http://www.eurekalert.org/pub_releases/2013-04/wifb-cma040513.php

Cry me a river of possibility: Scientists design new adaptive material inspired by tears

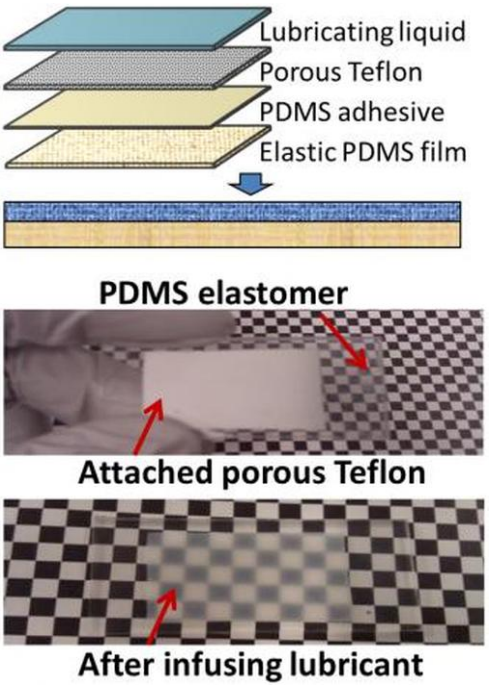
Tunable material system designed by Harvard team is easily adaptable for diverse applications in fuel transport, textiles, optical systems, and more

Imagine a tent that blocks light on a dry and sunny day, and becomes transparent and water-repellent on a dim, rainy day. Or highly precise, self-adjusting contact lenses that also clean themselves. Or pipelines that can optimize the rate of flow depending on the volume of fluid coming through them and the environmental conditions outside.

A team of researchers at the Wyss Institute at Harvard University and Harvard's School of Engineering and Applied Sciences (SEAS) just moved these enticing notions much closer to reality by designing a new kind of adaptive material with tunable transparency and wettability features, as reported yesterday in the online version of Nature Materials.

"The beauty of this system is that it's adaptive and multifunctional," said senior author Joanna Aizenberg, Ph.D., a Core Faculty member at the Wyss Institute and the Amy Smith Berylson Professor of Materials Science at SEAS.

The new material was inspired by dynamic, self-restoring systems in Nature, such as the liquid film that coats your eyes. Individual tears join up to form a dynamic liquid film with an obviously significant optical function that maintains clarity, while keeping the eye moist, protecting it against dust and bacteria, and helping to transport away any wastes – doing all of this and more in literally the blink of an eye.



This is the design of the liquid-infused dynamic material. The bottom two photographs show the dry and lubricated elastic substrates (transparent when at rest). **Wyss Institute at Harvard University and Harvard's School of Engineering and Applied Sciences (SEAS)**

The bioinspired material is a continuous liquid film that coats, and is infused in, an elastic porous substrate – which is what makes it so versatile. It is based on a core concept: any deformation of the substrate – such as stretching, poking, or swelling - changes the size of the pores, which causes the liquid surface to change its shape. With this design architecture in place, the team has thus far demonstrated the ability to dynamically control – with great precision – two key functions: transparency and wettability, said Xi Yao, Ph.D, Wyss Institute and SEAS postdoctoral fellow, and lead author of the study.

Sitting at rest, the material is smooth, clear and flat; droplets of water or oil on its surface flow freely off of the material. Stretching the material makes the fluid surface rougher, Yao explained. The rough surface makes it opaque for one thing, and enables one to do something never possible before: It offers the ability to make every droplet of oil or water that is placed on it reversibly start and stop in their tracks. This capability is far superior to the "switchable wettability" of other adaptive materials that exist today, Yao said, which simply switch between two states – from hydrophobic (water-hating) to hydrophilic (water-loving).

"In addition to transparency and wettability, we can fine-tune basically anything that would respond to a change in surface topography, such as adhesive or anti-fouling behavior," Yao said. They can also design the porous elastic solid such that it responds dynamically to temperature, light, magnetic or electric fields, chemical signals, pressure, or other environmental conditions, he said.

The material is a next generation of a materials platform that Aizenberg pioneered a few years ago called SLIPS. SLIPS stands for Slippery Liquid-Infused Porous Surfaces, and is a coating that repels just about anything with which it comes into contact – from oil to water and blood.

But whereas SLIPS is a liquid-infused rigid porous surface, "the new material is a liquid-infused elastic porous surface, which is what allows for the fine control over so many adaptive responses above and beyond its ability to repel a wide range of substances. A whole range of surface properties can now be tuned, or switched on and off on demand, through stimulus-induced deformation of the elastic material," Aizenberg said.

"This sophisticated new class of adaptive materials being designed by the Institute's Adaptive Materials Technologies platform led by Joanna Aizenberg have the potential to be game-changers in everything from oil and gas pipelines, to microfluidic and optical systems, building design and construction, textiles, and more," said Wyss Founding Director Donald Ingber, M.D., Ph.D.

The work was supported by the Air Force Office of Scientific Research (AFOSR), the Office of Naval Research (ONR) and the Wyss Institute for Biologically Inspired Engineering at Harvard University.

In addition to Yao and Aizenberg, the paper's coauthors included Wyss Core Faculty member L. Mahadevan, Ph.D., who is also the Lola England de Valpine Professor of Applied Mathematics at SEAS, and Professor of Organismic and Evolutionary Biology and Professor of Physics at Harvard University; Wyss Institute and SEAS Postdoctoral Fellow Yuhang Hu, Ph.D.; SEAS Staff Scientist Alison Grinthal, Ph.D.; and Tak-Sing Wong, Ph.D., formerly a Postdoctoral Fellow at the Wyss Institute and now an Assistant Professor at The Pennsylvania State University.

http://www.bbc.co.uk/news/science-environment-22063337

Curiosity rover traces loss of Martian air

Mars rover Curiosity is investigating a big crater on Mars' equator

Jonathan Amos By Jonathan Amos Science correspondent, BBC News, Vienna

The degree to which Mars' atmosphere has thinned over time is evident in exquisite new measurements from Nasa's Curiosity rover. It has analysed the different types, or isotopes, of argon atoms in the planet's air.

The study shows how a heavier version of the element has built up relative to a lighter one during Mars' history. It is confirmation that a substantial portion of the planet's original atmosphere has escaped into space.

Scientists think that perhaps as much as 95% of the gaseous shroud Mars started out with billions of years ago has gone. All of the key components in the present-day air show a leaning towards heavier isotopes. Curiosity itself has already demonstrated this to be the case with its measurements of oxygen, carbon dioxide, and also of water vapour.

But the new analysis of the ratio of argon-36 to argon-38 is particularly incisive because the element is so unreactive. There is no significant way for the ratio between the two to change other than through the preferential loss of the lightest isotope to space.

"We've been waiting for this result for a long time," said Prof Sushil Atreya from the University of Michigan, Ann Arbor, US. "Argon is chemically inert. It does not interact with the surface; it does not exchange with the interior [of the planet]. So it's the cleanest, clearest signal of escape," he told BBC News.

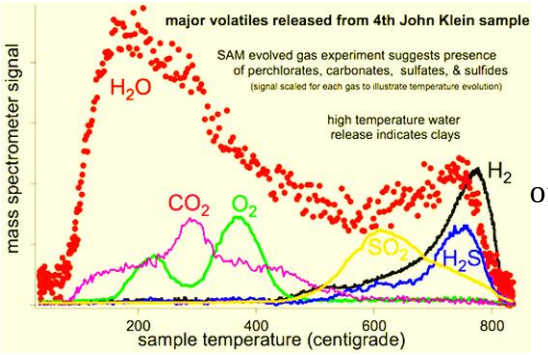
Prof Atreya was speaking here in Vienna at the European Geosciences Union General Assembly.

He is a co-investigator on the Sample Analysis at Mars (SAM) experiment. This is a large, sophisticated laboratory tucked away inside the belly of Curiosity. As well as studying rock specimens, it can also suck in the air to examine the concentration of gases that are present.

Argon forms a very small fraction of the modern Martian atmosphere at just 5.3 parts per million.

To make its latest measurement, SAM actually had to amplify the argon in its sample chambers by removing other, more dominant gases - the first time it has used such a procedure on the mission. The test showed there are 4.2 atoms of argon-36 for every one of argon-38.

By way of comparison, the ratio is 5.5 to one in the atmospheres of the Sun and Jupiter, which can be considered the baseline for when the Solar System formed. But Mars has no global magnetic field to protect atoms and molecules at the top of its atmosphere from being stripped away by the solar wind, and it is the lightest versions of those air atoms and molecules that are most readily eroded.



The Curiosity data is very precise and resolves the large uncertainties in previous measurements acquired by the Viking landers in the 1970s and from the study of Martian meteorites.

"We've been seeing the same kind of behaviour in the carbon dioxide isotopes and the water isotopes - they're all telling us the same story; that gases have been escaping from Mars over time, and the argon isotope just really nails it," Prof Atreya said.

The observation is important because a thicker atmosphere in the past could have allowed liquid water to be stable at the surface of the Red Planet, and this could have assisted any life that might have been present.

Today, the air pressure is so low that any exposed water would rapidly boil away. Some researchers doubt Mars ever had an atmosphere suitable to retain water on its surface for very long, but the Curiosity project scientist said he did not share this view.

As the Sample Analysis at Mars (SAM) suite of instruments on NASA's Curiosity Mars rover heats a sample, ***gases are released (or "evolved") from the sample and can be identified using SAM's quadrupole mass spectrometer. This graphic shows the principal gases evolved from the fourth portion of powder delivered to SAM from the sample material collected when Curiosity first drilled into the "John Klein" target rock in the "Yellowknife Bay" area of Mars' Gale Crater.***

The mass spectrometer signal is scaled separately for each gas so that the same graph can illustrate the patterns for various gases showing what temperatures caused the gas to be released. These evolved gases and the temperatures at which they evolved suggest the presence of hydrated minerals, carbonates, perchlorates, sulfates and sulfides, and clays in the rock-powder sample. Credit: NASA/JPL-Caltech

Prof John Grotzinger argued that the rocks now being observed by Curiosity looked like they were formed under stable conditions. "We see these mudstones and we see the textures that indicate stratification," he told BBC News. "It's kind of hard to imagine that [these textures] would be preserved if the mud was boiling - if the water in the mud was boiling."
Curiosity landed on Mars' equator in August last year. It is investigating a deep crater, looking for evidence that the Red Planet may once have had the conditions to allow simple microbial life to flourish. The US space agency will launch a new mission to Mars at the end of the year called Maven. This satellite will address specifically the issue of atmosphere loss. Its high altitude measurements will complement perfectly the studies conducted by Curiosity at the surface.

http://www.eurekalert.org/pub_releases/2013-04/vt-rfa040813.php

Researchers find avian virus may be harmful to cancer cells

Veterinary scientists find virus combats prostate cancer cells

A study at the Virginia-Maryland Regional College of Veterinary Medicine has identified a chicken-killing virus as a promising treatment for prostate cancer in humans.
Researchers have discovered that a genetically engineered Newcastle disease virus, which harms chickens but not humans, kills prostate cancer cells of all kinds, including hormone-resistant cancer cells. The work of Dr. Elankumaran Subbiah, an associate professor of virology in the Department of Biomedical Sciences and Pathobiology at Virginia Tech, along with Dr. Siba Samal, associate dean and chairman of the University of Maryland's Department of Veterinary Medicine, and Shobana Raghunath, a graduate student in Subbiah's laboratory, appears in the April 2013 issue of the Journal of Virology.
"This potential treatment is available for immediate pre-clinical and clinical trials, but these are typically not done at the university level," Subbiah said. "We are looking for commercial entities that are interested in licensing the technology for human clinical trials and treatment. Newcastle disease virus has yet to be tested as a treatment for prostate cancer in patients."
About one in six men will develop prostate cancer. Patients typically receive hormone treatments or chemotherapy, both of which have adverse side effects. Subbiah hopes that the development of new treatment methodologies will not only better fight prostate cancer, but also lessen the side effects commonly associated with hormone treatments and chemotherapy.
Newcastle disease virus affects domestic and wild bird species, especially chickens, and is one of the most economically important viruses to the poultry industry.
Although it can cause mild conjunctivitis and flu-like symptoms in humans who have been in close contact with infected birds, it does not pose a threat to human health.
Scientists first documented the cancer-fighting properties of Newcastle disease virus in the 1950s, but it is only with recent advances in reverse genetics technology that they have turned to the genetically engineered virus as a possible treatment.
"We modified the virus so that it replicates only in the presence of an active prostate-specific antigen and, therefore, is highly specific to prostate cancer. We also tested its efficacy in a tumor model in vitro," Subbiah said. "The recombinant virus efficiently and specifically killed prostate cancer cells, while sparing normal human cells in the laboratory, but it would take time for this to move from the discovery phase to a treatment for prostate cancer patients."
Earlier human clinical trials for other types of cancer with naturally occurring strains of Newcastle disease virus required several injections of the virus in large quantities for success. Subbiah believes that the recombinant virus would be able to eradicate prostate cancer in much lower doses. It would also seek out metastatic prostate cancer cells and remove them. Because it is cancer cell-type specific, "the recombinant virus will be extremely safe and can be injected intravenously or directly into the tumor," Subbiah added.
Subbiah received a $113,000 concept award from the U.S. Department of Defense to develop his prostate cancer treatment under a Congressionally directed medical research program. He is seeking additional foundation and corporate funds to take his research to the next level.
The researchers have also received a National Institutes of Health exploratory grant to develop the cell type-specific Newcastle disease virus for several other types of cancer cells, including breast, pancreas, brain, prostate, and multiple myeloma. "Although the virus can potentially treat many different types of cancer, we are focusing on these five," Subbiah said.

http://www.eurekalert.org/pub_releases/2013-04/uosf-nsf040813.php

New study finds plant proteins control chronic disease in Toxoplasma infections

University of South Florida-led research sheds light on malaria-related parasite's transition from acute to chronic stage

Tampa, FL - A new discovery about the malaria-related parasite Toxoplasma gondii -- which can threaten babies, AIDS patients, the elderly and others with weakened immune function -- may help solve the mystery of how this single-celled parasite establishes life-long infections in people.

The study, led by a University of South Florida research team, places the blame squarely on a family of proteins, known as AP2 factors, which evolved from the regulators of flowering in plants.

In findings published today in the Proceedings of the National Academy of Sciences, the researchers demonstrate AP2 factors are instrumental in flipping a developmental "switch" that transitions the parasite from a rapidly dividing form destructive to healthy tissue to a chronic stage invisible to the immune system. They identified one factor, AP2IX-9, that appears to restrict development of Toxoplasma cysts that settle quietly in various tissues, most commonly the host's brain.

A better understanding of how the switch mechanism works may eventually lead to ways to block chronic Toxoplasma infections, said study principal investigator Michael White, PhD, professor of global health and molecular medicine at USF Health and a member of the Center of Drug Discovery and Innovation, a Florida Center of Excellence at USF.

White and his colleagues are among the world's leading experts in T. gondii, combining approaches from biochemistry, genetics and structural biology to look for new ways to combat the parasitic disease toxoplasmosis.

No drugs or vaccines currently exist to treat or prevent the chronic stage of the disease. The T. gondii parasites may remain invisible to the immune system for years and then reactivate when immunity wanes, boosting the risk for recurrent disease.

"The evolutionary story of Toxoplasma is fascinating," White said. "We were blown away to find that the AP2 factors controlling how a flower develops and how plants respond to poor soil and water conditions have been adapted to work within an intracellular human parasite."

Ages ago the ancestors of malaria parasites genetically merged with an ancestor of plants, and the primitive plant donated its AP2 factors to the future malaria family.

"Our study showed that, like the AP2 factors help a plant survive a stressful environment, the AP2 factors of T. gondii help the parasite decide when the time is right to grow or when to form a tissue cyst that may lie dormant in people for many years," White said.

Toxoplasmosis, the infection caused T. gondii, is commonly associated with the medical advice that pregnant women should avoid contact with litter boxes. That's because infected cats play a big role in spreading the disease. The tiny organism thrives in the guts of cats, producing countless egg-like cells that are passed along in the feces and can live in warm moist soil or water for months.

People can acquire toxoplasmosis several ways, usually by exposure to the feces of cats or other infected animals, by eating undercooked meat of infected animals, or drinking water contaminated with T. gondii.

Up to 30 percent of the world's population is estimated to be infected with the T. gondii parasite. In some parts of the world, including places where sanitation is poor and eating raw or undercooked meat is customary, nearly 100 percent of people carry the parasite, White said.

Few experience flu-like symptoms because the immune system usually prevents the parasite from causing illness, but for those who are immune deficient the consequences can be severe.

The disease may be deadly in AIDS patients, organ transplant recipients, patients receiving certain types of chemotherapy, and infants born to mothers infected with the parasite during or shortly before pregnancy. Recently, toxoplasmosis has been linked to mental illness, such as schizophrenia and other diseases of dementia, and changes in behavior.

Because it is common, complex and not easily killed with standard disinfection measures, the toxoplasma parasite is a potential weapon for bioterrorists, White added.

The USF-led study was supported by grants from the National Institutes of Health. White's team worked with researchers at Princeton University, Albert Einstein College of Medicine, and Indiana University School of Medicine. Joshua Radke, a PhD student in the USF Health Department of Molecular Medicine, was a first author of the study.

Article citation: "ApiAP2 transciption factor restricts development of the Toxoplasma tissue cyst;" Joshua B. Radke, Oliver Lucas, Erandi K. DeSilva, YanFen Ma, William J. Sullivan, Jr., Louis M. Weiss, Manuel Llinas, and Michael W. White; Proceedings of the National Academy of Sciences; http://www.pnas.org/cgi/doi/10.1073/pnas.1300059110

http://www.eurekalert.org/pub_releases/2013-04/acs-net030713.php

New evidence that natural substances in green coffee beans help control blood sugar levels

Scientists today described evidence that natural substances extracted from unroasted coffee beans can help control the elevated blood sugar levels and body weight that underpin type 2 diabetes.

NEW ORLEANS - Their presentation on chlorogenic acids -- widely available as a dietary supplement -- was part of the 245th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society, being held here this week.

