Miniature livers 'grown in lab'

Organ for transplant There is a shortage of organs for transplant

Scientists have managed to produce a small-scale version of a human liver in the laboratory using stem cells.

The success increases hope that new transplant livers could be manufactured, although experts say that this is still many years away. The team from Wake Forest University Baptist Medical Center presented its findings at a conference in Boston. UK experts said it was an "exciting development" but it was not yet certain a fully-functioning liver was possible.

The demand for transplant livers far exceeds the number of available organs, and in recent years, research has focused on ways to use cell technology to support failing organs in the body, or even one day replace them.

Their building block is the stem cell, a "master cell" which can, in certain conditions, divide to produce different types of body tissue. However, constructing a three-dimensional organ from stem cells is a difficult task.

'Technical hurdles'

The method used by the Wake Forest researchers, and other teams around the world, is to form new liver tissue on a scaffold made from the structure of an existing liver.

In this case, a detergent was used to strip away the cells from the liver, leaving only the collagen framework which supported them, and a network of tiny blood vessels.

The new stem cells - in this case, immature liver cells and endothelial cells, to produce a new lining for the blood vessels - were gradually introduced.

After a week in a "bioreactor", which nurtured the cells with a mixture of nutrients and oxygen, the scientists saw widespread cell growth within the structure, and even signs of some normal functions in the tiny organ.

Professor Shay Soker, who led the research, said: "We are excited about the possibilities this research represents, but must stress that we're at an early stage, and many technical hurdles must be overcome before it could benefit patients.

"Not only must we learn how to grow billions of liver cells at one time in order to engineer livers large enough for patients, we must determine whether these organs are safe to use."

UK researchers welcomed the findings, which are being presented to the American Association for the Study of Liver Diseases. Professor Mark Thursz, from Imperial College London, said the results were "encouraging".

"The report suggests that the authors have overcome one of the major hurdles in creating an artificial liver - to generate functioning human liver cells in a 'natural' liver structure. It is clear that the cells are growing well, but the next step is to show that they are functioning like normal human liver tissue."

Dr Mark Wright, from Southampton University added: "In an era of increasing liver disease and death with a chronic shortage of liver transplants this represents an exciting development in an important field of work.

"The researchers appear to have made the step of combining stem cell technology with bioengineering as a first step to producing artificial livers. Whilst 'off the shelf' new livers are clearly still a long way off, this work gives a glimmer of hope that this is no longer just the stuff of science fiction."

http://www.bbc.co.uk/news/health-11654943

How do we kill rogue cells?

Assassin's tricks revealed in Nature today

A team of Melbourne and London researchers have shown how a protein called perforin punches holes in, and kills, rogue cells in our bodies. Their discovery of the mechanism of this assassin is published today in the science journal Nature.

"Perforin is our body's weapon of cleansing and death," says project leader Prof James Whisstock from Monash University. "It breaks into cells that have been hijacked by viruses or turned into cancer cells and allows toxic enzymes in, to destroy the cell from within. Without it our immune system can't destroy these cells. Now we know how it works, we can start to fine tune it to fight cancer, malaria and diabetes," he says.

The first observations that the human immune system could punch holes in target cells was made by the Nobel laureate Jules Bordet over 110 years ago. But how?

Researchers from Monash University and the Peter MacCallum Cancer Centre in Melbourne, and Birkbeck College in London collaborated on the ten-year study to unravel the molecular structure and function of perforin—the protein responsible. The structure was revealed with the help of the Australian Synchrotron, and with powerful electron microscopes at Birkbeck. Combining the detailed structure of a single perforin molecule with the electron microscopy reconstruction of a ring of perforins forming a hole in a model membrane reveals how this protein assembles to punch holes in cell membranes.

The new research has confirmed that the important parts of the perforin molecule are quite similar to those in toxins deployed by bacteria such as anthrax, listeria and streptococcus. "The molecular structure has survived

for close to two billion years, we think," says Prof Joe Trapani, head of the Cancer Immunology Program at Peter Mac. "This work is a dramatic illustration of the importance of the synchrotron," says Whisstock. "We simply couldn't have done it without this wonderful facility."

The weapon of death is a powerful molecule. If perforin isn't working properly the body can't fight infected cells. And there is evidence from mouse studies, says Trapani, that defective perforin leads to an upsurge in malignancy, particularly leukaemia.

Perforin is also the culprit when the wrong cells are marked for elimination, either in autoimmune disease conditions, such as early onset diabetes, or in tissue rejection following bone marrow transplantation.

