rock can slip by them for days to weeks. This one obviously did," astronomer John Tonry of the Institute for Astronomy at the University of Hawaii told NBC News Friday.

Tonry is one of the key players in a NASA-backed effort to build ATLAS (Asteroid Terrestrial-impact Last Alert System), two observatories in Hawaii that can simultaneously scan the entire visible sky twice a night.

"If ATLAS were up and running we might very well have seen" the meteor that hit Russia, he said, and "could have provided one to two days' warning."

However, he adds, the success of detection "depends on a couple of assumptions." One is that it's not cloudy. Another is that the asteroid doesn't go over the South Pole, "where ATLAS cannot see."

Telescopes, Tony said, "can only see the sky above the horizon, obviously. A telescope that's sited in the northern hemisphere (which ATLAS will be) cannot see all the way to the South Pole of the sky." And, "if the asteroid were coming from that direction, there's a good chance that it would never rise above the horizon for a northern telescope before it hits."

While it would "easy to build multiple copies of ATLAS and put some in the south, and spread them out so they see different weather patterns ... that's for the future," he said.

Dozens were hospitalized and nearly 1,000 residents suffered minor injuries from fallen debris and the impact of the meteor's powerful landing. NBC's Tom Costello reports.

The ATLAS telescopes are "just now" being built, Tonry said; ATLAS should "start running around the end of 2014 and be fully operational by the end of 2015." NASA has provided \$5 million in funding for ATLAS.

At one time, NASA considered launching an asteroid-hunting probe, but that didn't go forward because of the cost, estimated at \$500 million almost a decade ago.

Other private efforts are in the works, too.

Last year, leaders of the nonprofit B612 Foundation, including Apollo astronaut Rusty Schweickart, started a campaign to fund and launch a space telescope that will hunt for potential killer asteroids over the course of five and a half years.

Another venture, from a group called Planetary Resources, ultimately wants to do asteroid mining, but says its first step is to "launch an orbital fleet of 'personal space telescopes' capable of looking out into the heavens or back down on Earth," wrote Alan Boyle, NBC News.com's Science editor last year.

[http://www.sciencedaily.com/releases/2013/02/130214193826.htm?](http://www.sciencedaily.com/releases/2013/02/130214193826.htm)

Customized Device Tailored to Patient's Individual Anatomy Now Used to Repair Abdominal Aortic Aneurysm Without Surgery

New graft customized to patient's individual anatomy allows them to have a quick recovery

An abdominal aortic aneurysm -- a bulge in the large artery that carries blood away from the heart -- can be immediately life-threatening if it grows large enough to rupture. The chance of survival when it ruptures is less than 10 percent.

Many people who find out they have that risk are able to have a minimally invasive repair. But up to 30 percent instead face a major open surgery with a long recovery because of the location of the aneurysm. Now a new

graft customized to their individual anatomy allows them, too, to have a quick recovery. The Johns Hopkins Hospital is one of the first hospitals in the United States now offering the procedure.

Ronald Rolett, a retired physician from North Carolina, learned that he had an abdominal aortic aneurysm four years ago from a routine ultrasound screening. He then had follow-up ultrasound tests every six months and the bulge continued to grow. In September 2012, it had reached a critical size: 5.9 centimeters, and he says, "That was the alarm bell. I decided that something had to be done."

On January 11, 2013, Rolett became the first patient at The Johns Hopkins Hospital -- and at any hospital in the mid-Atlantic region -- to have an aneurysm repaired in a minimally invasive way using a graft that was made to fit his specific anatomy.

Because of the location of his aneurysm, without that customized graft, he would have needed a much more extensive, open surgery with a long recovery. He also faced a greater risk of kidney failure with an open operation since his kidney function was abnormal.



This CT scan shows the patient's ballooning aorta . When it gets large enough, the vessel is in danger of a life-threatening rupture. (Credit: The Johns Hopkins Hospital)

There are two methods to repair an abdominal aortic aneurysm to prevent it from rupturing:

The traditional "open" surgery approach that requires several months to recover.

An endovascular repair -- a minimally invasive procedure that has become more common in recent years. Doctors attach a synthetic graft to a catheter and then feed it through an artery in the groin to the damaged section of aorta to prevent the vessel from rupturing. The grafts commonly used today come in different sizes and are pulled off the shelf.

Previously, many of those people who were fortunate enough to have their aneurysm identified prior to rupture could not have the endovascular repair because their aneurysm was located too close to the renal arteries. For them, the only option has been open surgery, which carries higher risk of heart attack and kidney failure. "We need at least 5 millimeters to 10 millimeters of length between the renal arteries and the aneurysm in order to secure the stent-graft in place in most patients," says Johns Hopkins vascular surgeon James Black. Only a few dozen surgeons nationwide, including Black, have been trained to repair abdominal aortic aneurysms with a new type of graft that was FDA-approved in April 2012. Johns Hopkins is one of a select group of hospitals in the United States now offering this new approach to patients.

The new graft looks similar to the traditional endovascular graft made of a polyester fabric encased by a stainless steel scaffold.

However, it is different from the off-the-shelf graft because of fenestrations -- two tiny holes fabricated in the graft to accommodate the renal arteries, helping to keep the graft in place, as well as a scallop-shaped cut to supply blood to the superior mesenteric artery, which carries blood to the intestines.

"We do a substantial amount of planning before the endovascular operation to ensure that the graft will be engineered correctly to match the patient's individual anatomy," says Black. "The planning process includes making a 3-D image and model of the patient's aorta using computed tomography (CT)."

The fabrication of each graft takes about five weeks, but for patients it's worth the wait to have a less invasive repair. They can go home from the hospital three days later and get back to their normal activities in two weeks compared with a four- to eight-week recovery following open surgery.

Patients have a CT scan one to two months after the procedure and then are followed annually.

Patients who are eligible for the new customized graft repair include those whose aneurysms approach within 5 millimeters of the renal arteries and have large enough vessels to deliver the stent-graft to the appropriate location.

"At Hopkins, we perform close to 100 open abdominal aortic aneurysm repairs each year for patients who are not eligible for the minimally invasive option," says Black.

"With the new fenestrated stent-graft, we will be able to spare many of those patients a big operation and a long recovery."

Rolett is pleased that he was able to have his abdominal aortic aneurysm repaired in the minimally invasive way. "I spent three nights in the hospital, and after two weeks, I no longer had any discomfort and was able to get back to my normal activities."