Joe Vinson, Ph.D., who led the research, pointed out that type 2 diabetes, the most common form of diabetes, is an increasing global health problem. In the United States alone, almost 26 million have the disease, in which the pancreas does not produce enough of the insulin that enables the body to use sugar, or cells resist the effects of that insulin. Blood sugar levels rise, increasing the risk of heart attacks, stroke and other health problems. Current treatments focus on oral medications that stimulate insulin secretions and/or reduce insulin resistance, dietary changes that control blood sugar levels and weight loss that reduces insulin resistance.

"A simple natural pill or capsule that would both help control blood sugar and foster weight loss at the same time would be a major advance in the treatment of type 2 diabetes," Vinson said. "Our own research and studies published by other scientists suggest that such a treatment may, indeed, exist. There is significant epidemiological and other evidence that coffee consumption reduces the risk of type 2 diabetes.

"One large study indicated a 50 percent risk reduction for people who drank seven cups of coffee a day compared to those who drank only two cups a day. I am trying to make the coffee and diabetes story as clear as possible for the public. The evidence points to chlorogenic acids as the active ingredients in coffee that both prevent diabetes and improve glucose control in normal, pre-diabetic and diabetic people."

Chlorogenic acids are a family of substances that occur naturally in apples, cherries, plums, dried plums and other fruits and vegetables. Vinson, who is with the University of Scranton in Pennsylvania, pointed out that coffee — due to its popularity as a beverage — is a major dietary source of these substances. Large amounts of chlorogenic acids exist in green, or unroasted, coffee beans. However, the high temperatures used to roast coffee beans to make them suitable for use in coffee breaks down much of the chlorogenic acids. Thus, the focus has been on using concentrated extracts of green coffee beans, which contain higher amounts of chlorogenic acids.

In a previous study, Vinson found that overweight or obese people who took such an extract lost about 10 percent of their body weight in 22 weeks. The new study sought to document the effects of various doses of a commercial green coffee extract on the blood sugar levels of 56 men and women with normal blood sugar levels. They got a glucose tolerance test to see how their bodies responded to the sugar. Then over a period of time, they took 100, 200, 300 or 400 milligrams (mg) of the extract in a capsule with water. Follow-up glucose tolerance tests showed how the green coffee extract affected their responses.

"There was a significant dose-response effect of the green coffee extract and no apparent gastrointestinal side effects," Vinson said. "All doses of green coffee extract produced a significant reduction in blood sugar relative to the original blank glucose challenge. The maximum blood glucose occurred at 30 minutes and was 24 percent lower than the original with the 400 mg of green coffee extract and the blood glucose at 120 minutes was 31 percent lower."

Vinson acknowledged funding from Applied Food Sciences, Inc., which markets a green coffee antioxidant product.

Abstract

There are now numerous epidemiological studies indicating that coffee consumption, especially decaffeinated coffee, will reduce the risk of all-cause mortality, heart failure and type 2 diabetes and Parkinson's disease. The studies' results are usually J-curves indicating an optimal consumption of 2-4 cups/day. The question then arises, what is/are the bioactive substance(s) in coffee -- Our study of antioxidants in foods and beverages indicated the coffee is the #1 source of polyphenol antioxidants in the US diet and this has been borne out in several European countries. Recent studies indicate that coffee consumption acutely increases human plasma antioxidant capacity. Other investigators have found multiple evidence of chlorogenic acid metabolites and colonic bacterial degradation products in plasma and urine after drinking coffee and green coffee extract. A recent study in India with obese subjects showed a significant weight loss and body fat reduction after consuming capsules containing a green coffee extract which was high in chlorogenic acids. Roasting is known to greatly reduce the levels of these compounds in the beverage coffee. One mechanism for the weight loss is purported to be the inhibition of glucose-6-phosphatase which forces lipids to be used as energy to compensate for the decrease in glucose release from glycogenolysis in the liver. As evidence for coffee's diabetes and heart disease protection we will present a new human study demonstrating a dose-response green coffee extract inhibition of glucose absorption during a glucose tolerance test in normal subjects. Studies with rats and humans have shown that the caffeine in coffee contributes to hyperglycemia after glucose consumption. The green coffee extract which is very low in caffeine and should be studied with pre-diabetes and type 2 diabetic subjects as a means to improve their blood glucose control.

http://www.eurekalert.org/pub_releases/2013-04/plos-ngf040513.php

New guidelines for writing abstracts will help authors summarise their research

New guidelines for writing abstracts will help authors summarise their research

A new extension to the PRISMA guideline on reporting systemic reviews and meta-analyses (types of studies that analyse information from many studies) will help authors to give a more robust summary (abstract) of their study and is detailed by an international group of researchers in this week's PLOS Medicine.

These guidelines for abstracts of systemic reviews and meta-analyses are important, as the abstract is the most frequently read part of most papers and these types of studies are particularly important for influencing evidence-based research.

New guidelines are necessary as despite published guidance on writing the abstract in previous guidelines (the PRISMA Statement); evaluations show that reporting of systematic reviews in journal and conference abstracts is poor.

An international group of researchers (the PRISMA for Abstracts Group) developed the new consensus-based reporting guidelines to give authors a checklist and framework for summarising their systematic review into the essentials for an abstract that will meet the needs of many readers.

The authors say: "Abstracts should not replace full articles in informing decision making, but for time-pressed readers and those with limited access to full text reports, the abstract must stand alone in presenting a clear and truthful account of the research."

They continue: "The PRISMA for Abstracts checklist will guide authors in presenting an abstract that facilitates a quick assessment of review validity, an explicit summary of results, facilitates pre-publication or conference selection peer review, and enables efficient perusal of electronic search results."

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Competing Interests: TL is employed by The Cochrane Collaboration. TL is an editor (unpaid) for the Cochrane Airways Group. The authors have declared that no other competing interests exist.

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http://www.eurekalert.org/pub_releases/2013-04/ehs-gsa040713.php

Google searches about mental illness follow seasonal patterns

New study in the American Journal of Preventive Medicine reports

San Diego, CA - A new study published in the May issue of the American Journal of Preventive Medicine finds that Google searches for information across all major mental illnesses and problems followed seasonal patterns, suggesting mental illness may be more strongly linked with seasonal patterns than previously thought.

Monitoring population mental illness trends has been an historic challenge for scientists and clinicians alike. Typically, telephone surveys are used to try to glimpse inside the minds of respondents, but this approach is limited because respondents may be reluctant to honestly discuss their mental health. This approach also has high material costs. As a result, investigators have not had the data they need.

"The Internet is a game changer," said lead investigator John W. Ayers, PhD, MA, of the Graduate School of Public Health at San Diego State University. "By passively monitoring how individuals search online we can figuratively look inside the heads of searchers to understand population mental health patterns."

Using Google's public database of queries, the study team identified and monitored mental health queries in the United States and Australia for 2006 through 2010. All queries relating to mental health were captured and then grouped by type of mental illness, including ADHD (attention deficit-hyperactivity disorder), anxiety, bipolar, depression, eating disorders (including anorexia or bulimia), OCD (obsessive compulsive disorder), schizophrenia, and suicide. Using advanced mathematical methods to identify trends, the authors found all mental health queries in both countries were consistently higher in winter than summer.

The research showed eating disorder searches were down 37 percent in summers versus winters in the U.S., and 42 percent in summers in Australia. Schizophrenia searches decreased 37 percent during U.S. summers and by 36 percent in Australia.

Bipolar searches were down 16 percent during U.S. summers and 17 percent during Australian summers; ADHD searches decreased by 28 percent in the U.S. and 31 percent in Australia during summertime. OCD searches were down 18 percent and 15 percent, and bipolar searches decreased by 18 percent and 16 percent, in the U.S. and Australia respectively.

Searches for suicide declined 24 and 29 percent during U.S. and Australian summers and anxiety searches had the smallest seasonal change – down 7 percent during U.S. summers and 15 percent during Australian summers.

While some conditions, such as seasonal affective disorder, are known to be associated with seasonal weather patterns, the connections between seasons and a number of major disorders were surprising. "We didn't expect to find similar winter peaks and summer troughs for queries involving every specific mental illness or problem we studied, however, the results consistently showed seasonal effects across all conditions – even after adjusting for media trends," said James Niels Rosenquist, MD, PhD, a psychiatrist at Massachusetts General Hospital.

"It is very exciting to ponder the potential for a universal mental health emollient, like Vitamin D (a metabolite of sun exposure). But it will be years before our findings are linked to serious mental illness and then linked to mechanisms that may be included in treatment and prevention programs," said Ayers. "Is it biologic, environmental, or social mechanisms explaining universal patterns in mental health information seeking? We don't know."

"Our findings can help researchers across the field of mental health generate additional new hypotheses while exploring other trends inexpensively in real-time," said Benjamin Althouse, a doctoral candidate at Johns Hopkins Bloomberg School of Public Health and researcher on the study. "For instance, moving forward, we can explore daily patterns in mental health information seeking … maybe even finding a 'Monday effect.' The potential is limitless."

Dr. Daniel Ford, vice dean for clinical investigation in the Johns Hopkins University School of Medicine, and Jon-Patrick Allem, doctoral student at University of Southern California Keck School of Medicine, also contributed to the study.

http://www.sciencedaily.com/releases/2013/04/130409211857.htm

Face-To-Face Negotiations Favor the Powerful

If you are negotiating with someone who has more power than you it is a good idea to avoid face-to-face meetings.

That is the conclusion of research presented today, Wednesday 10 April 2013, by Michael Taylor from Imperial College London at the Annual Conference of the British Psychological Society in Harrogate.

Michael Taylor and his fellow researchers conducted two studies in which the same negotiation was conducted face-to-face and in a sophisticated 3D virtual simulation. In the first study 74 people took part in a two-sided negotiation in which one party had more power than the other. In the second, 63 people conducted a three-sided negotiation where they were playing the part of people at different levels in a hierarchy.

The results of the first study showed that the side with less power did better in the virtual negotiations than the face-to-face ones. In the second study, the least powerful side outperformed the other two in the virtual negotiations but not in the face-to-face ones.

Michael Taylor says: "It looks as though it is a good idea for less powerful parties to negotiate from remote locations rather than face-to-face. When people negotiate from further apart, it affects their whole way of thinking. This can mean the contextual details of the negotiations, such as power hierarchies, have less impact on the outcome. This has implications for team negotiation and shared decision-making in the workplace."

http://www.sciencedaily.com/releases/2013/04/130410082154.htm

Art Can Change Your World, Experts Say

Newcastle University researchers have shown it's never too late to change your mind.

As we get older, we're more likely to be thought of as 'set in our ways', but researchers have discovered that art can in fact fundamentally change our sense of who we are.

For the initial project, they took groups of older people to major exhibitions in the North East of England to discover how they responded to contemporary visual art and whether these effects lasted beyond the initial encounter.

"The widely held belief that older people are stuck in their ways is not borne out at all by our findings," explained Andrew Newman, principal investigator. "Three visits to a gallery is nothing and yet we saw a rapid change in opinions. It wasn't unusual for participants to go from initially being uncertain to talking knowledgeably about the art by the final visit."

For many taking part it was their first experience of contemporary visual art and they were initially unable to understand the artworks in terms of what the artist intended to communicate.

However, they quickly begun to use their own life histories -- such as childhood memories and holidays -- to make sense of them, enabling a sense of continuity between then and now.

For example, one 79-year-old had given up knitting after she had a stroke and moved into sheltered accommodation. She picked up some needles again at the Knitted Lives exhibition in the Shipley Art Gallery in Gateshead and was able to knit successfully, enabling her to re-establish links with her previous life. It also had a positive effect on the present as she went on to help set up a knitting group in the sheltered accommodation.

Mr Newman and colleague Anna Goulding, of the International Centre for Cultural and Heritage Studies, are heading to the Museum of Modern Art in New York this month (April) to share their research on how older people's lives can be improved through engagement with contemporary visual art.
As part of this research, they have produced a short film that shows a more creative way of working in art galleries. "Unlike many projects in this field, this is not about reminiscence, it's about using the imagination to create something new," said Ms Goulding. "Art can take us out of our normal lives and enable us to change our thinking, which can have a profound influence on how we relate to the world around us."
The New Dynamics of Ageing programme funded the research and a follow-on project about developing informed arts policy and intervention guidance that could have significant implications for museums and galleries.
"These institutions could have a greater role to play in an ageing society," said principal investigator Mr Newman. "Visits can be personally and collectively beneficial for older visitors and help them have a positive sense of self, which is crucial for successful ageing and helping to maintain self-esteem."
They are now building upon this work with a £1.5m AHRC Communities, Cultures, Health and Wellbeing research project, led by Bangor University. They will look at how the visual arts can enrich the lives of older people with dementia by reconnecting them with their communities.
"Many people believe it takes a major life event to change the trajectory we're on, especially as we approach older age, but we found that art can actually have a similar effect in a remarkably short space of time," added Mr Newman. "We were surprised to find that our sense of art is quite fundamental to our make-up."

http://www.eurekalert.org/pub_releases/2013-04/cndi-fqf040913.php

First genetic factor in prostate cancer prognosis identified

CNIO researchers, together with scientists in the United Kingdom, have revealed that hereditary mutations in the BRCA2 gene predispose patients to a worse evolution of the illness and a greater risk of developing metastasis

Patients with prostate cancer and hereditary mutations in the BRCA2 gene have a worse prognosis and lower survival rates than do the rest of the patients with the disease. This is the main conclusion to come out of a study published this week in the Journal of Clinical Oncology, in which David Olmos, Head of the Prostate Cancer and Genitourinary Tumours Clinical Research Unit at the Spanish National Cancer Research Centre (CNIO), has taken part in, along with Elena Castro, a member of the Unit, and British researchers at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust.
According to Olmos: "Whilst the majority of patients with prostate cancer have an excellent prognosis, one of the biggest challenges we face in daily clinical practice is the difficulty of identifying those patients in which the illness can be fatal".
In order to search for genetic markers that offer clues as to the evolution of the illness, the study's authors examined 61 patients with prostate cancer who were also carriers of mutations in the BRCA2 gene (a gene that suppresses tumours and that protects DNA), 18 patients with mutations in BRCA1 (a gene whose function is similar to BRCA2) and 1,940 patients in which the presence of mutations in both genes had been excluded.

The Largest Study To Date

The magnitude of the study makes it one of the largest studies carried out so far in prostate cancer patients carrying BRCA1 or BRCA2 mutations; these genes are traditionally known for being responsible for familial breast and ovarian cancer syndrome.
Patient analyses showed that BRCA1 and BRCA2 gene mutation carriers were at greater risk for having more advanced prostate cancer at the time of diagnosis, as well as of developing metastasis.
Furthermore, within the subgroup of patients in which the disease had not spread at the time of diagnosis, 23% of carriers of mutations in these genes developed metastasis over the following five years, compared to 7% of those patients who were not carriers. Five years after diagnosis, 19% of BRCA2 mutation carriers with early-stage disease had died, compared with 4% of the non-carriers; there were no significant differences between BRCA1 mutation carriers and non-carriers.
Castro, the first author of the article, says: "These data turn the BRCA2 gene into the first genetic factor for prostate cancer prognosis", to which she adds: "The results of this study suggest the need for a paradigm shift in the clinical management of patients with prostate cancer who are carriers of mutations in the BRCA genes; current treatment standards for these patients appear to be insufficient and there are no specific action guidelines".
"Now that we have managed to identify patients with potentially lethal disease, our next challenge is to explore the most adequate treatments with the least side effects that have a real impact on survival", says Olmos.

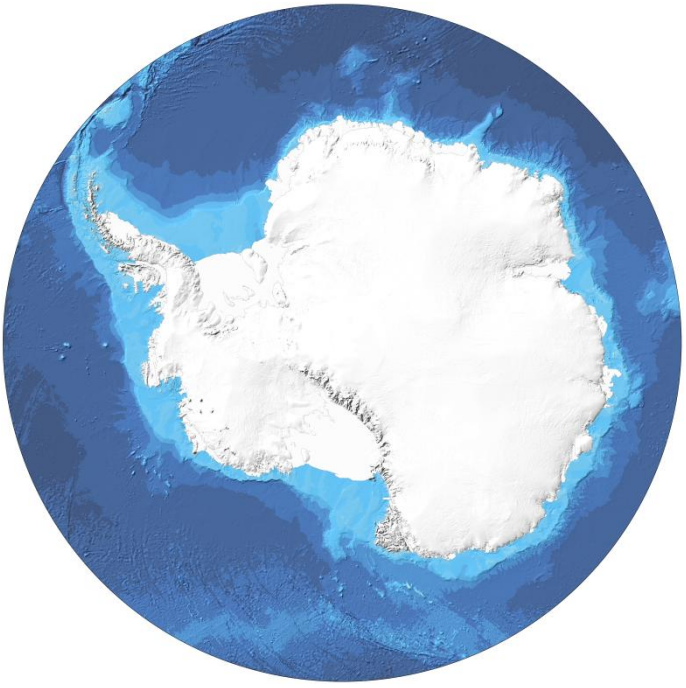
Prostate cancer is the second most common type of cancer in men worldwide, although in developed countries it is the most frequently found tumour. This is the case in Spain, where more than 25,000 new cases are diagnosed each year, making it the third cause of cancer-related deaths in men.

Over the past few decades, an increase in cases has been observed due, above all, to longer life expectancies and the widespread use of the PSA (Prostate-Specific Antigen) screening test in the general population. Fortunately, a decrease in mortality for this disease has also been observed, due to the majority of diagnoses being carried out at an early stage and due to improved treatments. Even so, there are still cases in which the disease is fatal and efforts as well as resources are being dedicated to identifying those patients with the worst prognosis and to establishing the most appropriate therapeutic strategies.

http://www.eurekalert.org/pub_releases/2013-04/haog-ncs040913.php

New chart shows the entire topography of the Antarctic seafloor in detail for the first time

Reliable information on the depth and floor structure of the Southern Ocean has so far been available for only few coastal regions of the Antarctic.



Bremerhaven/Germany - An international team of scientists under the leadership of the Alfred Wegener Institute, Helmholtz Centre for Polar and Marine Research, has for the first time succeeded in creating a digital map of the entire Antarctic seafloor. The International Bathymetric Chart of the Southern Ocean (IBCSO) for the first time shows the detailed topography of the seafloor for the entire area south of 60°S. An article presented to the scientific world by IBCSO has now appeared online in the scientific journal Geophysical Research Letters. The IBCSO data grid and the corresponding Antarctic chart will soon be freely available in the internet and are intended to help scientists amongst others to better understand and predict sea currents, geological processes or the behaviour of marine life.