So the researchers are now investigating ways to boost perforin for more effective cancer protection and therapy for acute diseases such as cerebral malaria. And with the help of a $1 million grant from the Wellcome Trust they are working on potential inhibitors to suppress perforin and counter tissue rejection.

The lead authors are Ruby Law from Monash University, Natalya Lukoyanova from Birkbeck College, London, and Ilia Voskoboinik from the Peter MacCallum Cancer Centre and the University of Melbourne. The project leaders are: Joe Trapani (Peter Mac), Helen Saibil (Birkbeck) and James Whisstock (Monash). The research was supported by the above institutions, the NHMRC, the ARC , the UK Biotechnology and Biological Sciences Research Council and the Wellcome Trust.

http://www.eurekalert.org/pub_releases/2010-10/sip-hdw102910.php

Mars volcanic deposit tells of warm and wet environment

PROVIDENCE, R.I. [Brown University] — Roughly 3.5 billion years ago, the first epoch on Mars ended. The climate on the red planet then shifted dramatically from a relatively warm, wet period to one that was arid and cold. Yet there was at least one outpost that scientists think bucked the trend.

A team led by planetary geologists at Brown University has discovered mounds of a mineral deposited on a volcanic cone less than 3.5 billion years ago that speak of a warm and wet past and may preserve evidence of one of the most recent habitable microenvironments on Mars.

Observations by NASA's Mars Reconnaissance Orbiter enabled researchers to identify the mineral as hydrated silica, a dead ringer that water was present at some time. That fact and the mounds' location on the flanks of a volcanic cone provide the best evidence yet found on Mars for an intact deposit from a hydrothermal environment — a steam fumarole or a hot spring. Such environments may have provided habitats for some of Earth's earliest life forms.

"The heat and water required to create this deposit probably made this a habitable zone," said J.R. Skok, a graduate student at Brown and lead author of the paper in Nature Geoscience. "If life did exist there, this would be a promising spot where it would have been entombed — a microbial mortuary, so to speak."

No studies have determined whether Mars has ever supported life, but this finding adds to accumulating evidence that at some times and in some places, Mars hosted favorable environments for microbial life. The deposit is located in the sprawling, flat volcanic zone known as Syrtis Major and was believed to have been left during the early Hesperian period, when most of Mars was already turning chilly and arid.

"Mars is just drying out," Skok said, "and this is one last hospitable spot in a cooling, drying Mars."

Concentrations of hydrated silica have been identified on Mars previously, including a nearly pure patch found by NASA's Mars Exploration Rover Spirit in 2007. However, this is the first found in an intact setting that clearly signals the mineral's origin.

"You have spectacular context for this deposit," Skok said. "It's right on the flank of a volcano. The setting remains essentially the same as it was when the silica was deposited."

The small, degraded cone rises about 100 meters from the floor of a shallow bowl named Nili Patera. The patera spans about 50 kilometers (30 miles) in Syrtis Major of equatorial Mars. Before the cone formed, free-flowing lava blanketed nearby plains. The collapse of an underground magma chamber from which lava had emanated created the bowl. Subsequent lava flows, still with a runny texture, coated the floor of Nili Patera. The cone grew from even later flows, apparently after evolution of the underground magma had thickened its texture so that the erupted lava would mound up.

"We can read a series of chapters in this history book and know that the cone grew from the last gasp of a giant volcanic system," said John "Jack" Mustard, professor of geological sciences and a co-author of the paper, who is Skok's thesis adviser at Brown. "The cooling and solidification of most of the magma concentrated its silica and water content."

Observations by cameras on the Mars Reconnaissance Orbiter revealed patches of bright deposits near the summit of the cone, fanning down its flank, and on flatter ground in the vicinity. The Brown researchers partnered with Scott Murchie of Johns Hopkins University Applied Physics Laboratory to analyze the bright exposures with the Compact Reconnaissance Imaging Spectrometer for Mars (CRISM) instrument on the orbiter.

Silica can be dissolved, transported and concentrated by hot water or steam. Hydrated silica identified by the spectrometer in uphill locations — confirmed by stereo imaging — indicates that hot springs or fumaroles fed by underground heating created these deposits. Silica deposits around hydrothermal vents in Iceland are among the best parallels on Earth.