The new bathymetric chart of the Southern Ocean is an excellent example of what scientists can achieve if researchers from around the world work across borders. "For our IBCSO data grid, scientists from 15 countries and over 30 research institutions brought together their bathymetric data from nautical expeditions. We were ultimately able to work with a data set comprising some 4.2 billion individual values", explains IBCSO editor Jan Erik Arndt, bathymetric expert at the Alfred Wegener Institute in Bremerhaven.

Collecting bathymetric data, as with the German research vessel Polarstern with its multibeam echo sounding system, was nowhere near enough, however, to develop a useful, three-dimensional model of the seafloor: "The ocean south of the 60th parallel extends over an area of some 21 million square kilometres and is therefore around 60 times as large as the Federal Republic of Germany. Reliable bathymetric data have so far existed for only 17 per cent of this area. The largest data gaps, for example, are in the deep sea regions of the south Indian Ocean and the South Pacific and in areas which experience difficult sea ice conditions throughout the year in some places, such as in the Weddell Sea", says Jan Erik Arndt.

For this reason the mappers did not just take the trouble to digitize old Antarctic nautical charts and to convert satellite data. They also used a mathematical trick by interpolating the data set. "We treated every existing measurement point like a tent pole to a certain extent and arithmetically covered these poles with a tarpaulin. In this way we obtained approximate values about the height of the tarpaulin between the poles", explains the AWI specialist for data modeling. This work was worth it: the IBCSO data grid has a resolution of 500 times 500 metres. This means that one data point reflects the depth of a sea area of 500 times 500 metres – a feature that leads to impressive degree of detail.

Where older models only offer a glimpse of a mountain in the deep sea, IBCSO shows an elevation with sharp ridge crests and deep channels in the slopes. A formerly flat point at the bottom of the Riiser-Larsen Sea can now be identified as an offshoot, some 300 metres deep, of the underwater Ritscher Canyon which runs along a length of over 100 kilometres from the south west to the north. And not far away from today's shelf ice edge of the large Getz ice shelf the furrows are to be seen quite clearly which were ploughed into the seafloor by the ice tongue as it grew.

Using this degree of detail IBCSO is primarily intended to push ahead with research: "The depth data of the Southern Ocean are of great interest to polar researchers from many disciplines. The 3D data grids of the seafloor enable oceanographers to model currents and the movement of the deep Antarctic water which is of such great importance. Geologists are able to recognise the structures of geological processes more easily. Biologists may be able to better estimate the regions in which certain biological communities may emerge or whether, for example, seals dive to the bottom of the sea in a certain area in search of food", explains Jan Erik Arndt.
However, despite the elation about the new model and its chart, it should not be forgotten that more than 80 per cent of the area of the South Polar Sea is still unchartered. Jan Erik Arndt: "We hope that as our data grid becomes better known in the scientific world, other scientists will be more willing to provide us with their data of current and future depth measurements in the South Polar Sea. The chances are not bad. A few new research ice breakers are currently being built around the world and every one of them will presumably be equipped with a modern multibeam echo sounder in the same way as Polarstern."
Both the IBCSO data grid and a digital print template of the chart (dimensions: 100 centimetres times 120 centimetres) will be available for downloading to everyone soon on the project website at http://www.ibcso.org.

http://www.scientificamerican.com/article.cfm?id=dont-sleep-it-off

Don't Sleep It Off

Dozing immediately after trauma might make the memories worse

By Tori Rodriguez

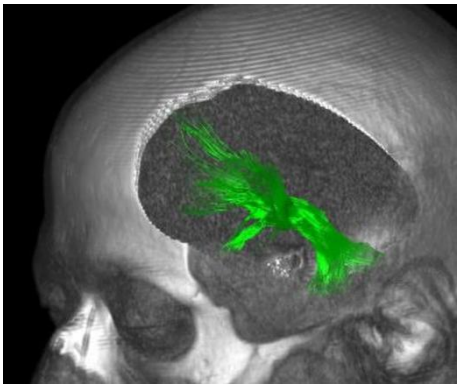
It may be tempting to seek solace in slumber after a traumatic event, but a study from the October 2012 issue of Neuropsychopharmacology found that sleeping too soon after trauma might lead to increased post-traumatic stress disorder symptoms. Two groups of rodents were exposed to a predator's scent, a traumatic event for a mouse. For six hours afterward, one group was prevented from sleeping, whereas a control group was not. The sleep-deprivation group displayed fewer physiological markers of stress than the control group and less PTSD-like behavior, such as freezing and a heightened startle response.
Researchers believe that sleep deprivation disrupts the consolidation of trauma memories - a hypothesis that jibes with the current understanding of the role of sleep in strengthening emotional memories. (Once that memory is ingrained, however, sleep could provide an opportunity for treatment; see the story at the right.)
Sleep deprivation can also reduce the impact of traumatic brain injury (TBI), according to a study published in the November 2012 issue of Neuroscience Letters. Rats with TBI sustained less damage when they were kept awake for 24 hours after the injury. Taken together, these findings suggest that after a violent, traumatic event - such as a car accident - staying awake for a while could afford both physical and mental protection.

http://www.eurekalert.org/pub_releases/2013-04/uob-ssi040913.php

Sensational success in patients with major depression

For the first time, physicians from the Bonn University Hospital have stimulated patients' medial forebrain bundles

Researchers from the Bonn University Hospital implanted pacemaker electrodes into the medial forebrain bundle in the brains of patients suffering from major depression with amazing results: In six out of seven patients, symptoms improved both considerably and rapidly. The method of Deep Brain Stimulation had already been tested on various structures within the brain, but with clearly lesser effect. The results of this new study have now been published in the renowned international journal "Biological Psychiatry."
After months of deep sadness, a first smile appears on a patient's face. For many years, she had suffered from major depression and tried to end her life several times. She had spent the past years mostly in a passive state on her couch; even watching TV was too much effort for her.



The medial forebrain bundle is highlighted in green. **Volker Arnd Coenen/Uni Freiburg**

Now this young woman has found her joie de vivre again, enjoys laughing and travelling. She and an additional six patients with treatment resistant depression participated in a study involving a novel method for addressing major depression at the Bonn University Hospital.

Considerable amelioration of depression within days

Prof. Dr. Volker Arnd Coenen, neurosurgeon at the Department of Neurosurgery (Klinik und Poliklinik für Neurochirurgie), implanted electrodes into the medial forebrain bundles in the brains of subjects suffering from major depression with the electrodes being connected to a brain pacemaker. The nerve cells were then stimulated by means of a weak electrical current, a method called Deep Brain Stimulation. In a matter of days,

in six out of seven patients, symptoms such as anxiety, despondence, listlessness and joylessness had improved considerably. "Such sensational success both in terms of the strength of the effects, as well as the speed of the response has so far not been achieved with any other method," says Prof. Dr. Thomas E. Schläpfer from the Bonn University Hospital Department of Psychiatry und Psychotherapy (Bonner Uniklinik für Psychiatrie und Psychotherapie).

Central part of the reward circuit

The medial forebrain bundle is a bundle of nerve fibers running from the deep-seated limbic system to the prefrontal cortex. In a certain place, the bundle is particularly narrow because the individual nerve fibers lie close together. "This is exactly the location in which we can have maximum effect using a minimum of current," explains Prof. Coenen, who is now the new head of the Freiburg University Hospital's Department of Stereotactic and Functional Neurosurgery (Abteilung Stereotaktische und Funktionelle Neurochirurgie am Universitätsklinikum Freiburg). The medial forebrain bundle is a central part of a euphoria circuit belonging to the brain's reward system. What kind of effect stimulation exactly has on nerve cells is not yet known. But it obviously changes metabolic activity in the different brain centers.

Success clearly increased over that of earlier studies

The researchers have already shown in several studies that deep brain stimulation shows an amazing and–given the severity of the symptoms– unexpected degree of amelioration of symptoms in major depression. In those studies, however, the physicians had not implanted the electrodes into the medial forebrain bundle but instead into the nucleus accumbens, another part of the brain's reward system. This had resulted in clear and sustainable improvements in about 50 percent of subjects. "But in this new study, our results were even much better," says Prof. Schläpfer. A clear improvement in complaints was found in 85 percent of patients, instead of the earlier 50 percent. In addition, stimulation was performed with lower current levels, and the effects showed within a few days, instead of after weeks.

Method's long-term success proven

"Obviously, we have now come closer to a critical structure within the brain that is responsible for major depression," says the psychiatrist from the Bonn University Hospital. Another cause for optimism among the group of physicians is that, since the study's completion, an eighth patient has also been treated successfully. The patients have been observed for a period of up to 18 month after the intervention. Prof. Schläpfer reports, "The anti-depressive effect of deep brain stimulation within the medial forebrain bundle has not decreased during this period." This clearly indicates that the effects are not temporary. This method gives those who suffer from major depression reason to hope. However, it will take quite a bit of time for the new procedure to become part of standard therapy.

Publication: Rapid Effects of Deep Brain Stimulation for Treatment Resistant Major Depression, Biological Psychiatry, DOI: 10.1016/j.biopsych.2013.01.034

You can find a podcast on this topic at: http://www.uni-bonn.tv/podcasts/20130322_ST_Hirnstimulation-Schlaepfer.mp4/view

http://nyti.ms/15crEhM

Protein Linked to Development Problems

Mice lacking a protein have many of the same learning and memory defects as mice with Down syndrome

By DOUGLAS QUENQUA

The French geneticist Jérôme Lejeune discovered more than 50 years ago that Down syndrome is caused by the presence of an extra copy of chromosome 21. But to this day it has remained a mystery why that results in impaired physical and cognitive development. Now researchers at the Sanford-Burnham Medical Research Institute think they have found a clue.

The scientists, who were investigating Alzheimer's disease, found that mice that lacked a protein known as SNX27 had many of the same learning and memory defects as mice with Down syndrome. Looking at the brains of people with the syndrome, the researchers discovered that they, too, lacked SNX27.

While chromosome 21 is not directly involved in SNX27 production, it does encode a regulator - miR-155 - that inhibits production. According to the study, published in the journal Nature Medicine, levels of miR-155 in the brains of people with Down syndrome correlate almost exactly with the decrease in SNX27.

"In the brain, SNX27 keeps certain receptors on the cell surface - receptors that are necessary for neurons to fire properly," said the study's senior author, Huaxi Xu, in a statement released by the institute. "So in Down syndrome, we believe lack of SNX27 is at least partly to blame for developmental and cognitive defects."

To test their findings, Dr. Xu's team introduced more SNX27 to mice with Down syndrome. As they expected, the mice showed immediate improvements in cognitive function and behavior. Now the researchers are investigating molecules that might increase production of SNX27 in the human brain.

http://www.eurekalert.org/pub_releases/2013-04/kc-n-sfc040913.php

Study finds copper reduces 58 percent of healthcare-acquired infections

4-year study proves Antimicrobial Copper metal surfaces are capable of saving patient lives

New York, NY - New research has revealed that the use of Antimicrobial Copper surfaces in hospital rooms can reduce the number of healthcare-acquired infections (HAIs) by 58% as compared to patients treated in Intensive Care Units with non-copper touch surfaces. In the United States, 1 out of every 20 hospital patients develops an HAI, resulting in an estimated 100,000 deaths per year. Although numerous strategies have been developed to decrease these infections, Antimicrobial Copper is the only strategy that works continuously, has been scientifically proven to be effective and doesn't depend on human behavior, according to a recently published study in the SHEA Journal of Infection Control and Hospital Epidemiology.

"The implications of this study are critical," said Dr. Harold Michels, Senior Vice President of the Copper Development Association (CDA). "Until now, the only attempts to reduce HAIs have required hand hygiene, increased cleaning and patient screening, which don't necessarily stop the growth of these bacteria the way copper alloy surfaces do. We now know that copper is the game-changer: it has the potential to save lives."

Intensive Care Units See the Benefit of Copper Alloys

The study, funded by the U.S. Department of Defense, was conducted in the Intensive Care Units (ICUs) of three major hospitals: The Medical University of South Carolina, Memorial Sloan-Kettering Cancer Center in New York City and the Ralph H. Johnson Veterans Affairs Medical Center in Charleston, South Carolina. To determine the impact of copper alloy surfaces on the rate of HAIs, copper-surfaced objects were placed in each ICU, where patients are at higher risk due to the severity of their illnesses, invasive procedures and frequent interaction with healthcare workers. Patients were randomly placed in available rooms with or without copper alloy surfaces, and the rates of HAIs were compared. A total of 650 patients and 16 rooms (8 copper and 8 standard) were studied between July 12, 2010 and June 14, 2011.

Results of this study, that appeared last July in the Journal of Clinical Microbiology, found that Antimicrobial Copper can continuously kill 83% of bacteria that cause HAIs within two hours, including strands resistant to antibiotics. The study compared copper to equivalent non-copper touch surfaces during active patient care between routine cleaning and sanitizing.

"Copper alloy surfaces offer an alternative way to reduce the increasing number of HAIs, without having to worry about changing healthcare worker behavior," said Dr. Michael Schmidt, Vice Chairman of Microbiology and Immunology at the Medical University of South Carolina and one of the authors of the study. "Because the antimicrobial effect is a continuous property of copper, the regrowth of deadly bacteria is significantly less on these surfaces, making a safer environment for hospital patients."

In study results, 46 patients developed an HAI, while 26 patients became colonized with MRSA or VRE. Overall, the proportion of patients who developed an HAI was significantly lower among those assigned to intensive care rooms with objects fabricated using copper alloys. There are currently hundreds of Antimicrobial Copper healthcare-related products available today, including IV poles, stretchers, tray tables and door hardware.

This study was so successful that an interdisciplinary team from UCLA began replicating this research in July 2012. The team is testing ICUs with Antimicrobial Copper at Ronald Reagan UCLA Medical Center.

For more information about Antimicrobial Copper, visit http://www.antimicrobialcopper.com.

About the Copper Development Association

The Copper Development Association Inc. is the market development, engineering and information services arm of the copper industry, chartered to enhance and expand markets for copper and its alloys in North America. Learn more on our blog.

http://www.eurekalert.org/pub_releases/2013-04/uobc-dni040513.php

Doctors not informed of harmful effects of medicines during sales visits

The majority of family doctors receive little or no information about harmful effects of medicines when visited by drug company representatives, according to an international study involving Canadian, U.S. and French physicians.

Yet the same doctors indicated that they were likely to start prescribing these drugs, consistent with previous research that shows prescribing behaviour is influenced by pharmaceutical promotion.

The study, which had doctors fill out questionnaires about each promoted medicine following sales visits, was published online today in the Journal of General Internal Medicine. It shows that sales representatives failed to provide any information about common or serious side effects and the type of patients who should not use the medicine in 59 per cent of the promotions. In Vancouver and Montreal, no potential harms were mentioned for 66 per cent of promoted medicines.

"Laws in all three countries require sales representatives to provide information on harm as well as benefits," says lead author Barbara Mintzes of the University of British Columbia. "But no one is monitoring these visits and there are next to no sanctions for misleading or inaccurate promotion."
Serious risks were mentioned in only six percent of the promotions, even though 57 per cent of the medications involved in these visits came with US Food and Drug Administration "black box" or Health Canada boxed warnings – the strongest drug warning that can be issued by both countries.
"We are very concerned that doctors and patients are left in the dark and patient safety may be compromised," says Mintzes, an expert on drug advertising in UBC's School of Population and Public Health.
Doctors in Toulouse were more likely to be told of a harmful effect in a promotional visit, compared to doctors in Canada and the U.S., according to the study. Researchers suggested that this may reflect stricter regulatory standards for promotion of medicines in France.
NB: Figures showing the study's key findings are available at https://www.dropbox.com/sh/gzo3d9uqy19rexl/ULFOzdk5d-.
Background | Drug Sales Visits Lack Details
About the study
The UBC-led study is the most comprehensive to date of the quality of pharmaceutical sales representative promotions to family physicians.
Researchers recruited physicians to participate using random samples from lists of primary care physicians at four sites – Vancouver, Montreal, Sacramento and Toulouse. Among 704 eligible physicians contacted, 255 (36 per cent) chose to participate. Information was collected on 1,692 drug promotions at sales visits between May 2009 to June 2010.
Doctors were asked to fill out a questionnaire about the information provided for each promoted medicine following each visit they received from pharmaceutical sales representatives. Sales representatives regularly visit doctors' offices to promote medicines by providing information, free samples and in some cases food and invitations to events. The study focused on how often information was provided about drug safety.
The team includes researchers from UBC, York University, University of Montreal, University of California, Davis and the University of Toulouse.
Third-party comment
Dr. Tom Perry, an internal medicine and clinical pharmacology specialist at the UBC Hospital in Vancouver, who is not part of the study, expressed concern about the findings:
"Doctors learn relatively little about drugs in medical school, and much of their exposure to pharmacology after graduation may be in the form of advertising. If they are unaware of the potential harms from drugs they prescribe, patients inevitably suffer the consequences." Perry also called for much stricter control of drug advertising in Canada.
Dr. Perry can be reached by pager 604-707-1427 or e-mail tperryjr@shaw.ca.

http://www.eurekalert.org/pub_releases/2013-04/uocd-ans_1040613.php

AACR news: Studies show increasing evidence that androgen drives breast cancer

Overwhelming evidence adds a major new target in breast cancer: Androgens including testosterone

Estrogen and progesterone receptors, and the gene HER2 – these are the big three markers and/or targets in breast cancer. Evidence presented at the AACR Annual Meeting 2013 adds a fourth: androgen receptors.
"This is a continuing line of work with all evidence pointing toward the addition of the androgen receptor as potential target and useful marker in all of the major subtypes of breast cancer," says Jennifer Richer, PhD, investigator at the University of Colorado Cancer Center and co-director of the CU Cancer Center Tissue Processing and Procurement Core.
The finding of androgen receptors (AR) as a potential target in breast cancer is especially important in light of its prevalence in breast cancers that don't express other hormone receptor targets or have developed resistance to treatments that target estrogen dependence. Overall, approximately 77 percent of breast cancers are positive for AR, including 88 percent of cancers that are estrogen receptor positive, 59 percent of those that are HER2 positive, and 20-32 percent of triple negative breast cancers.
The study presented this week explores the ability of estrogen-positive (ER+) breast cancers to develop resistance to anti-estrogen drugs by potentially developing an alternative addiction to AR – and hypothesizes that anti-androgen therapy, such as the drug enzalutamide (formerly MDV3100) as successful counters to breast cancers' evolution. First, Richer and colleagues used breast cancer tumor registries to discover that cancers with higher ratios of AR to ER protein had shorter time to relapse after anti-estrogen therapies. Cut off from their estrogen addition, these cancers may have turned to growth and survival via androgens instead.
The group then returned to the lab to explore the effects of anti-androgen therapies in cell lines and preclinical models.
"Remarkably, the anti-androgen drug enzalutamide had effects comparable to the anti-estrogen drug tamoxifen in breast cancer cells that expressed both ER and AR," Richer says. HER2 cell lines that were also AR+ showed promising responses as well.

"We are excited to move toward clinical trials of anti-androgen therapies in breast cancer," Richer says. "And this study shows that patients with a high AR/ER ratio who relapse while on estrogen targeting therapies might be good candidates for this kind of therapy."

http://www.eurekalert.org/pub_releases/2013-04/sumc-gch040813.php

Getting CLARITY: Hydrogel process developed at Stanford creates transparent brain

Combining neuroscience and chemical engineering, researchers at Stanford University have developed a process that renders a mouse brain transparent.

STANFORD, Calif. - The postmortem brain remains whole - not sliced or sectioned in any way - with its three-dimensional complexity of fine wiring and molecular structures completely intact and able to be measured and probed at will with visible light and chemicals.

The process, called CLARITY, ushers in an entirely new era of whole-organ imaging that stands to fundamentally change our scientific understanding of the most-important-but-least-understood of organs, the brain, and potentially other organs, as well. The process is described in a paper to be published online April 10 in Nature by bioengineer and psychiatrist Karl Deisseroth, MD, PhD, leading a multidisciplinary team, including postdoctoral scholar Kwanghun Chung, PhD.

"Studying intact systems with this sort of molecular resolution and global scope - to be able to see the fine detail and the big picture at the same time - has been a major unmet goal in biology, and a goal that CLARITY begins to address," Deisseroth said.

"This feat of chemical engineering promises to transform the way we study the brain's anatomy and how disease changes it," said Thomas Insel, MD, director of the National Institute of Mental Health. "No longer will the in-depth study of our most important three-dimensional organ be constrained by two-dimensional methods."

The research in this study was performed primarily on a mouse brain, but the researchers have used CLARITY on zebrafish and on preserved human brain samples with similar results, establishing a path for future studies of human samples and other organisms.

"CLARITY promises to revolutionize our understanding of how local and global changes in brain structure and activity translate into behavior," said Paul Frankland, PhD, a senior scientist in neurosciences and mental health at the Hospital for Sick Children Research Institute in Toronto, who was not involved in the research.

Frankland's colleague, senior scientist Sheena Josselyn, PhD, added that the process could turn the brain from "a mysterious black box" into something essentially transparent.

An inscrutable place

The mound of convoluted grey matter and wiring that is the brain is a complex and inscrutable place. Neuroscientists have struggled to fully understand its circuitry in their quest to comprehend how the brain works, and why, sometimes, it doesn't.

CLARITY is the result of a research effort in Deisseroth's lab to extract the opaque elements - in particular the lipids - from a brain and yet keep the important features fully intact. Lipids are fatty molecules found throughout the brain and body. In the brain, especially, they help form cell membranes and give the brain much of its structure. Lipids pose a double challenge for biological study, however, because they make the brain largely impermeable both to chemicals and to light.

Neuroscientists would have liked to extract the lipids to reveal the brain's fine structure without slicing or sectioning, but for one major hitch: removing these structurally important molecules causes the remaining tissue to fall apart.

Prior investigations have focused instead on automating the slicing/sectioning approach, or in treating the brain with organic molecules that facilitate the penetration of light only, but not macromolecular probes. With CLARITY, Deisseroth's team has taken a fundamentally different approach.

"We drew upon chemical engineering to transform biological tissue into a new state that is intact but optically transparent and permeable to macromolecules," said Chung, the paper's first author.

This new form is created by replacing the brain's lipids with a hydrogel. The hydrogel is built from within the brain itself in a process conceptually similar to petrification, using what is initially a watery suspension of short, individual molecules known as hydrogel monomers. The intact, postmortem brain is immersed in the hydrogel solution and the monomers infuse the tissue. Then, when "thermally triggered," or heated slightly to about body temperature, the monomers begin to congeal into long molecular chains known as polymers, forming a mesh throughout the brain. This mesh holds everything together, but, importantly, it does not bind to the lipids.

With the tissue shored up in this way, the team is able to vigorously and rapidly extract lipids through a process called electrophoresis. What remains is a 3-D, transparent brain with all of its important structures - neurons, axons, dendrites, synapses, proteins, nucleic acids and so forth - intact and in place.

Going things one better

CLARITY then goes one better. In preserving the full continuity of neuronal structures, CLARITY not only allows tracing of individual neural connections over long distances through the brain, but also provides a way to gather rich, molecular information describing a cell's function is that is not possible with other methods.

"We thought that if we could remove the lipids nondestructively, we might be able to get both light and macromolecules to penetrate deep into tissue, allowing not only 3-D imaging, but also 3-D molecular analysis of the intact brain," said Deisseroth, who holds the D.H. Chen Professorship.

Using fluorescent antibodies that are known to seek out and attach themselves only to specific proteins, Deisseroth's team showed that it can target specific structures within the CLARITY-modified - or "clarified" - mouse brain and make those structures and only those structures light up under illumination. The researchers can trace neural circuits through the entire brain or explore deeply into the nuances of local circuit wiring. They can see the relationships between cells and investigate subcellular structures. They can even look at chemical relationships of protein complexes, nucleic acids and neurotransmitters.

"Being able to determine the molecular structure of various cells and their contacts through antibody staining is a core capability of CLARITY, separate from the optical transparency, which enables us to visualize relationships among brain components in fundamentally new ways," said Deisseroth, who is one of 15 experts on the "dream team" that will map out goals for the $100 million brain research initiative announced April 2 by President Obama.

And in yet another significant capability from a research standpoint, researchers are now able to destain the clarified brain, flushing out the fluorescent antibodies and repeating the staining process anew using different antibodies to explore different molecular targets in the same brain. This staining/destaining process can be repeated multiple times, the authors showed, and the different data sets aligned with one another.

Opening the door

CLARITY has accordingly made it possible to perform highly detailed, fine-structural analysis on intact brains - even human tissues that have been preserved for many years, the team showed. Transforming human brains into transparent-but-stable specimens with accessible wiring and molecular detail may yield improved understanding of the structural underpinnings of brain function and disease.

Beyond the immediate and apparent benefit to neuroscience, Deisseroth cautioned that CLARITY has leapfrogged our ability to deal with the data. "Turning massive amounts of data into useful insight poses immense computational challenges that will have to be addressed. We will have to develop improved computational approaches to image segmentation, 3-D image registration, automated tracing and image acquisition," he said.

Indeed, such pressures will increase as CLARITY could begin to support a deeper understanding of large-scale intact biological systems and organs, perhaps even entire organisms.

"Of particular interest for future study are intrasystem relationships, not only in the mammalian brain but also in other tissues or diseases for which full understanding is only possible when thorough analysis of single, intact systems can be conducted," Deisseroth said. "CLARITY may be applicable to any biological system, and it will be interesting to see how other branches of biology may put it to use."

Other co-authors include undergraduate student Jenelle Wallace; graduate students Sung-Yon Kim, Kelly Zalocusky, Joanna Mattis, Aleksandra Denisin and Logan Grosenick; research assistants Sandhiya Kalyanasundaram, Julie Mirzabekov, Sally Pak and Charu Ramakrishnan; postdoctoral scholars Aaron Andalman, PhD, and Tom Davidson, PhD; former undergraduate student Hannah Bernstein; and former staff scientist Viviana Gradinaru.

The research is supported by the National Institute of Mental Health (grant MH099647); the National Science Foundation; the Simons Foundation; the President and Provost of Stanford University; the Wiegers, Snyder, Reeves, Gatsby and Yu foundations; the DARPA REPAIR program; and the Burroughs Wellcome Fund.

http://www.bbc.co.uk/news/health-22086086

Organ donation soars over past five years, says NHS Blood and Transplant

The number of people donating organs after death has risen 50% since 2008.

By Anna-Marie Lever Health reporter, BBC News

More than 1,200 people in the UK donated their organs in the last year, leading to about 3,100 transplants.

The increase has been largely credited to the network of specialist nurses who approach and support bereaved relatives in hospitals.

But with the numbers on the organ donation register remaining unchanged, the NHS Blood and Transplant service is still asking people to sign up.

Sally Johnson, from NHS Blood and Transplant, said: "The NHS has worked hard to ensure every potential donor is identified, that the organ donation register is checked, and that families are approached.

Refusal rate

"But the NHS can't do it on its own. We need a transformation in donor and family consent because the UK's family refusal rate remains one of the highest in Europe."

Last year, 125 families overruled an individual's intention to donate.

Ms Johnson said: "It is important families know their relative is signed up to the register. On the worst day of their lives, don't let families guess"

In 2008, the UK's health ministers accepted the recommendations of the Organ Donation Taskforce. These included better identification of potential donors, improved referral of potential donors and improved care of donors to increase the number of organs available - around three organs were retrieved last year for every donor.

The Role of a Specialist Nurse

Andrea Bradley, at Morriston Hospital Swansea, decided to become an organ donation nurse after her father received a corneal transplant. She is the first person to suggest approaching a bereaved family about organ donation.

"You are asking a family to make a decision at the most difficult time of their lives. I give them all the information and hold nothing back.

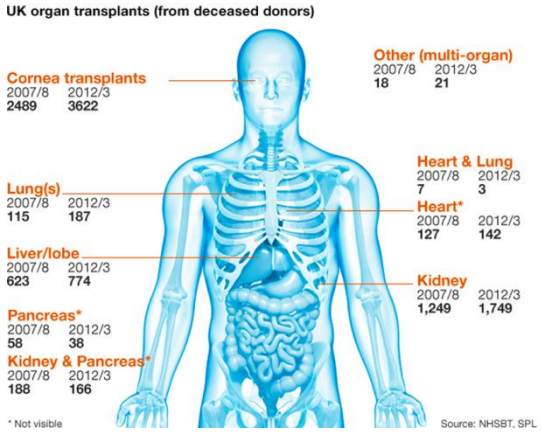
"Most are in shock- it is an art form to gauge if the family understands what you are saying. No one has ever been angry with me when I suggest the possibility of organ donation.

"If donation goes ahead I stay with the patient throughout, putting their information on the system to find a match, going to theatre with them and then the chapel of rest. I ring the family, if they would like to know I tell them what was retrieved. Later I meet with them and can tell them how the people who received the organs are doing."

Each donor has the potential to help nine people through donation of a heart, lungs, two kidneys, pancreas, liver and small bowel and two corneas.

Since the Taskforce report recommendations five years ago, Scotland and Northern Ireland have seen the largest increases in deceased donors- 74% and 82% respectively.

And the actual number of transplants in the UK is up by 30% - the difference between the increase in donors and transplants is partly down to organs from some who wish to donate being unsuitable because of factors such as age and obesity.



Opt-out system

But with three people in the UK dying a day because of a lack of donor organs, many experts believe more need to be done.

Dr Vivienne Nathanson from the British Medical Association says the donation system needs an overhaul. Referring to recent research she said: "[We] concluded the best way forward for the UK was to introduce an opt-out system with safeguards."

The plan would mean people were deemed to consent to organ donation, unless they object during their lifetime. This system is being considered for introduction in Wales in two years time

Ministers in Northern Ireland recently announced the intention to consult on public attitudes towards organ donation, including the introduction of an opt-out system.

http://www.eurekalert.org/pub_releases/2013-04/uoca-fom040913.php

First objective measure of pain discovered in brain scan patterns by CU-Boulder study

For the first time, scientists have been able to predict how much pain people are feeling by looking at images of their brains, according to a new study led by the University of Colorado Boulder.

The findings, published today in the New England Journal of Medicine, may lead to the development of reliable methods doctors can use to objectively quantify a patient's pain. Currently, pain intensity can only be measured based on a patient's own description, which often includes rating the pain on a scale of one to 10. Objective measures of pain could confirm these pain reports and provide new clues into how the brain generates different types of pain.

The new research results also may set the stage for the development of methods using brain scans to objectively measure anxiety, depression, anger or other emotional states. "Right now, there's no clinically acceptable way to measure pain and other emotions other than to ask a person how they feel," said Tor Wager, associate professor of psychology and neuroscience at CU-Boulder and lead author of the paper.

The research team, which included scientists from New York University, Johns Hopkins University and the University of Michigan, used computer data-mining techniques to comb through images of 114 brains that were taken when the subjects were exposed to multiple levels of heat, ranging from benignly warm to painfully hot. With the help of the computer, the scientists identified a distinct neurologic signature for the pain.

"We found a pattern across multiple systems in the brain that is diagnostic of how much pain people feel in response to painful heat," Wager said.

Going into the study, the researchers expected that if a pain signature could be found it would likely be unique to each individual. If that were the case, a person's pain level could only be predicted based on past images of his or her own brain. But instead, they found that the signature was transferable across different people, allowing the scientists to predict how much pain a person was being caused by the applied heat, with between 90 and 100 percent accuracy, even with no prior brain scans of that individual to use as a reference point.
The scientists also were surprised to find that the signature was specific to physical pain. Past studies have shown that social pain can look very similar to physical pain in terms of the brain activity it produces. For example, one study showed that the brain activity of people who have just been through a relationship breakup - and who were shown an image of the person who rejected them - is similar to the brain activity of someone feeling physical pain.
But when Wager's team tested to see if the newly defined neurologic signature for heat pain would also pop up in the data collected earlier from the heartbroken participants, they found that the signature was absent.
Finally, the scientists tested to see if the neurologic signature could detect when an analgesic was used to dull the pain. The results showed that the signature registered a decrease in pain in subjects given a painkiller.
The results of the study do not yet allow physicians to quantify physical pain, but they lay the foundation for future work that could produce the first objective tests of pain by doctors and hospitals. To that end, Wager and his colleagues are already testing how the neurologic signature holds up when applied to different types of pain.
"I think there are many ways to extend this study, and we're looking to test the patterns that we've developed for predicting pain across different conditions," Wager said. "Is the predictive signature different if you experience pressure pain or mechanical pain, or pain on different parts of the body?
"We're also looking towards using these same techniques to develop measures for chronic pain. The pattern we have found is not a measure of chronic pain, but we think it may be an 'ingredient' of chronic pain under some circumstances. Understanding the different contributions of different systems to chronic pain and other forms of suffering is an important step towards understanding and alleviating human suffering."
The study was funded by the National Institute on Drug Abuse, the National Institute of Mental Health and the National Science Foundation.

http://www.bbc.co.uk/news/world-europe-22066905

Parkinson's patients test Irish set dancing benefits

People with Parkinson's disease have taken to the dance floor to see if Irish set dancing can improve their symptoms.

It is part of an international study being led by the University of Limerick. Results are yet to be analysed but in a previous study, patients fell less often and were more mobile after regular set dancing lessons.
Benefits may be down to exercise, the strong rhythm of Irish music and the sociability of group dances.
The research could potentially lead to people worldwide being offered traditional Irish set dancing as part of their Parkinson's treatment.

Music lift

Masters student Joanne Shanahan, a qualified set dance instructor, led an exercise programme twice a week for eight weeks in a pilot study.
Eight patients with mild to moderate Parkinson's took part and were compared against a control group. One of them, Mary, spoke to the BBC but did not want her surname to be made public.
She was diagnosed with Parkinson's eight years ago and it causes her to drag her right leg behind her when she walks, as well as making her joints stiff.
"With the music it kind of lifted you somehow," she said. "I would walk out better than I walked in."
Her husband Pat noted that set dancing helped Mary get better at "little things" like putting her own shoes on.
Mary has now pledged to join regular set dancing classes.
"I feel this is definitely helping me," Mary said. "I'm going to join up and keep it going."
Lecturer Amanda Clifford said the "enjoyment factor" of set dancing is "key". "There's theory to support that this is beneficial and we have seen this in some (other) studies," she said. But she warned that she and her team are still analysing results from a pilot study.

'Fluent' dance

Parkinson's research first turned to set dancing after an Italian doctor had a chance encounter in a County Clare village.
Daniele Volpe is an Irish folk music enthusiast and plays the guitar. While playing at an annual traditional music festival in Feakle, he saw a man walk in using a cane. Dr Volpe recognised the symptoms of Parkinson's, but was amazed when the man set aside his cane to start dancing in a "fluent" way.