"The habitable zone would have been within and alongside the conduits carrying the heated water," Murchie said. *NASA funded the research.*

http://www.eurekalert.org/pub_releases/2010-10/bu-mvd102910.php

Arthritis drugs could help prevent memory loss after surgery

Anti-inflammatory drugs currently used to treat diseases such as rheumatoid arthritis may also help prevent cognitive decline after surgery, according to a new study led by researchers at UCSF and colleagues at Imperial College, London.

The research explains for the first time why many patients experience memory loss or other forms of cognitive dysfunction after surgery or critical illness, a process the researchers traced to a specific inflammatory response in the brain.

The findings could lead directly to human clinical trials in as short as 12 months, the authors said. Their work appears in an upcoming issue of the Proceedings of the National Academy of Sciences and will be online at http://www.pnas.org/papbyrecent.shtml.

For years, anesthesiologists and neurologists have struggled to explain why some patients, especially the elderly, experience confusion, learning disorders and memory loss after surgery.

While typically short-term, this delirium occurs widely in intensive care units, affecting between 28 and 92 percent of hospitalized patients, depending on their age, health status and type of surgery, the authors said. It also has been linked to poorer surgical outcomes, as well as an increased risk of mortality, inability to cope and possible permanent dementia.

Until now, no one has clearly understood what caused the disorder or how to treat it, according to senior author Mervyn Maze, MB ChB, Professor and Chair of the UCSF Department of Anesthesiology and Perioperative Care. The new research not only linked that response to an immune protein called tumor necrosis factor (TNF-α), a cytokine, but also identified a likely drug therapy to prevent it, he said.

"Antibody therapies already are widely used against cytokines to prevent or treat inflammation, so we know that these are effective in humans," said Maze, who began the research as a member of the Imperial College faculty before joining UCSF. "This study suggests that one day we also might be able to use these therapies as a single, pre-surgical dose to prevent cognitive decline in susceptible patients."

Previous studies have linked post-operative cognitive decline with the rise in blood levels of interleukin-1 beta (IL-1β), a molecule involved in inflammation. For this study, Maze and his colleagues studied a protein called tumor necrosis factor (TNF-α), which is known to regulate the immune system's inflammatory response before interleukin-1 is produced.

Working with Sir Marc Feldmann, MB, PhD, FRS – a pioneer in cytokine research in inflammatory disorders and professor at the Kennedy Institute of Rheumatology at Imperial College, London – the team gave a single dose of anti-TNF monoclonal antibody to mice using a model of orthopedic surgery. They found that it successfully acted as a prophylaxis against this disorder, decreasing blood levels of IL-1β, while limiting inflammation in the brain and eliminating behavioral indications of cognitive decline.

The research suggests that the TNF protein acts "upstream" of IL-1 and triggers a cascade of immune responses during surgery that provokes the production of IL-1 in the brain, Maze said. That in turn contributes to cognitive decline after surgery or critical illness.

"This is an important observation, as it demonstrates that cytokines are potential therapeutic targets in a wider range of diseases, not just autoimmune disease and cancer for which they are known targets," Feldmann said. "Moreover, effective therapeutics already are available, with a known safety profile and modest cost if used short term."

The lead author on the paper was Niccolò Terrando, PhD, a postdoctoral fellow in Maze's lab and scholar in the Department of Anesthetics, Pain Medicine and Intensive Care in the Imperial College London. Co-authors on the paper include Claudia Monaco, MD, PhD; Brian M.J. Foxwell, PhD (deceased); and Feldmann, all of the Kennedy Institute of Rheumatology, Imperial College London.

The study was supported by the Westminster Medical School Research Trust, in London, the Mathilda and Terence Kennedy Institute of Rheumatology Trust, and Arthritis Research United Kingdom. The authors disclose no conflicts of interest in this work.

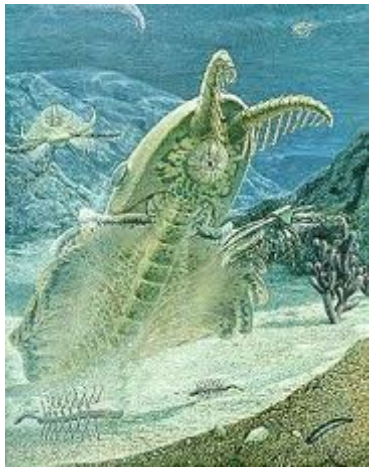
http://www.eurekalert.org/pub_releases/2010-11/uoc--adc102910.php

Earth's first great predator wasn't

Boulder, CO, USA - The meters-long, carnivorous "shrimp" from hell that once ruled the seas of Earth a half billion years ago may have been a real softy, it turns out. A new 3-D modeling of the mouth parts of the Anomalocaris, along with evidence that these parts were not hard like teeth, but flexible, shows that the famed predator could not have been munching on the hard shells of trilobites and other such creatures of the early seas.