He teamed up with Dublin-based researcher Timothy Lynch and on Dr Volpe's return to Venice, they sent 24 patients with Parkinson's to weekly set dancing classes for six months.
When measured against a control group, all of them saw improvement in balance, mobility and quality of life. They found it easier to change direction and to start moving again after they had stopped.
In 20 years of sending patients to the gym, to swimming and to treadmill-based rehabilitation, he said "this was the first time that all the patients gave very high compliance to the treatment".
Other dance forms including tango, ballet and foxtrot have been investigated as possible aids for Parkinson's patients. But the steady rhythm of Irish folk music acts as an "acoustic cue", Dr Volpe said, bypassing the Parkinson's trouble spots in the brain and helping patients to overcome their symptoms for the duration of the dance. And he is optimistic about people getting the therapy worldwide, because "everywhere you can listen to traditional Irish music".
The sociable nature of set dancing and the uniformity of the steps used also prompted improvements in patients' symptoms, Dr Volpe believes. He said: "I'm very happy that this dance can help people improve their quality of life. This is our job."
A larger research study led by the University of Limerick, with input from Meg Morris at the University of Melbourne, is due to be rolled out in Ireland in the coming months. And Parkinson's sufferers from Italy and Ireland will join to perform set dancing at the Feakle festival later this year.

http://www.eurekalert.org/pub_releases/2013-04/uom-sto041013.php

Some types of papilloma virus might prevent cervical cancer

Certain types of papilloma virus might actually prevent cervical cancer, according to a new study by researchers from The University of Manchester

Certain types of papilloma virus might actually prevent cervical cancer, according to a new study by researchers from The University of Manchester.
There are over 100 different types of human papilloma virus (HPV). Cervical cancer is known to be caused by infection with approximately 14 so-called "high-risk" types of this virus. Researchers from Manchester looked at the different types of HPV found in cervical smears and invasive cervical cancers from HIV positive and HIV negative women in Kenya. They found high numbers of a specific type of HPV (type 53) in normal cervical smears from HIV positive women, but this was rarely found in HIV negative women. This sub-type was also never found in cervical cancers from either HIV positive or negative women.
Dr Ian Hampson, a Senior Lecturer in Viral Oncology from The University of Manchester who lead the study, said: "It is well known that HIV increases the number of different types of HPV found in any one patient which implies that HIV opens the door for infection with multiple types of HPV. If only high-risk types are present these will undoubtedly accelerate progression to cancer whereas if other types (eg type 53) are also present they may actually compete with the high-risk types to inhibit progression to cervical cancer."
There are 270,000 deaths from cervical cancer globally each year with 85% of these occurring in countries with low resources. In Kenya it is the most common malignancy accounting for between 18 and 23 per cent of all diagnosed cases of cancer.
The study looked at women at samples taken from women in Kenya and results were analysed at The University of Manchester's Viral Oncology Laboratories based at the Saint Mary's Hospital. Completed by Dr Ian Hampson, Dr Lynne Hampson and Dr Innocent Orora Maranga the results have been published in The Open Virology Journal.
Dr Hampson said the study suggested one possible explanation for why, in spite of a large increase in the numbers of HPV infections in HIV positive African women, there was not a corresponding increase in numbers of cases of cervical cancer. This could also explain why another African study had actually shown the risk of developing one specific type of cervical cancer actually dropped in HIV-positive women, he said.
The researchers now plan to do more research in this area. "Our study was quite small and more research with larger sample numbers is now needed," Dr Hampson said. "We also need to work out exactly how one type of HPV might suppress the cancer causing properties of another. If it can be proved that HPV type 53 can inhibit the cancer-causing properties of other high-risk types of HPV, this could potentially form the basis of a simple biological therapy to prevent this disease. This could be extremely useful in low resource countries who cannot afford expensive HPV vaccines."
The work was published in the Open Virology Journal and was funded by the Humane Research Trust, The Janice Cholerton Post Graduate Support Fund, The Caring Cancer Trust, The Cancer Prevention Research Trust and United in Cancer UK. Dr Maranga was part-funded by awards from the International Atomic Energy Association and Wellbeing of Women.
To view the article, please click here: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3594704/

http://www.sciencedaily.com/releases/2013/04/130410154627.htm

Naturally-Occurring Substance Proves Effective Against Deadly Skin Cancer in Test Tube and Mice Studies

Gossypin as a treatment for melanoma,

For the first time, scientists have demonstrated the mechanism of action of gossypin, a naturally-occurring substance found in fruits and vegetables, as a treatment for melanoma, which causes the majority of deaths from skin cancer.

"We identified gossypin as a novel agent with dual inhibitory activity towards two common mutations that are the ideal targets for melanoma treatment," said Texas Biomed's Hareesh Nair, Ph.D.

At the moment, there is no single therapeutic agent or combination regimen available to treat all melanomas, of which about 76,000 new cases are diagnosed annually, according to the American Cancer Society.

"Our results indicate that gossypin may have great therapeutic potential as a dual inhibitor of mutations called BRAFV600E kinase and CDK4, which occur in the vast majority of melanoma patients. They open a new avenue for the generation of a novel class of compounds for the treatment of melanoma," Nair added.

His report, appearing in the March 29, 2013 issue of the journal Molecular Cancer Therapeutics, was funded by the Texas Biomedical Forum and the Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation.

Nair and his colleagues found that gossypin inhibited human melanoma cell proliferation, in vitro, in melanoma cell lines that harbor the two mutations. Gossypin stunted activities of the mutated genes, possibly through direct binding with them. It also inhibited the growth of various human melanoma cells. In addition, gossypin treatment for 10 days of human melanoma cell tumors with the mutations transplanted into mice reduced tumor volume and increased survival rate.

Further studies are planned by Nair's team to understand how the body absorbs gossypin and how it is metabolized. This idea has been discussed with the Cancer Therapy & Research Center at the UT Health Science Center San Antonio's Deva Mahalingam, M.D, Ph.D., who is interested in testing gossypin in melanoma patients.

S. Bhaskaran, K. V. Dileep, S. S. Deepa, C. Sadasivan, M. Klausner, N. K. Krishnegowda, R. R. Tekmal, J. L. VandeBerg, H. B. Nair. Gossypin as a Novel Selective Dual Inhibitor of v-raf Murine Sarcoma Viral Oncogene Homolog B1 and Cyclin-Dependent Kinase 4 for Melanoma. Molecular Cancer Therapeutics, 2013; 12 (4): 361 DOI: 10.1158/1535-7163.MCT-12-0965

http://www.eurekalert.org/pub_releases/2013-04/uoc--los040913.php

Launch of semi-synthetic artemisinin a milestone for malaria, synthetic biology

12-year route from UC Berkeley lab to market for yeast-derived drug precursor

Twelve years after a breakthrough discovery in his University of California, Berkeley, laboratory, professor of chemical engineering Jay Keasling is seeing his dream come true.

On April 11, the pharmaceutical company Sanofi will launch the large-scale production of a partially synthetic version of artemisinin, a chemical critical to making today's front-line antimalaria drug, based on Keasling's discovery.

The drug is the first triumph of the nascent field of synthetic biology and will be, Keasling hopes, a lifesaver for the hundreds of millions of people in developing countries who each year contract malaria and more than 650,000, most of them children, who die of the disease. Synthetic biology involves inserting a dozen or more genes into microbes to make them produce drugs, chemicals or biofuels that they normally would not.

Keasling and colleagues at Amyris, a company he cofounded in 2003 to bring the lab-bench discovery to the marketplace, will publish in the April 25 issue of Nature the sequence of genes they introduced into yeast that allowed Sanofi to make the chemical precursor of artemisinin. The paper will be available online April 10.

"It is incredible," said Keasling, who also serves as associate director for biosciences at Lawrence Berkeley National Laboratory and as CEO of the Joint Bioenergy Institute in Emeryville, Calif. "The time scale hasn't been that long, it just seems like a long time. There were many places along the way where it could have failed."

The yeast strain developed by Amyris based on Keasling's initial research and now used by Sanofi produces a chemical precursor of artemisinin, a compound that until now has been extracted from the sweet wormwood plant, Artemsia annua. Artemisinin from either sweet wormwood or the engineered yeast is then turned into the active antimalarial drug artesunate, and typically mixed with another antimalarial drug in what is called arteminsinin combination therapy, or ACT.

Global demand for artemisinin has increased since 2005, when the World Health Organization identified ACTs as the most effective malaria treatment available. Sanofi said that it is committed to producing semisynthetic artemisinin using a no-profit, no-loss production model, which will help to maintain a low price for developing

countries. Though the price of ACTs will vary from product to product, the new source for its key ingredient, in addition to the plant-derived supply, should lead to a stable cost and steady supply, Keasling said.

Key campus support

"This wouldn't have happened without lots of incredible support from the UC Berkeley campus," Keasling added, noting that the university pushed for royalty-free licensing of the process to Sanofi, which in turn will sell artemisinin at cost. "Some really dedicated people put their careers on the line for it, both at UC Berkeley and at Amyris."

The success is due in large part to two grants totaling $53.3 million from the Bill & Melinda Gates Foundation to OneWorld Health, the drug development program for PATH, an international nonprofit organization aiming to transform global health through innovation. OneWorld Health shepherded the drug's development out of Keasling's UC Berkeley lab to Amyris for scale-up and then to pharmaceutical firm Sanofi, based in France, for production.

"With commercial production of semi-synthetic artemisinin underway, we are poised to enable a more stable flow of key antimalarial treatments to those who need them most," said Ponni Subbiah, global program leader for drug development at PATH. "The success of this cross-sector collaboration demonstrates that, with a shared humanitarian goal and the dedication and perseverance of all partners, we can advance science to make a real impact in global health."

"Those three partners working together under a OneWorld Health umbrella has been an amazing collaboration," said Jack Newman, chief science officer of Amyris and a former post-doctoral fellow in Keasling's UC Berkeley lab. "Only through a partnership like that a research lab, a biotech focused on taking the discovery and turning it into something that's industrializable, and a commercial partner to take it to market are these types of results possible."

Keasling encourages other companies to license for free their synthetic processes to make artemisinin in order to ensure that needed doses are available worldwide. The yeast strain described in the Nature paper is licensed exclusively to Sanofi.

Ancient Chinese therapy

Sweet wormwood was used in ancient Chinese therapy to treat various illnesses, including fevers typical of malaria. In the 1970s, Chinese scientists rediscovered it and identified its active ingredient, artemisinin, and artemisinin is now extracted from sweet wormwood grown commercially in China, Southeast Asia and Africa. The quality, supply and cost have been unpredictable and inconsistent, however. Keasling's goal was to create a synthetic version with a stable and ideally lower price that could be produced in sufficient quantity to treat the 300-500 million cases of malaria that arise each year.

"The production of semisynthetic artemisinin will help secure part of the world's supply and maintain the cost of this raw material at acceptable levels for public health authorities around the world and ultimately benefit patients," said Dr. Robert Sebbag, vice-president of Access to Medicines at Sanofi. "This is a pivotal milestone in the fight against malaria."

The "semi-synthetic" artemisinin is chemically modified to an active drug, such as artesunate, and combined in ACT with another antimalarial drug to lessen the chance that the malaria parasite will develop resistance to artemisinin. Sanofi plans to produce 35 tons of artemisinin in 2013 and, on average, 50 to 60 tons a year by 2014, which will translate to between 80 and 150 million ACT treatments. Following regulatory approval expected later this year, semisynthetic artemisinin will be ready for rapid integration into the supply chain for antimalarial therapies, according to the company.

"This artemisinin produced by this semisynthetic process will substitute directly for the artemisnin from the plant, so there will be no difference in the final ACT product," Keasling said.

The 12-year tale started in Keasling's UC Berkeley lab with the discovery that implanting a combination of wormwood and yeast genes into bacteria made the bacteria produce a chemical that could be chemically converted to artemisinin. Further research turned up another gene in 2006 that, when inserted into yeast with the earlier genes, allowed Keasling and his team to synthesize small amounts of artemisinic acid, which is closer chemically to the actual drug. Using synthetic biology techniques from Keasling's lab, Amyris added that gene to yeast along with other plant genes to boost artemisinic acid production by a factor of 15, good enough to interest Sanofi.

The drug company developed its own proprietary photochemical process to convert artemisinic acid to artemisinin, hence the term semi-synthetic. In the Nature paper, the Amyris researchers describe an alternative, nonproprietary process for achieving the same result.

http://phys.org/news/2013-04-life-lithium-ion-batteries-electric.html

Understanding the life of lithium ion batteries in electric vehicles

How long before the battery pack dies

Scientists today answered a question that worries millions of owners and potential owners of electric and hybrid vehicles using lithium-ion batteries: How long before the battery pack dies, leaving a sticker-shock bill for a fresh pack or a car ready for the junk heap? Their answer, presented here at the 245th National Meeting & Exposition of the American Chemical Society (ACS), may surprise skeptics.

"The battery pack could be used during a quite reasonable period of time ranging from 5 to 20 years depending on many factors," said Mikael G. Cugnet, Ph.D., who spoke on the topic. "That's good news when you consider that some estimates put the average life expectancy of a new car at about eight years.

Cugnet explained that the lifespan depends mainly on the battery's temperature, state of charge and charge protocol. Battery performance begins to suffer as soon as the temperature climbs above 86 degrees Fahrenheit. "The higher the temperature, the lower the battery service life," he said. "A temperature above 86 degrees F affects the battery pack performance instantly and even permanently if it lasts many months like in Middle East countries." Cugnet also recommended that electric vehicle (EV) owners pay attention to how much their battery is charged, another factor in a battery's longevity. He reported that a fully-charged battery is more vulnerable to losing power at temperatures above 86 degrees F.

To test the limits of lithium-ion EV batteries, Cugnet's team reconstructed the experience of a typical EV battery in the laboratory. Using data gleaned from a real five-mile trip in an EV, they put EV battery packs and cells through simulated lifetimes of driving with cycles of draining and recharging. The researchers considered a battery to be beyond its useful lifespan when it had lost 20 percent of its full power.

The question of longevity matters to EV owners and manufacturers alike. The cost of the lithium-ion batteries that power these vehicles remains high, and an EV can cost twice as much as a gas or diesel equivalent. Customers want to make sure they get their money's worth, and manufacturers are eager to demonstrate that EVs are economical.

One obvious saving is the cost of fuel over a car's lifetime, but EV makers are also pushing so-called "second life" uses for batteries that could make them valuable even after they've lost too much power to be useful in cars. These applications could include backup power for computers and medical equipment, or electrical grid storage, which would go hand-in-hand with renewable power like wind or solar to keep electricity flowing even when environmental conditions aren't right. Another option is recycling a battery's components to make new batteries.

More information: Abstract

The market of Li-ion batteries is growing fast mainly due to the electric vehicle rebirth. However, the anticipated demand in electric vehicles is much lower than it was originally announced, since they can cost twice as much as similar gas-powered vehicles. Battery costs will unfortunately stay high until they can be made at high volumes. Among the various ways identified to decrease their price is the possibility of a battery second life in other applications, less demanding in power capability, such as utility storage. This means that batteries should not only be able to operate during the complete vehicle life, but also long after. Therefore, there is a need to investigate the way they degrade during rest (calendar life) and operation (cycle life) depending on the vehicle characteristics. This will help to improve the battery design, the battery management system, and consequently the electric vehicle competitiveness.

http://phys.org/news/2013-04-evolved-judgments-author.html

Not as evolved as we think: Adaptation neither stops nor makes value judgments, author says

"There is no 'progress' in evolution. No living thing is trying to get anywhere. And humans are not at the pinnacle of the evolutionary ladder."

Lest you think you're at the top of the evolutionary heap, looking down your highly evolved nose at the earth's lesser creatures, Marlene Zuk has a message for you: When it comes to evolution, there is no high or low, no better or worse. From evolution's standpoint, people are no more special than microbes evolved to survive in extreme surroundings that might kill mere humans.

Zuk, a professor of ecology, evolution, and behavior at the University of Minnesota, took aim Wednesday evening at popular misconceptions of evolution, the human kind in particular. The biggest misconception, she said, is that the process is linear, with a beginning and an end, and that human evolution is progressing somehow from worse to better.

Evolution, rather, is the continual adaptation of organisms to their surroundings. When the surroundings change, those life forms poorly adapted to the new environment perish, while those it suits survive.

"There is no 'progress' in evolution. No living thing is trying to get anywhere," Zuk said. "And humans are not at the pinnacle of the evolutionary ladder."

She also took aim at the notion that anything is ever "perfectly adapted" to its environment. Evolution, she said, is no engineer, building the perfect organism from scratch every time the environment changes. Rather, evolution is the ultimate tinkerer, always having to make do with the parts on hand. Its creations tend to be imperfect, just fit enough to survive.

Zuk, the author of a new book on the subject, "Paleofantasy: What Evolution Really Tells Us About Sex, Diet, and How We Live," spoke at the Harvard Museum of Natural History (HMNH) as part of its "Evolution Matters" lecture series. Zuk was introduced by Jane Pickering, executive director of the Harvard Museums of Science and Culture, of which the HMNH is part.

Zuk cast a jaundiced eye on the modern nostalgia for our rugged caveman days, saying that the idea that we were somehow "perfectly adapted" then isn't true - just a "paleofantasy" - and neither is the idea that we haven't evolved since and are somehow ill-suited to life today.

Those supposedly "perfectly adapted" cavemen were evolutionary compromises, just good enough to survive and pass their genes to the next generation. They might themselves have been nostalgic for the days when ancestors ran about on all fours, since walking upright can cause back pain, Zuk said. Or they might have bemoaned all the effort required to hunt for a living, longing to return to the days when humans scavenged other animals' kills. "Why stop there? Why not long to be aquatic, since life arose in the sea?" Zuk said. "All living things are full of compromises. We're jury-rigged."

The idea that our physical traits somehow make us better fitted to the ancient savannahs of Africa than to the demands of modern society is widespread in popular culture, Zuk said. It is evidenced in everything from the popular "Paleo diet," whose adherents only eat foods a caveman might, to the rise of barefoot running, to explanations of the obesity crisis, and of our darker emotions and desires.

Zuk illustrated her point with images from popular culture, showing a Glamour magazine cover offering "A Cavewoman's Guide to Good Health," a New York Times article about New Yorkers who model their lives on cavemen - giving blood regularly to mimic blood once lost in battle - and several versions of a common cartoon showing human evolution as a progression from chimpanzee to caveman to well-muscled, anatomically modern man to office slouch, hunched over a computer, or tubby, balding guy munching on a sub sandwich.

Human evolution is still happening, Zuk said. Researchers examining data from the Framingham Heart Study, which began in 1948, detected a large enough signal in the 14,000 study subjects to predict that, 10 generations on, women will be shorter, plumper, with lower cholesterol and blood pressure.

"Selection is continuing in our lives, as it was in our ancestors'," Zuk said.

There are other instances of recent human evolution, including the evolution of lactose tolerance in herding populations in Africa and Europe. Most mammals lose the enzyme lactase, which confers the ability to digest dairy, as they mature. But in these populations, the continued ability to use a readily available food source must have conferred enough added fitness for the gene to spread. And an increase in fitness doesn't have to be large, Zuk pointed out, to have a significant impact over long periods of time. Just a 3 percent fitness increase would result in a gene becoming widespread in a population in some 300 to 350 generations, a relative blink in evolutionary time. "Nobody heaves a sigh of genetic relief and then stops," Zuk said. No life form can say, "OK, we're not evolving. We can all now learn to knit."

http://www.eurekalert.org/pub_releases/2013-04/cp-mfi040513.php

Mutations found in individuals with autism interfere with endocannabinoid signaling in the brain

Mutations in individuals with autism inhibit brain molecules acting on endocannabinoid receptors

Mutations found in individuals with autism block the action of molecules made by the brain that act on the same receptors that marijuana's active chemical acts on, according to new research reported online April 11 in the Cell Press journal Neuron. The findings implicate specific molecules, called endocannabinoids, in the development of some autism cases and point to potential treatment strategies.

"Endocannabinoids are molecules that are critical regulators of normal neuronal activity and are important for many brain functions," says first author Dr. Csaba Földy, of Stanford University Medical School. "By conducting studies in mice, we found that neuroligin-3, a protein that is mutated in some individuals with autism, is important for relaying endocannabinoid signals that tone down communication between neurons." When the researchers introduced different autism-associated mutations in neuroligin-3 into mice, this signaling was blocked and the overall excitability of the brain was changed.

"These findings point out an unexpected link between a protein implicated in autism and a signaling system that previously had not been considered to be particularly important for autism," says senior author Dr. Thomas

Südhof, also of Stanford. "Thus, the findings open up a new area of research and may suggest novel strategies for understanding the underlying causes of complex brain disorders."
The results also indicate that targeting components of the endocannabinoid signaling system may help reverse autism symptoms.
The study's findings resulted from a research collaboration between the Stanford laboratories of Dr. Südhof and Dr. Robert Malenka, who is also an author on the paper.
Neuron, Foldy et al.: "Autism-Associated Neuroligin-3 Mutations Commonly Disrupt Tonic Endocannabinoid Signaling."

http://www.eurekalert.org/pub_releases/2013-04/uotw-sns040513.php

6 new Science papers describe how Au. Sediba walked, chewed and moved

Papers report on some of the most complete early human ancestral remains ever discovered

Johannesburg - A team of South African and international scientists from the Evolutionary Studies Institute (ESI) at the University of the Witwatersrand (Wits) and 15 other global institutions, are publishing six papers and an introduction by Prof. Lee Berger, the lead author and project leader, in the prestigious journal Science tomorrow, Friday, 12 April 2013.
The papers report on some of the most complete early human ancestral remains ever discovered. The 2-million-year-old fossils belong to the species Australopithecus sediba (Au. sediba) and provide what Berger, from the Wits Evolutionary Studies Institute, describes as "unprecedented insight into the anatomy and phylogenetic position of an early human ancestor".
The six papers represent the culmination of more than four years of research into the anatomy of Au. sediba based on the holotype and paratype skeletons commonly referred to as MH1 and MH2, as well as the adult isolated tibia referred to as MH4. The fossil remains were discovered at the site of Malapa in August of 2008, and the species was named in 2010 by Berger and his colleagues. The articles presented in Science complete the initial examination of the prepared material attributed to these three individuals.
The papers are entitled: Dental morphology and the phylogenetic "place" of Australopithecus sediba; Mandibular remains support taxonomic validity of Australopithecus sediba; The upper limb of Australopithecus sediba; Mosaic morphology in the thorax of Australopithecus sediba; The vertebral column of Australopithecus sediba; and The lower limb and the mechanics of walking in Australopithecus sediba, with the introduction entitled The Mosaic Anatomy of Australopithecus sediba.
In essence, the six studies describe how the 2-million-year-old Au. sediba walked, chewed and moved.
Berger summarises that Au. sediba provides us with the most comprehensive examination of the anatomy of a definitive single species of early hominin. "This examination of a large number of associated, often complete and undistorted elements, gives us a glimpse of a hominin species that appears to be mosaic in its anatomy and that presents a suite of functional complexes that are both different from that predicted for other australopiths, as well as that for early Homo.
Such clear insight into the anatomy of an early hominin species will clearly have implications for interpreting the evolutionary processes that affected the mode and tempo of hominin evolution and the interpretation of the anatomy of less well preserved species," says Berger.
"Aside from the 26 authors from 16 institutions involved in these publications, the team focusing its research efforts on Au. sediba and Malapa now numbers more than 100 researchers from around the world and represents one of the largest dedicated archaeological or palaeontological research programmes," says Prof. Loyiso Nongxa, Vice-Chancellor and Principal of the University of the Witwatersrand. Berger adds that the work undertaken to date, although only five years in the making (since the discovery of the site in mid-2008), represents some of the most extensive focused literature on a single early hominin species yet created.
Included in the recent discoveries from the site are a new species of fox, named by the team as Vulpes skinneri just three months ago, and the discovery of more than 300 early human ancestor remains, including parts of skeletons still encased in rock.
Berger concludes: "Discoveries such as Australopithecus sediba and the Malapa site demonstrate the need for further African based exploration in the rich fossil fields of southern Africa, and additionally demonstrate the tremendous promise of the palaeosciences on the continent."

AU. SEDIBA FACT SHEET ON SIX PAPERS

Introduction: Mosaic Anatomy Of Australopethicus Sediba

Prof. Lee Berger, researcher in the Wits Evolutionary Studies Institute (ESI) at the University of the Witwatersrand, project leader and lead author of the introduction entitled Mosaic Anatomy of Australopethicus Sediba, summarises that Au. sediba provides the most comprehensive examination of the anatomy of a definitive single species of early hominin.

"This examination of a large number of associated, often complete and undistorted elements, gives us a glimpse of a hominin species that appears to be mosaic in its anatomy and that presents a suite of functional complexes that are both different from that predicted for other australopiths, as well as that for early Homo," says Berger. "Such clear insight into the anatomy of an early hominin species will clearly have implications for interpreting the evolutionary processes that affected the mode and tempo of hominin evolution and the interpretation of the anatomy of less well preserved species."

Dental Morpholohy And The Phylogenetic "Place" Of Australopethicus Sediba

The first paper, by lead author Prof. Joel Irish from the Research Centre for Evolutionary Anthropology and Palaeoecology at Liverpool John Moores University in the United Kingdom and his co-authors, examines non-metric dental traits in Au. sediba.

The study concludes that the species is distinct from east African australopiths, but is close to Au. africanus, thus forming a southern African australopith clade.

The latter, in turn, shares a number of derived states with a clade comprising four fossil samples of the genus Homo. This surprising result has significant implications for our present understanding of hominin phylogeny through the terminal Pliocene, and alludes to the possibility that Au. sediba, and perhaps Au. africanus are not descendant from the Au. afarensis lineage.

Irish noted that even though the results of this study were surprising and were bound to be viewed as controversial given the long held hypotheses relating to the origins of the genus Homo he would have come to the same conclusion.

"The extreme age and rarity of these fossils naturally draws enhanced interest in and scrutiny of any new findings. Based on the evidence, I would have come up with the same conclusions whether the samples were three million or 30 years old. If I had found that Au. sediba was totally distinct from all other hominins, I would have been just has happy to report that," says Irish.

Manidbular Remains Support Taxonomic Validity Of Australopethicus Sediba

Prof. Darryl de Ruiter from the Department of Anthropology, Texas A&M and the Evolutionary Studies Institute at the University of the Witwatersrand, and his co-authors examine new mandibular material attributable to MH2, including the previously unknown mandibular incisors and premolars of Au. sediba held in a spectacular new mandibular specimen associated with the female paratype specimen.

The study concludes, as is seen elsewhere in the cranium and skeleton, these mandibular remains share similarities with other australopiths, but can be differentiated from the southern African ape-man Au. africanus in both size and shape, as well as in their unique ontogenetic growth trajectory.

"These results add further support to the claim that Au. sediba is taxonomically distinct from the temporally – and geographically – close species Au. africanus. Where the Au. sediba mandibles differ from those of Au. africanus, they appear most similar to representatives of early Homo," says De Ruiter.

He adds that "everywhere we look in these skeletons, from the jaws on down to the feet, we see evidence of the transition from australopith to Homo; everywhere we see evidence of evolution."

The Upper Limb Of Australopethicus Sediba

In the third paper by Prof. Steven Churchill from the Department of Evolutionary Anthropology at Duke University and the Evolutionary Studies Institute at University of the Witwatersrand, he and his co-authors describe new, remarkably well preserved upper limb elements of Au. sediba.

The paper announces the first complete (or nearly complete) and undistorted humerus, radius, ulna, scapula, clavicle and manubrium (a frontal chest bone) yet described from the early hominin record, all associated with one individual.

The authors note that with the exception of the hand skeleton (which exhibits a suite of derived features that may signal enhanced manipulative capabilities relative to earlier australopiths), the upper limbs of the Malapa hominins are largely primitive in their morphology. Au. sediba thus shares with other australopiths an upper limb that was well-suited for arboreal or other forms of climbing and possibly suspension, though perhaps more so than has been previously suggested for any other member of this genus.

Churchill adds that "it is possible that the climbing features in the skeleton of Australopithecus sediba and other australopiths are functionally unimportant primitive traits retained from a more arboreal ancestor. Even so, it is curious that these features persist unchanged for several million years, only to abruptly disappear with the emergence of the genus Homo."

Mosaic Morphology In The Thorax Of Australopethicus Sediba

Remains of the rib cage of Au. sediba are described in the fourth paper by Dr Peter Schmid and his co-authors at the Evolutionary Studies Institute at the University of the Witwatersrand and the University of Zurich.

Their findings reveal a mediolaterally-narrow upper thorax like that of the large-bodied apes, and unlike the broad, cylindrical chest seen in humans. In conjunction with the largely complete remains of the shoulder girdle, Schmid notes that "the morphological picture that emerges is one of a conical thorax with a high shoulder joint that produces in Au. sediba an ape-like "shrugged" shoulder appearance, and thus a configuration that is perhaps uniquely australopith, and that would not have been conducive to human-like swinging of the arms during bipedal striding and running".
The research however shows that the less well-preserved elements of the lower rib cage suggest a degree of human-like, mediolateral narrowing to the lower thorax. This indicates a surprising and rather unsuspected mosaic anatomy in the chest that is not like that observed in H. erectus or H. sapiens.

The Vertebral Column Of Australopethicus Sediba

Dr Scott Williams from the Center for the Study of Human Origins, Department of Anthropology, New York University and co-authors on the fifth paper describing the vertebral column of Au. sediba is the first paper to analyse elements of the cervical, thoracic, lumbar, and sacral regions of the vertebral column in Au. sediba. Among the material described is a remarkably articulated lumbar vertebral region that shows a human-like curvature of the lower back. Williams notes that "the adult female is the first early hominin skeleton that preserves an intact terminal thoracic region and this provides critical information on the transition in inter-vertebral joints, and, by inference, mobility of the lower back".
The study also demonstrates that Au. sediba had the same number of lumbar vertebrae as modern humans, but possessed a functionally longer and more flexible lower back. In addition, morphological indicators of strong lumbar curvature suggest that Au. sediba was derived in this regard relative to Au. africanus and more similar to the Nariokotome Homo erectus skeleton.

The Lower Limb And The Mechanics Of Walking In Australopethicus Sediba

The sixth paper by Dr Jeremy DeSilva and his co-authors at Boston University and the Evolutionary Studies Institute at the University of the Witwatersrand describes the lower limb anatomy of Au. sediba is described and a specific biomechanical hypothesis is proposed as to how this species walked.
"The female Australopithecus sediba preserves a heel, ankle, knee, hip and lower back- all of the ingredients necessary to reconstruct how she walked with remarkable precision. Even the famous Lucy skeleton only preserves two of these five (ankle and hip)", says DeSilva.
In isolation, the anatomies of the heel, mid-foot, knee, hip, and back are unique and curious, but in combination, they are internally consistent for a biped walking with a hyper-pronating gait.
"The implications of this study are that multiple forms of bi-pedalism were once practiced by our early hominin ancestors," adds Berger.

http://www.eurekalert.org/pub_releases/2013-04/sri-sfi040913.php

Study finds interferon, one of the body's proteins, induces persistent viral infection

The findings suggest a new approach to clearing infections from AIDS to hepatitis

LA JOLLA, CA - Scientists at The Scripps Research Institute (TSRI) have made a counterintuitive finding that may lead to new ways to clear persistent infection that is the hallmark of such diseases as AIDS, hepatitis B and hepatitis C.
The study, reported in the April 12, 2013 issue of the journal Science, focused on the activity of the body's type 1 interferon (IFN-I) proteins. Since its discovery over 50 years ago, IFN-I has been believed to be an especially powerful antiviral agent that marshals the immune system's response against the body's foreign invaders. But in the new study, the TSRI scientists document in mice that IFN-I initiates persistent infection and limits the generation of an effective antiviral immune response.
"Our findings illuminate an unexpected role for IFN-I protein(s) in persistent infections, which has major implications for how we treat these infections," said Michael B. A. Oldstone, a professor in the Department of Immunology and Microbial Science at TSRI and senior investigator for the study.
Mystery of Immune Suppression
For decades, Oldstone and other virologists around the world have been trying to understand how some viruses manage to persist in their hosts.
One big clue, discovered only in recent years, is that some of these viruses are especially effective at getting into cells of the immune system known as dendritic cells. These cells serve as key detectors of infection and normally respond to viral infection by producing IFN-I proteins. They also produce both immune-enhancing proteins (cytokines/chemokines) to drive forward a vigorous immune response, as well as immune-suppressing

proteins including interleukin-10 (IL-10) and PD-1, which act as a braking system that balances the immune response to keep within healthy (non-autoimmune) limits.
Persistent viruses can use this immune-suppressing effect for their own purposes. In several experimental models of persistent infections and in humans with persistent infections, a rise in IL-10 and PD-L1 is followed by declines in the function and numbers of antiviral T-cells. Many of the surviving T cells are rendered ineffectual - a phenomenon called "T-cell exhaustion" or "hyporesponsiveness."

A Surprising Observation

To better understand how this immune-suppressing response develops, Oldstone and his team, including first authors John R. Teijaro and Cherie Ng, along with Brian Sullivan, looked in detail at the early events in a persistent viral infection. The team used a now-standard animal model that Oldstone developed almost 30 years ago: laboratory mice infected with lymphocytic choriomeningitis virus (LCMV) Clone (Cl) 13 strain.
One initial observation surprised them. "A day after infection, bloodstream levels of IFN-I were at least several times higher in the persistent infection, compared to a non-persistent LCMV infection," said Teijaro.
The persistent LCMV Cl 13 strain also turned out to be much better at infecting plasmacytoid dendritic cells - which are considered the principal source of IFN-I proteins during viral infections. By contrast, the LCMV Armstrong (ARM) 53b strain, from which Cl 13 was derived, generated significantly less IFN-I and did not induce a persistent infection but rather generated antiviral effector CD8 T cells; this infection was terminated within 7 to 10 days. Cl 13 differs from ARM by only three amino acids (protein building blocks) of which just two are important; one in the glycoprotein for binding and entry into dendritic cells and the other in the viral polymerase that enhances viral replication.

Earlier Clearance and Fewer Malfunctions

The production of IFN-Is by plasmacytoid dendritic cells has been considered a normal and beneficial part of the immune reaction to a viral infection. "We usually think of IFN-I proteins as antiviral proteins, so that more IFN is better," said Ng. Indeed, when she and Teijaro used a monoclonal antibody to block IFN-I-alpha-beta (-α-β) receptor, activity just prior to or after infection with Cl 13, they observed a sharp drop in the production of IL-10 and PD-L1, loss of excessive cytokine/chemokine expression (cytokine storm) and maintenance of normal secondary lymphoid tissue architecture.
But the scientists found over the longer term a sharp drop in levels of immune-suppressing IL-10, as well as PD-L1, both inducers of T-cell exhaustion, was associated with restoration of antiviral immune response and virus clearance. And although blocking the IFN-I-α-β receptor led to higher bloodstream levels of virus in the first days after infection, it soon brought about a stronger, infection-clearing response.
"Even when we blocked IFN-I-α-β receptor after a persistent infection had been established and T-cell exhaustion had set in, we still saw a significantly earlier clearance of the virus," Ng said.
Blocking IFN-I-α-β receptor also prevented or reversed other immune malfunctions caused by the persistent LCMV strain, including a disruption of the structure of the spleen tissue and diminished T cell entry and maintenance within lymphoid structures in the spleen that contain dendritic cells. The interaction of dendritic cells with T cells is necessary to generate antiviral effector CD8 and CD4 T cells. "We saw a restoration of this lymphoid architecture, as well as an increase in a subset of antiviral T cells, natural killer cells and dendritic cells, and restoration of antiviral CD4 T cell function," said Teijaro.

Potentially Broad Applications

Oldstone and his team now plan to study IFN-I signaling pathways in further detail. In particular, they hope to determine whether the IFN-I-α-β receptor blocking strategy can work against chronic viral infections in humans. The scientists will also seek small pharmacologic molecules with the same function.
"Most of our findings in the LCMV model mirror what has been observed in human persistent infections, namely the upregulation of IL-10 and PD-L1, and the disruption of lymphoid architecture," said Oldstone.
Conceivably, the IFN-I-α-β receptor-blocking strategy could have broad clinical applications. In terms of viruses alone, chronic HIV, hepatitis B and hepatitis C infections collectively are found in hundreds of millions of people worldwide. Other common persistent viruses include Epstein-Barr virus, cytomegalovirus and cancer-causing human papilloma virus. Researchers have estimated that the average person at any one time carries at least several persistent, often silent viral infections.

Other contributors to the study, "Persistent LCMV infection is controlled by blockade of type 1 interferon signaling," were Kathleen C. F. Sheehan and Robert D. Schreiber of Washington School of Medicine at St. Louis; and Megan J. Welch, Andrew M. Lee, and Juan Carlos de la Torre of TSRI.

The study was supported by the National Institutes of Health grants AI009484, AI057160 and AI077719, as well as an American Heart Association Fellowship (11POST7430106).

http://www.eurekalert.org/pub_releases/2013-04/uom-sia041113.php

Self-medication in animals much more widespread than believed

The practice of animal self-medication is a lot more widespread than previously thought

Mark Hunter

ANN ARBOR - It's been known for decades that animals such as chimpanzees seek out medicinal herbs to treat their diseases. But in recent years, the list of animal pharmacists has grown much longer, and it now appears that the practice of animal self-medication is a lot more widespread than previously thought, according to a University of Michigan ecologist and his colleagues.

Animals use medications to treat various ailments through both learned and innate behaviors. The fact that moths, ants and fruit flies are now known to self-medicate has profound implications for the ecology and evolution of animal hosts and their parasites, according to Mark Hunter, a professor in the Department of Ecology and Evolutionary Biology and at the School of Natural Resources and Environment.