What's more, there is no evidence from fossilized stomach contents or feces that Anomalocaris' ate anything hard enough to leave a fossilized trace. In fact it was this lack of fossil evidence backing any dietary preference – right alongside other animals that do show fragments of what they ate in their gullets – which inspired the investigation, said paleontologist James "Whitey" Hagadorn of the Denver Museum of Nature & Science.

Hagadorn will be presenting his team's discoveries about Anomalocaris on Monday, Nov. 1, at the annual meeting of the Geological Society of America in Denver.



"It was supposed to roam around the Cambrian seas gobbling up trilobites and everything else," said Hagadorn. But the pineapple-like whorl of mouth parts and the associated whisker-like appendages of Anomalocaris all appear to have been bendable, in the fossil remains, he said. They are not mineralized like the exoskeletons of the trilobites they were supposedly eating.

His suspicions prompted Hagadorn to develop a 3-D, finite element analysis model of the Anomalocaris mouth. This allowed for testing just how the mouth worked and how much force it could create – in other words, how strong a bite it had. The model turned up some surprises.

"It couldn't even close its mouth," said Hagadorn. And there was no practical way these mouth parts could create the force needed to break open a modern lobster shell nor a shrimp shell, which were used as analogues for a trilobite carapace in the model.

Another interesting discovery made along the way came from studying more than 400 Anomalocaris mouths. In none of them did Hagadorn find any signs of wear. That's strange because if they were genuine teeth there would be chips, scratches and other signs they were being used to munch on hard-shelled animals.

The model, gut contents, feces and wear all suggest Anomalocaris was not a trilobite eater. But they fail to help explain what this impressive beast from the Cambrian was eating.

"Maybe it ingested things and then spit them out," Hagadorn speculated. Another possibility is that it somehow broke down the food it was eating into very fine particles before ingesting it. At this point the only thing that appears certain is that the famed biggest predator of the early Cambrian is more mysterious than ever.

Paper No. 125-1: PUTTING ANOMALOCARIS ON A SOFT-FOOD DIET?
Abstract link: http://gsa.confex.com/gsa/2010AM/finalprogram/abstract_181965.htm Session No. 125: Paleontology V - Predation and Biological Interactions http://gsa.confex.com/gsa/2010AM/finalprogram/session_27553.htm

http://www.eurekalert.org/pub_releases/2010-11/gsoa-efg103110.php

Inhaled steroids increase diabetes risk, say Lady Davis Institute researchers

Benefits outweigh risks for asthmatics, but COPD patients should think twice

Patients taking inhaled corticosteroids are at increased risk of developing type 2 diabetes, and more so with higher doses, say researchers at the Jewish General Hospital's Lady Davis Institute for Medical Research (LDI) In Montreal. The risk is of special concern for patients suffering from chronic obstructive pulmonary disorder (COPD), and much less significant for asthmatics.

"These medications are very effective in asthma, so the benefits clearly outweigh the risk for asthmatics," said Dr. Samy Suissa, Director of the Centre for Clinical Epidemiology at the LDI, and lead author of the study published in the American Journal of Medicine. "However, their effectiveness is questionable in COPD, where they are also used in higher doses. This is a very different risk/benefit situation."

Inhaled corticosteroids are administered in the form of aerosol sprays and micropowders, and include drugs like fluticasone (Flonase®, Advair®), budesonide (Pulmicort®, Rhinocort®) and beclometasone (QVAR®, Beclovent®), among others.

Oral corticosteroids like predinisone have long been known to increase the risk of diabetes, but this is the first time the effect has been observed with the inhaled form.

Suissa and his colleagues used the extensive databases of Quebec's provincial health insurance board to study a cohort of nearly 400,000 patients treated for COPD or asthma. They determined that inhaled corticosteroids increased the rate of onset of diabetes from 14 people per 1000 to 19 per 1000, or 34 percent, every year of use. In other words, 5 additional people for every 1000 users in the study – people who otherwise would not have been affected – developed diabetes from the use of the drug.

"These are not insubstantial numbers," said Dr. Suissa, also a professor of epidemiology and biostatistics at McGill University in Montreal. "Over a large population the absolute numbers of affected people are significant.

"We recommend that physicians reserve the use of inhaled steroids for the patients who truly benefit from these medications, namely asthmatics, and curb their use in COPD to the few patients for whom they are indicated. In all cases, patients using high doses should be assessed for possible hyperglycemia and the lowest effective dose targeted."

http://www.eurekalert.org/pub_releases/2010-11/jgh-isi110110.php

New strain of 'high-runner' rats uniquely resistant to disease -- all disease!

New research in the FASEB Journal explains sophisticated animal model system that allows for in-depth exploration of gene function and expression as related directly or indirectly to all diseases

Everybody knows that if you're physically fit, you're less likely to get a wide range of diseases. What most people don't know is that some people are "naturally" in better shape than others, and this variation in conditioning makes it difficult to test for disease risk and drug effectiveness in animal models. A new research paper published in the November 2010 print issue of The FASEB Journal (http://www.faseb.org) started out as a study to explain the strong statistical link between low aerobic exercise capacity and common diseases, but ultimately led to an animal model that breaks through the limitations of current systems that target single disease pathways.

Because common disease risks arise from complex interactions of many genetic pathways, future animal model systems, like this one, must account for multiple pathways. The animal model developed in this study can be used to evaluate mechanisms by which positive and negative environmental effects influence disease risks and explore a wide variety of pathways, rather than focusing on a single target.

"We hope that our approach of using a more realistic animal model system of disease risks will lead to information that is explanatory and ultimately predictive of mechanisms underlying disease," said Heikki Kainulainen, Ph.D., co-author of the study from the Neuromuscular Research Center at the University of Jyväskylä in Finland. "This seems to be the only path for developing diagnostics and therapeutics that have high efficacy."

To create this animal model, researchers bred high-runners with high-runners and low¬-runners with low-runners to divide and concentrate the genes for these traits in two groups of rats. After 11 generations of selection, "high-runner" rats could run three times as far as the "low-runner" rats. The low-runner rats appeared to be at a higher risk for disease than the high-runner rats. Genetic analysis of the two groups of rats revealed that the expression levels of seven functionally related groups of genes correlated with differences in aerobic running traits and disease risks between the low- and high- runner rats. This makes the low-runner and high-runner rat model system a valuable tool to explore mechanisms underlying disease risks at all levels of biological organization.

"Genes that increase resistance to common diseases in high-runner rats are also present across species," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "As our understanding of disease grows in complexity, so does our need for animal models that can mimic disease susceptibility in humans."

http://www.eurekalert.org/pub_releases/2010-11/foas-nso110110.php

Scientists turn a new leaf to discover a compound in daffodils that targets brain cancer

New research in the FASEB Journal suggests that narciclagsine, a natural compound found in daffodil bulbs, markedly reduces cancer cell proliferation and migration

When looking for new ways to treat aggressive brain cancers, an international team of scientists turned a new leaf and "discovered" the lowly daffodil. A new research study published in the November 2010 print issue of The FASEB Journal (http://www.fasebj.org) offers hope that a natural compound found in daffodil bulbs, called narciclasine, may be a powerful therapeutic against biologically aggressive forms of human brain cancers.

"We are planning to move a narciclasine derivative toward clinical trials in oncology within a three to four year period in order to help patients with brain cancers, including gliomas, as well as brain metastases," said Robert Kiss, Ph.D., co-author of the study from the Laboratory of Toxicology at the Institute of Pharmacy at the Université Libre de Bruxelles in Brussels, Belgium. "We hope narciclasine could be given to brain cancer patients in addition to conventional therapies."

To make this discovery, Kiss and colleagues used computer-assisted techniques to identify targets for narciclasine in cancer cells. The strongest potential candidate to emerge was the eEF1A elongation factor. Researchers then grafted human melanoma brain metastatic cells into the brains of genetically altered mice.

Results showed that the injected mice survived significantly longer when treated with narciclasine than those mice left untreated. The researchers believe that narciclasine selectively inhibits the proliferation of very aggressive cancer cells, while avoiding adverse effects on normal cells. Narciclasine could be used in the near future to combat brain cancers, including gliomas, and metastases such as melanoma brain metastases.

"Scientists have been digging in odd corners to find effective treatments for brain cancer for decades, and now they've found one in daffodils." said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal, "It doesn't mean that you should eat daisies or daffodils for what ails you, but that modern medicinal chemistry can pluck new chemicals from stuff that grows in the garden. This is a good one!"

http://www.eurekalert.org/pub_releases/2010-11/foas-sta110110.php

Slight change in wind turbine speed significantly reduces bat mortality

Study shows a 1 percent annual energy loss and 44-93 percent reduction in bat fatalities

While wind energy has shown strong potential as a large-scale, emission-free energy source, bat and bird collisions at wind turbines result in thousands of fatalities annually. Migratory bats, such as the hoary bat, are especially at risk for collision with wind turbines as they fly their routes in the forested ridges of the eastern U.S. This loss not only impacts the immediate area, but is also detrimental to ecosystem health nationwide—that is, bats help with pest management, pollination and the dispersal of numerous plant seeds.