In addition, because plants remain the most promising source of future pharmaceuticals, studies of animal medication may lead the way in discovering new drugs to relieve human suffering, Hunter and two colleagues wrote in a review article titled "Self-Medication in Animals," to be published online today in the journal Science. "When we watch animals foraging for food in nature, we now have to ask, are they visiting the grocery store or are they visiting the pharmacy?" Hunter said. "We can learn a lot about how to treat parasites and disease by watching other animals."

Much of the work in this field has focused on cases in which animals, such as baboons and woolly bear caterpillars, medicate themselves. One recent study has suggested that house sparrows and finches add high-nicotine cigarette butts to their nests to reduce mite infestations.

But less attention has been given to the many cases in which animals medicate their offspring or other kin, according to Hunter and his colleagues. Wood ants incorporate an antimicrobial resin from conifer trees into their nests, preventing microbial growth in the colony. Parasite-infected monarch butterflies protect their offspring against high levels of parasite growth by laying their eggs on anti-parasitic milkweed.

Hunter and his colleagues suggest that researchers in the field should "de-emphasize the 'self' in self-medication" and base their studies on a more inclusive framework.

"Perhaps the biggest surprise for us was that animals like fruit flies and butterflies can choose food for their offspring that minimizes the impacts of disease in the next generation," Hunter said. "There are strong parallels with the emerging field of epigenetics in humans, where we now understand that dietary choices made by parents influence the long-term health of their children."

The authors argue that animal medication has several major consequences on the ecology and evolution of host-parasite interactions. For one, when animal medication reduces the health of parasites, there should be observable effects on parasite transmission or virulence. For example, when gypsy moth caterpillars consume foliage high in certain toxic compounds, transmission of viruses between the caterpillars is reduced, facilitating moth outbreaks.

In addition, animal medication should affect the evolution of animal immune systems, according to Hunter and his colleagues. Honeybees are known to incorporate antimicrobial resins into their nests. Analysis of the honeybee genome suggests that they lack many of the immune-system genes of other insects, raising the possibility that honeybees' use of medicine has been partly responsible - or has compensated - for a loss of other immune mechanisms.

The authors also note that the study of animal medication will have direct relevance for human food production. Disease problems in agricultural organisms can worsen when humans interfere with the ability of animals to medicate, they point out. For example, increases in parasitism and disease in honeybees can be linked to selection by beekeepers for reduced resin deposition by their bees. A reintroduction of such behavior in managed bee colonies would likely have great benefits for disease management, the authors say.

The first author of the Science paper is Jacobus de Roode of Emory University. The other author is Thierry Lefevre of the Institut de Recherche pour le Developpement in France.

http://www.eurekalert.org/pub_releases/2013-04/nesc-spa041213.php

Study proposes alternative way to explain life's complexity

Evolution skeptics argue that some biological structures, like the brain or the eye, are simply too complex for natural selection to explain.

Durham, NC - Biologists have proposed various ways that so-called 'irreducibly complex' structures could emerge incrementally over time, bit by bit. But a new study proposes an alternative route. Instead of starting from simpler precursors and becoming more intricate, say authors Dan McShea and Wim Hordijk, some structures could have evolved from complex beginnings that gradually grew simpler - an idea they dub "complexity by

subtraction." Computer models and trends in skull evolution back them up, the researchers show in a study published this week in the journal Evolutionary Biology.
Some biological structures are too dizzyingly complex to have emerged stepwise by adding one part and then the next over time, intelligent design advocates say. Consider the human eye, or the cascade that causes blood to clot, or the flagellum, the tiny appendage that enables some bacteria to get around. Such all-or-none structures, the argument goes, need all their parts in order to function. Alter or take away any one piece, and the whole system stops working. In other words, what good is two thirds of an eye, or half of a flagellum?
For the majority of scientists, the standard response is to point to simpler versions of supposedly 'irreducibly complex' structures that exist in nature today, such as cup eyes in flatworms. Others show how such structures could have evolved incrementally over millions of years from simpler precursors. A simple eye-like structure - say, a patch of light-sensitive cells on the surface of the skin - could evolve into a camera-like eye like what we humans and many other animals have today, biologists say.
"Even a very simple eye with a small number of parts would work a little. It would be able to detect shadows, or where light is coming from," said co-author Dan McShea of Duke University.
In a new study, McShea and co-author Wim Hordijk propose an alternative route. Instead of emerging by gradually and incrementally adding new genes, cells, tissues or organs over time, what if some so-called 'irreducibly complex' structures came to be by gradually losing parts, becoming simpler and more streamlined? Think of naturally occurring rock arches, which start as cliffs or piles of stone and form when bits of stone are weathered away. They call the principle 'complexity by subtraction.'
"Instead of building up bit by bit from simple to complex, you start complex and then winnow out the unnecessary parts, refining them and making them more efficient as you go," McShea said.
A computer model used by co-author Wim Hordijk supports the idea. In the model, complex structures are represented by an array of cells, some white and some black, like the squares of a checkerboard. In this class of models known as cellular automata, the cells can change between black and white according to a set of rules. Using a computer program that mimics the process of inheritance, mutation, recombination, and reproduction, the cells were then asked to perform a certain task. The better they were at accomplishing the task, the more likely they were to get passed on to the next generation, and over time a new generation of rules replaced the old ones. In the beginning, the patterns of black and white cells that emerged were quite complex. But after several more generations, some rules 'evolved' to generate simpler black and white cell patterns, and became more efficient at performing the task, Hordijk said.
We see similar trends in nature too, the authors say. Summarizing the results of previous paleontological studies, they show that vertebrate skulls started out complex, but have grown simpler and more streamlined. "For example, the skulls of fossil fish consist of a large number of differently-shaped bones that cover the skull like a jigsaw puzzle," McShea said. "We see a reduction in the number of skull bone types in the evolutionary transitions from fish to amphibian to reptile to mammal." In some cases skull bones were lost; in other cases adjacent bones were fused. Human skulls, for example, have fewer bones than fish skulls.
Computer simulations like Hordijk's will allow scientists to test ideas about how often 'complexity by subtraction' happens, or how long it takes. The next step is to find out how often the phenomenon happens in nature.
"What we need to do next is pick an arbitrary sample of complex structures and trace their evolution and see if you can tell which route they proceeded by, [from simple to complex or the opposite]. That will tell us whether this is common or not," McShea added.
McShea, D. and W. Hordijk (2013). "Complexity by subtraction." Evolutionary Biology. http://dx.doi.org/10.1007/s11692-013-9227-6

http://www.eurekalert.org/pub_releases/2013-04/uow-nbf041213.php

New bird flu strain seen adapting to mammals, humans

A genetic analysis of the avian flu virus responsible for at least nine human deaths in China portrays a virus evolving to adapt to human cells, raising concern about its potential to spark a new global flu pandemic.

Terry Devitt

MADISON – The collaborative study, conducted by a group led by Masato Tashiro of the Influenza Virus Research Center, National Institute of Infectious Diseases, and Yoshihiro Kawaoka of the University of Wisconsin-Madison and the University of Tokyo, appears in the current edition (April 11, 2013) of the journal Eurosurveillance. The group examined the genetic sequences of H7N9 isolates from four of the pathogen's human victims as well as samples derived from birds and the environs of a Shanghai market.
"The human isolates, but not the avian and environmental ones, have a protein mutation that allows for efficient growth in human cells and that also allows them to grow at a temperature that corresponds to the upper

respiratory tract of humans, which is lower than you find in birds," says Kawaoka, a leading expert on avian influenza.
The findings, drawn from genetic sequences deposited by Chinese researchers into an international database, provide some of the first molecular clues about a worrisome new strain of bird flu, the first human cases of which were reported on March 31 by the Chinese Center for Disease Control and Prevention. So far, the new virus has sickened at least 33 people, killing nine. Although it is too early to predict its potential to cause a pandemic, signs that the virus is adapting to mammalian and, in particular, human hosts are unmistakable, says Kawaoka.
Access to the genetic information in the viruses, he adds, is necessary for understanding how the virus is evolving and for developing a candidate vaccine to prevent infection.
Influenza virus depends on its ability to attach to and commandeer the living cells of its host to replicate and spread efficiently. Avian influenza rarely infects humans, but can sometimes adapt to people, posing a significant risk to human health.
"These viruses possess several characteristic features of mammalian influenza viruses, which likely contribute to their ability to infect humans and raise concerns regarding their pandemic potential," Kawaoka and his colleagues conclude in the Eurosurveillance report.
Kawaoka, a faculty member in the UW-Madison School of Veterinary Medicine who also holds a faculty appointment at the University of Tokyo, explains that the majority of the viruses in the study - from both humans and birds - display mutations in the surface protein hemagglutinin, which the pathogen uses to bind to host cells. Those mutations, according to Kawaoka, allowed them to easily infect human cells.
In addition, the isolates from patients contained another mutation that allows the virus to efficiently replicate inside human cells. The same mutation, Kawaoka notes, lets the avian virus thrive in the cooler temperatures of the human upper respiratory system. It is in the cells of the nose and throat that flu typically gains a hold in a mammalian or human host.
Kawaoka and his colleagues also assessed the response of the new strain to drugs used to treat influenza, discovering that one class of commonly used antiviral drugs, ion channel inhibitors which effectively bottle up the virus in the cell, would not be effective; the new strain could be treated with another clinically relevant antiviral drug, oseltamivir.
In addition to Kawaoka and Tashiro, co-authors of the Eurosurveillance report include Tsutomu Kageyama, Seiichiro Fujisaki, Emi Takashita, Hong Xu, Shinya Yamada, Yuko Uchida, Gabriele Neumann and Takehiko Saito. The work was supported by Grants-in-Aid for Pandemic Influenza Research and Grant-in-Aid for Specially Promoted Research from the Ministry of Health, Labour and Welfare, Japan; by the NIAID Center for Research on Influenza Pathogenesis (CRIP, HHSN266200700010C); by a Grant-in-Aid for Specially Promoted Research, by the Japan Initiative for Global Research Network on Infectious Diseases from the Ministry of Education, Culture, Sports, Science, and Technology, Japan; and by ERATO, Japan.

http://www.sciencedaily.com/releases/2013/04/130412132229.htm

The Power of Cocoa Polyphenols Against Neurodegenerative Diseases

Epidemiological studies have indicated that dietary habits and antioxidants from diet can influence the incidence of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases.

In the recent years, a number of papers have reported on neuroprotective effects of polyphenols in cell and animal models. However, the majority of these studies have focused only on the anti-oxidant properties of these compounds and less on the mechanism/s of action at cellular and molecular levels.
Now, a new study from the Sbarro Health Research Organization (SHRO, Center for Biotechnology, Temple University, Philadelphia PA USA) and the University of L'Aquila (Italy) shows that cocoa polyphenols triggers neuroprotection by activating BDNF survival pathway, both on Aß plaque treated cells and on Aß oligomers treated cells, resulting in the counteraction of neurite dystrophy.
The findings, published on Journal of Cellular Biochemistry, may have important implications for prevention of cognitive impairment in elderly and in neurodegenerative diseases in counteracting disease's progression. "Our studies indicate for the first time the cocoa polyphenols do not act only as mere anti-oxidant but they, directly or indirectly, activate the BDNF survival pathway counteracting neuronal death" says Annamaria Cimini of the University of L'Aquila, lead author of the study.
"Understanding the preventive potential and the mechanism of action of functional food may provide a means to limit cognitive impairment progression" says Antonio Giordano, founder and director of the Sbarro Institute for Cancer Research and Molecular Medicine.

http://www.bbc.co.uk/news/health-22106939

Why are school nurses important?

School nurses were once seen simply as nit seekers, but children's safety and emotional wellbeing are now their primary concern.

By Philippa Roxby Health reporter, BBC News

The government has announced that children will help to train school nurses in how to provide the best support as part of a "strengthened and more tailored school nursing service". Yet there are only 1,200 of them in England, and about 20,000 primary and secondary schools. So why is their role still so important?

The poor health of army recruits in the 1890s is thought to have created the need for nurses to look after the health of children and young people.

In the early 1900s, these public health nurses were concerned with hygiene and the spread of disease, frequently dealing with outbreaks of flu and cholera.

White coats

The first school nurse worked in Bolton, caring for the poor in their own homes, and then in the 1960s and 70s school nurses began wearing white coats, answering to doctors and brandishing nit combs.

But the "Nitty Nora" image of school nurses combing through children's hair is one the profession has long been trying to shed.

"The role has always been about promoting public health with children and families," says Sharon White, professional officer with the School and Public Health Nurses Association (SAPHNA), which represents school nurses.

"But their work now covers around 50 different facets, ranging from acne to sexual exploitation, self harm to sleep problems - all those issues centred around the holistic health of children."

Team work

Immunising children, measuring their height and weight, running drop-in clinics and teaching part of the PSHE (personal, social and health education) curriculum are just a few more of the jobs they can be asked to do.

Depending on the needs of the local population, school nursing resources have to be focused on some areas more than others.

They do not work alone either. Qualified school nurses are part of a team of health professionals who help share the load.

"Sometimes the school nurse may seem invisible, but she is spending time on the neediest, complex families and on safeguarding issues," says Sharon White."And there's a difference between accessibility and invisibility."

School nurses say they have a unique position working with children aged from five to 19 years. They can have one-to-one conversations with them in a way that teachers often feel unable to do. They also offer greater confidentiality - and a link between home and school.

'Approachable'

Helen Ross is an executive board member of SAPHNA. She started school nursing in 1989 and has seen many changes since then.

She and her team now spend 70% of their time on trying to protect children, which she says is the right thing to do following the cases of Baby P and Victoria Climbie,

"School nurses are approachable and non-judgemental. We're in a position to be able to support young people - and they have a voice we must listen to."

The Department of Health's new vision for school nursing wants to take this further by making nurses more visible and more relevant.

It started with a promise last year to make it easier to contact school nurses, by texting them to make appointments. Now 300 young people will be chosen to help shape the services which school nurses provide.

Nurse numbers

Caroline Voogd, the editor of the British Journal of School Nursing, understands why this is important.

"Visibility has been poor. Involving young people ensures that they know the school nurse exists."

But it is still a small workforce. While there were 2,415 registered school nurses in England in 2008, according to the Nursing and Midwifery Council, numbers went down to 1,138 in May 2010 - then up again a little to 1,216 by the end of 2012.

Even if services are as made as efficient as possible, Voogd believes there should still be more qualified school nurses. "You can increase performance and productivity but that only goes so far. School nurses can play a massive part in public health but there need to be more of them."

http://www.sciencedaily.com/releases/2013/04/130412132321.htm

L-Carnitine Significantly Improves Patient Outcomes Following Heart Attack, Study Suggests

L-carnitine significantly improves cardiac health in patients after a heart attack, say a multicenter team of investigators in a study published today in Mayo Clinic Proceedings.

Their findings, based on analysis of key controlled trials, associate L-carnitine with significant reduction in death from all causes and a highly significant reduction in ventricular arrhythmias and anginal attacks following a heart attack, compared with placebo or control.

Heart disease is the leading cause of death in the United States. Although many of the therapies developed in recent decades have markedly improved life expectancy, adverse cardiovascular events such as ventricular arrhythmias and angina attacks still occur frequently after an acute myocardial infarction (heart attack).

It is known that during ischemic events L-carnitine levels are depleted. Investigators sought to determine the effects of targeting cardiac metabolic pathways using L-carnitine to improve free fatty acid levels and glucose oxidation in these patients. By performing a systematic review and meta-analysis of the available studies published over several decades, they looked at the role of L-carnitine compared with placebo or control in patients experiencing an acute myocardial infarction.

L-carnitine is a trimethylamine which occurs in high amounts in red meat and is found in certain other foods, and is also widely available as an over-the-counter nutritional supplement which is claimed to improve energy, weight loss, and athletic performance. Its potential role in treating heart disease was first reported in the late 1970s. A comprehensive literature search yielded 153 studies, 13, published from 1989-2007, were deemed eligible. All the trials were comparison trials of L-carnitine compared with placebo or control in the setting of acute myocardial infarction.

This systematic review of the 13 controlled trials in 3,629 patients, involving 250 deaths, 220 cases of new heart failure, and 38 recurrent heart attacks, found that L-carnitine was associated with:

- ***Significant 27% reduction in all-cause mortality (number needed to treat 38)***
- ***Highly significant 65% reduction in ventricular arrhythmias (number needed to treat 4)***
- ***Significant 40% reduction in the development of angina (number needed to treat 3)***
- ***Reduction in infarct size***

There were numerically fewer myocardial reinfarctions and heart failure cases associated with L-carnitine, but this did not reach statistical significance.

First author James J. DiNicolantonio, PharmD, Wegmans Pharmacy, Ithaca, NY, observes, "Although therapies for acute coronary syndrome (ACS), including percutaneous coronary intervention, dual antiplatelet therapy, b-blockers (BBs), statins, angiotensin-converting enzyme inhibitors (ACEIs), omega-3 fatty acids, and cardiac rehabilitation, have markedly improved clinical outcomes, adverse cardiovascular (CV) events still occur too frequently after ACS. One promising therapy for improving cardiac health involves using L-carnitine to improve free fatty acid levels and glucose oxidation."

"The potential mechanisms responsible for the observed beneficial impact of L-carnitine in acute myocardial infarction are likely multifactorial and may, in part, be conferred through the ability of L-carnitine to improve mitochondrial energy metabolism in the heart by facilitating the transport of long-chain fatty acids from the cytosol to the mitochondrial matrix, where b-oxidation occurs, removing toxic fatty acid intermediates, reducing ischemia induced by long-chain fatty acid concentrations, and replenishing depleted carnitine concentrations seen in ischemic, infarcted, and failing myocardium," says DiNicolantonio.

L-carnitine is proven to be safe and is readily available over the counter. The investigators agree that the overall results of this meta-analysis support the potential use of L-carnitine in acute myocardial infarction and possibly in secondary coronary prevention and treatment, including angina. They advocate for a larger randomized, multicenter trial to be performed to confirm these results in the modern era of routine revascularization and other intensive medical therapies following acute myocardial infarction. But, says DiNicolantonio, "L-carnitine therapy can already be considered in selected patients with high-risk or persistent angina after acute myocardial infarction who cannot tolerate treatment with ACE inhibitors or beta blockers, considering its low cost and excellent safety profile."

These findings may seem to contradict those reported in a study published earlier this month in Nature Medicine by Robert A. Koeth and others (link below), which demonstrated that metabolism by intestinal microbiota of dietary L-carnitine produced trimethylamine N-oxide (TMAO) and accelerated atherosclerosis in mice. They also noted that omnivorous human subjects produced more TMAO than did vegans or vegetarians following ingestion of L-carnitine, and suggested a possible direct link between L-carnitine, gut bacteria, TMAO, and atherosclerosis and risk of ischemic heart disease.

"The Nature Medicine paper is of interest," agrees senior investigator Carl J. Lavie, M.D.,FACC,FACP,FCCP, Medical Director of the Cardiac Rehabilitation and Prevention Center at the John Ochsner Heart and Vascular Institute at the University of Queensland School of Medicine in New Orleans, "but the main study reported there was in animals, and unlike our study, lacks hard outcomes." He also notes that "there are various forms of 'carnitine' and our relatively large meta-analysis specifically tested L-carnitine on hard outcomes in humans who had already experienced acute myocardial infarction."

James J. DiNicolantonio, Carl J. Lavie, Hassan Fares, Arthur R. Menezes and James H. O'Keefe. L-Carnitine in the Secondary Prevention of Cardiovascular Disease: Systematic Review and Meta-analysis. Mayo Clinic Proceedings, June 2013; Volume 88, Issue 6 DOI: 10.1016/j.mayocp.2013.02.007

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http://nyti.ms/YmoK2s

DNA Project Aims to Make Public a Company's Data on Cancer Genes

Anyone in the United States who wants to know if she has mutations in two breast cancer genes has little choice of where to be tested. One company alone has patents on the genes, and that company pretty much controls the market.

By GINA KOLATA

On Monday, the Supreme Court will take up the issue of whether companies can own patents on genes. But there is another issue, often overlooked, that might make the patent question beside the point. No matter which way the patent decision goes, the company, Myriad Genetics, will still own the largest database that tells patients what various mutations mean.

With 17 years of experience, millions of tests looking for thousands of mutations in the genes, and a $500 million investment, the company was able to amass a huge database that tells which DNA changes increase cancer risk and by how much, and which are inconsequential blips in DNA. And it is keeping that data to itself.

Some genetics researchers are furious and have now figured out a way to get the data anyway. Every time Myriad sends out a report on a gene test, it specifies not just the mutations it found but also what they mean. As a result, Myriad's data on each of the mutations is scattered in millions of reports in the hands of doctors and patients. If the geneticists could just gather those reports, they say, they can recreate Myriad's database.

So they started a grass-roots project, Sharing Clinical Reports, and are asking cancer clinics and doctors to provide them with all the Myriad data they have from patients who have been tested.

None of the data have names of patients or other identifiers, so confidentiality is not an issue, advocates say. But their task is huge because the amount of data needed is vast. The project's leader, Dr. Robert L. Nussbaum, chief of the division of genomic medicine at the University of California, San Francisco, estimates that with about 1,000 mutations collected so far, he has only about 1.5 percent of what Myriad has.

"Myriad is probably laughing at me, saying, 'Here is this little flea,' " Dr. Nussbaum said.

The story began in 1996, when Myriad got patents on the two isolated DNA molecules known as the BRCA1 and BRCA2 genes and provided a test to determine if the genes carried mutations. The company realized, though, that it would be crucial to figure out how risky each mutation was.

That sort of analysis requires linking the mutations to people's cancer history. Obtaining that data is a momentous project, said Mark Capone, president of Myriad Genetic Laboratories, a wholly owned Myriad subsidiary. In 1996, the company classified 40 percent of mutations as being of uncertain significance because it did not have enough information to know what they meant. By 2004, the figure was down to 20 percent. Now it is just 3 percent.

Mr. Capone explained how the work is done. The company finds a mutation and is not certain what it means. To find out, it needs to see the same mutation in at least 20 other people, asking whether they had cancer and, if so, what type. So Myriad offers free testing to other family members to get more information.

Until 2004, Myriad posted its data on a site for researchers. But, Mr. Capone said, the company became aware of problems with the way its data were being used. For example, he said, the person running the database part time updated it only every couple of months. And the database included risk estimates submitted by laboratories all over the world, not just by Myriad.

"We might classify a mutation one way, and someone else might call it something different," Mr. Capone said. That is fine if the data were being used as intended — for research purposes only. But instead, they were being used to tell patients their cancer risk and to make major medical decisions.

Myriad's database, Mr. Capone said, is highly regulated. "We can only use our database to provide clinical results for patients who had their genes sequenced in our lab," he said. So, he said, when the company became aware of how the research database was being used, "we had to act — we didn't have any choice."
Myriad stopped posting its data.
Dr. Nussbaum does not buy that argument. "The Myriad approach is a big black box," he said. "It's a 'trust us, we know best' approach." And, he said, "it is contrary to the public health."
One thing it does is preclude independent second opinions, said Sherri Bale, managing director of GeneDX, a gene testing company working with Dr. Nussbaum. Yet the consequences of some mutations are so dire that women may have their breasts and ovaries removed to protect themselves from cancer. "You are going to remove my breasts, you are going to remove my ovaries? Let me ask one other person," Dr. Bale said.
Myriad disagrees, though, saying it has licensed to LabCorp the ability to independently use its technology to search for mutations. Myriad then uses its data to say what the mutations mean.
But having one company control the data for genes is contrary to the way medicine is developing, said Heidi Rehm, a Harvard geneticist who also is working with Dr. Nussbaum.
In the not so recent past, she said, when it was difficult and expensive to determine the DNA letters that make up a gene, individual laboratories would study one or two genes and become the world's expert on them.
Today, doctors and researchers are scanning all of a patient's genes and the old system is crumbling. No one can know enough to interpret the results without a public database.
"Now it is, 'I have 22,000 genes and have to stay on top of 50 million variants,' " Dr. Rehm said. "There is just no way a single laboratory can manage that." And if companies control the data on the interpretation of results, doctors, clinical laboratories and researchers are in a quandary.
Dr. Rehm, Dr. Nussbaum, Dr. Bale and others now are working with the National Institutes of Health to start a public database of variants in all the genes that have been studied. But first, they are working on the Myriad issue.
The Myriad project began about a year ago when Dr. Nussbaum decided he and others could take matters into their own hands.
Working from home at night and on weekends, with the volunteer help of two genetics counselors, he began contacting geneticist friends and people he knew at large clinics, asking them to send in Myriad reports.
"I would say, 'How about pulling your results?' They would say, 'It's a big pain.' So I would tell them, 'I will pay you 33 cents for each variant,' " Dr. Nussbaum said, explaining that a clinic would usually end up getting about $50 if it sent in all of its patients' mutations and their interpretations. Most then agreed to do it, assigning a student who needed extra money.
Clinics that sent in at least 200 unique genetic variants would get an iPad mini.
The funds for these inducements were supplied by Peter Kolchinsky, managing director of RA Capital Management in Boston.
Dr. Kolchinsky, a scientist by training, said he would like to see many gene testing labs compete on the basis of cost, speed and customer service. But they would all share data on interpreting alterations in genes rather than creating what he called "gene- or disease-specific trade secret monopolies."
"That works for Coke, not for cancer," Dr. Kolchinsky said.

http://www.eurekalert.org/pub_releases/2013-04/cwru-osc041213.php

Ordinary skin cells morphed into functional brain cells

Scientists at CWRU School of Medicine discover new technique that holds promise for the treatment of multiple sclerosis and cerebral palsy

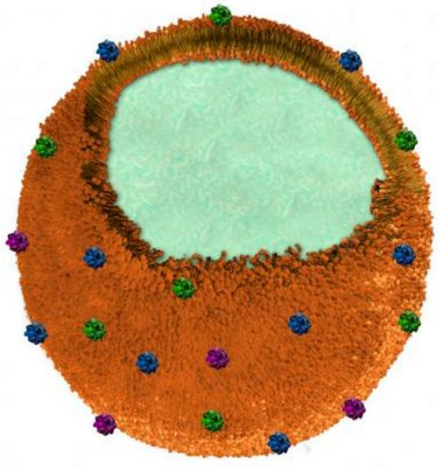
Researchers at Case Western Reserve School of Medicine have discovered a technique that directly converts skin cells to the type of brain cells destroyed in patients with multiple sclerosis, cerebral palsy and other so-called myelin disorders.
This discovery appears today in the journal Nature Biotechnology.
This breakthrough now enables "on demand" production of myelinating cells, which provide a vital sheath of insulation that protects neurons and enables the delivery of brain impulses to the rest of the body. In patients with multiple sclerosis (MS), cerebral palsy (CP), and rare genetic disorders called leukodystrophies, myelinating cells are destroyed and cannot be replaced.
The new technique involves directly converting fibroblasts - an abundant structural cell present in the skin and most organs - into oligodendrocytes, the type of cell responsible for myelinating the neurons of the brain.

"Its 'cellular alchemy,'" explained Paul Tesar, PhD, assistant professor of genetics and genome sciences at Case Western Reserve School of Medicine and senior author of the study. "We are taking a readily accessible and abundant cell and completely switching its identity to become a highly valuable cell for therapy."
In a process termed "cellular reprogramming," researchers manipulated the levels of three naturally occurring proteins to induce fibroblast cells to become precursors to oligodendrocytes (called oligodendrocyte progenitor cells, or OPCs).
Tesar's team, led by Case Western Reserve researchers and co-first authors Fadi Najm and Angela Lager, rapidly generated billions of these induced OPCs (called iOPCs). Even more important, they showed that iOPCs could regenerate new myelin coatings around nerves after being transplanted to mice—a result that offers hope the technique might be used to treat human myelin disorders.
When oligodendrocytes are damaged or become dysfunctional in myelinating diseases, the insulating myelin coating that normally coats nerves is lost. A cure requires the myelin coating to be regenerated by replacement oligodendrocytes.
Until now, OPCs and oligodendrocytes could only be obtained from fetal tissue or pluripotent stem cells. These techniques have been valuable, but with limitations.
"The myelin repair field has been hampered by an inability to rapidly generate safe and effective sources of functional oligodendrocytes," explained co-author and myelin expert Robert Miller, PhD, professor of neurosciences at the Case Western Reserve School of Medicine and the university's vice president for research. "The new technique may overcome all of these issues by providing a rapid and streamlined way to directly generate functional myelin producing cells."
This initial study used mouse cells. The critical next step is to demonstrate feasibility and safety using human cells in a lab setting. If successful, the technique could have widespread therapeutic application to human myelin disorders.
"The progression of stem cell biology is providing opportunities for clinical translation that a decade ago would not have been possible," said Stanton Gerson, MD, professor of Medicine-Hematology/Oncology at the School of Medicine and director of the National Center for Regenerative Medicine and the UH Case Medical Center Seidman Cancer Center. "It is a real breakthrough."
Additional co-authors of the publication include Case Western Reserve School of Medicine researchers Anita Zaremba, Krysta Wyatt, Andrew Caprariello, Daniel Factor, Robert Karl, and Tadao Maeda.
The research was supported by funding from the National Institutes of Health, the New York Stem Cell Foundation, the Mt. Sinai Health Care Foundation and Case Western Reserve University School of Medicine.

http://www.eurekalert.org/pub_releases/2013-04/uoc--nsu041013.php

Nanosponges soak up toxins released by bacterial infections and venom

Nanosponge " capable of safely removing a broad class of dangerous toxins from the bloodstream



Engineers at the University of California, San Diego have invented a "nanosponge" capable of safely removing a broad class of dangerous toxins from the bloodstream – including toxins produced by MRSA, E. coli, poisonous snakes and bees. These nanosponges, which thus far have been studied in mice, can neutralize "pore-forming toxins," which destroy cells by poking holes in their cell membranes. Unlike other anti-toxin platforms that need to be custom synthesized for individual toxin type, the nanosponges can absorb different pore-forming toxins regardless of their molecular structures. In a study against alpha-haemolysin toxin from MRSA, pre-innoculation with nanosponges enabled 89 percent of mice to survive lethal doses.
Administering nanosponges after the lethal dose led to 44 percent survival. The team, led by nanoengineers at the UC San Diego Jacobs School of Engineering, published the findings in Nature Nanotechnology April 14.

Engineers at the University of California, San Diego have invented a "nanosponge" capable of safely removing a broad class of dangerous toxins from the bloodstream, including toxins produced by MRSA, E. Coli, poisonous snakes and bees. The nanosponges are made of a biocompatible polymer core wrapped in a natural red blood cell membrane.
Zhang Research Lab

"This is a new way to remove toxins from the bloodstream," said Liangfang Zhang, a nanoengineering professor at the UC San Diego Jacobs School of Engineering and the senior author on the study. "Instead of creating specific treatments for individual toxins, we are developing a platform that can neutralize toxins caused

by a wide range of pathogens, including MRSA and other antibiotic resistant bacteria," said Zhang. The work could also lead to non-species-specific therapies for venomous snake bites and bee stings, which would make it more likely that health care providers or at-risk individuals will have life-saving treatments available when they need them most.
The researchers are aiming to translate this work into approved therapies. "One of the first applications we are aiming for would be an anti-virulence treatment for MRSA. That's why we studied one of the most virulent toxins from MRSA in our experiments," said "Jack" Che-Ming Hu, the first author on the paper. Hu, now a post-doctoral researcher in Zhang's lab, earned his Ph.D. in bioengineering from UC San Diego in 2011.
Aspects of this work will be presented April 18 at Research Expo, the annual graduate student research and networking event of the UC San Diego Jacobs School of Engineering.
Nanosponges as Decoys
In order to evade the immune system and remain in circulation in the bloodstream, the nanosponges are wrapped in red blood cell membranes. This red blood cell cloaking technology was developed in Liangfang Zhang's lab at UC San Diego. The researchers previously demonstrated that nanoparticles disguised as red blood cells could be used to deliver cancer-fighting drugs directly to a tumor. Zhang also has a faculty appointment at the UC San Diego Moores Cancer Center.
Red blood cells are one of the primary targets of pore-forming toxins. When a group of toxins all puncture the same cell, forming a pore, uncontrolled ions rush in and the cell dies.
The nanosponges look like red blood cells, and therefore serve as red blood cell decoys that collect the toxins. The nanosponges absorb damaging toxins and divert them away from their cellular targets. The nanosponges had a half-life of 40 hours in the researchers' experiments in mice. Eventually the liver safely metabolized both the nanosponges and the sequestered toxins, with the liver incurring no discernible damage.
Each nanosponge has a diameter of approximately 85 nanometers and is made of a biocompatible polymer core wrapped in segments of red blood cells membranes.
Zhang's team separates the red blood cells from a small sample of blood using a centrifuge and then puts the cells into a solution that causes them to swell and burst, releasing hemoglobin and leaving RBC skins behind. The skins are then mixed with the ball-shaped nanoparticles until they are coated with a red blood cell membrane.
Just one red blood cell membrane can make thousands of nanosponges, which are 3,000 times smaller than a red blood cell. With a single dose, this army of nanosponges floods the blood stream, outnumbering red blood cells and intercepting toxins.
Based on test-tube experiments, the number of toxins each nanosponge could absorb depended on the toxin. For example, approximately 85 alpha-haemolysin toxin produced by MRSA, 30 stretpolysin-O toxins and 850 melittin monomoers, which are part of bee venom.
In mice, administering nanosponges and alpha-haemolysin toxin simultaneously at a toxin-to-nanosponge ratio of 70:1 neutralized the toxins and caused no discernible damage.
One next step, the researchers say, is to pursue clinical trials.
The research was funded by the National Science Foundation (DMR-1216461) and the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK095168).

http://www.bbc.co.uk/news/health-22123386

Scientists make 'laboratory-grown' kidney

A kidney "grown" in the laboratory has been transplanted into animals where it started to produce urine, US scientists say.

By James Gallagher Health and science reporter, BBC News

Similar techniques to make simple body parts have already been used in patients, but the kidney is one of the most complicated organs made so far. A study, in the journal Nature Medicine, showed the engineered kidneys were less effective than natural ones. But regenerative medicine researchers said the field had huge promise.
Kidneys filter the blood to remove waste and excess water. They are also the most in-demand organ for transplant, with long waiting lists.
The researchers' vision is to take an old kidney and strip it of all its old cells to leave a honeycomb-like scaffold. The kidney would then be rebuilt with cells taken from the patient. This would have two major advantages over current organ transplants.
The tissue would match the patient, so they would not need a lifetime of drugs to suppress the immune system to prevent rejection. It would also vastly increase the number of organs available for transplant. Most organs which are offered are rejected, but they could be used as templates for new ones.

Scaffolding

The rat kidney was grown in the laboratory

Researchers at Massachusetts General Hospital have taken the first steps towards creating usable engineered kidneys. They took a rat kidney and used a detergent to wash away the old cells. The remaining web of proteins, or scaffold, looks just like a kidney, including an intricate network of blood vessels and drainage pipes. This protein plumbing was used to pump the right cells to the right part of the kidney, where they joined with the scaffold to rebuild the organ. It was kept in a special oven to mimic the conditions in a rat's body for the next 12 days.

When the kidneys were tested in the laboratory, urine production reached 23% of natural ones.

The team then tried transplanting an organ into a rat. Once inside the body, the kidney's effectiveness fell to 5%.

Yet the lead researcher, Dr Harald Ott, told the BBC that restoring a small fraction of normal function could be enough: "If you're on haemodialysis then kidney function of 10% to 15% would already make you independent of haemodialysis. It's not that we have to go all the way."

He said the potential was huge: "If you think about the United States alone, there's 100,000 patients currently waiting for kidney transplants and there's only around 18,000 transplants done a year.

"I think the potential clinical impact of a successful treatment would be enormous."

'Really impressive'

There is a huge amount of further research that would be needed before this is even considered in people.

The technique needs to be more efficient so a greater level of kidney function is restored. Researchers also need to prove that the kidney will continue to function for a long time. There will also be challenges with the sheer size of a human kidney. It is harder to get the cells in the right place in a larger organ.

Prof Martin Birchall, a surgeon at University College London, has been involved in windpipe transplants produced from scaffolds.He said: "It's extremely interesting. It is really impressive. "They've addressed some of the main technical barriers to making it possible to use regenerative medicine to address a really important medical need."

He said that being able to do this for people needing an organ transplant could revolutionise medicine: "It's almost the nirvana of regenerative medicine, certainly from a surgical point of view, that you could meet the biggest need for transplant organs in the world - the kidney."