Since turbine towers and non-spinning turbine blades do not kill bats, some scientists have proposed shutting off or reducing the usage of wind turbines during peak periods of migration in the late summer and early fall months when bat activity and fatalities are highest.

In a study to be published online November 1, 2010 in Frontiers in Ecology and the Environment (e-View), a journal of the Ecological Society of America, Edward Arnett from Bat Conservation International in Austin, Texas and colleagues examined the effects of changes in wind turbine speed on bat mortality during the low-wind months of late summer and early fall.

Currently, most wind turbines in the U.S. are programmed to begin rotating and producing power once wind speed has reached approximately 8 to 9 miles per hour (mph)—the wind speed at which turbines begin generating electricity to the power grid is known as the cut-in speed. Wind turbines with a low cut-in speed run more frequently than those set at higher cut-in speeds since they begin rotating at lower wind speeds.

The researchers found that, by raising the cut-in speed to roughly 11 mph, bat fatalities were reduced by at least 44 percent, and by as much as 93 percent, with an annual power loss of less than one percent. That is, programming the turbines to rotate only when the wind reached approximately 11 mph or higher caused the turbines to rotate less frequently and, therefore, killed significantly fewer bats. Because this was performed during months with seasonably low wind speeds already, the overall energy loss was marginal when the researchers calculated the annual power output.

"This is the only proven mitigation option to reduce bat kills at this time," said Arnett. "If we want to pursue the benefits associated with wind energy, we need to consider the local ecological impacts that the turbines could cause. We have already seen a rise in bat mortality associated with wind energy development, but our study shows that, by marginally limiting the turbines during the summer and fall months, we can save bats as well as promote advances in alternative energy."

Arnett and colleagues monitored 12 of the 23 turbines at the Casselman Wind Project in Somerset County, Pennsylvania in the Appalachian Mountain region and recorded bat fatalities for 25 summer and fall nights in both 2008 and 2009. The researchers analyzed the fatalities following nights when the turbines were fully operational and when the turbines were set to the less sensitive cut-in speeds of roughly 11 mph and 14.5 mph. In both years, the researchers found at least one fresh bat carcass every night that the turbines were fully operational. Specifically, the researchers reported a mortality rate that was, on average, 3.6 to 5.4 times higher at the fully functioning turbines compared with the turbines set to the altered cut-in speeds.

According to John Hayes, co-author of the study from the University of Florida, "the findings are important step forward in building a comprehensive energy strategy with reduced environmental impacts."

"Rarely do you see such a win-win result in a study," said Arnett. "There is a simple, relatively cost-effective solution here that could save thousands of bats. This is good news for conservation and for wind energy development."

http://www.eurekalert.org/pub_releases/2010-11/esoa-sci110110.php

New drug may provide more cost-effective stroke prevention than warfarin, Stanford/VA study shows

STANFORD, Calif. — A newly approved drug may be a cost-effective way to prevent stroke in patients with an irregular heart rhythm — and may also offer patients better health outcomes than the commonly prescribed, but

potentially risky, blood thinner warfarin. That's according to a new analysis from researchers at the Stanford University School of Medicine and the Veterans Affairs Palo Alto Health Care System.

"Dabigatran is the first new drug in 20 years to be approved for stroke prevention in atrial fibrillation, and we wanted to see if it could be cost-effective even before it made its debut in the United States," said cardiac electrophysiologist Mintu Turakhia, MD, MAS, a VA investigator and an instructor of medicine at Stanford. Turakhia is senior author of the research that will appear Nov. 2 in the Annals of Internal Medicine.

"We found that for the average patient — 65 years and older with a risk of stroke — this drug has the potential to be a cost-effective alternative to warfarin, depending on how it is priced," said first author James Freeman, MD, MPH, a cardiology fellow at Stanford.

The researchers hope their findings will help guide decisions by physicians, insurance payers and policy-makers about the drug, dabigatran, which the U.S. Food and Drug Administration approved on Oct. 19 for the prevention of stroke in patients with atrial fibrillation. "We now have sufficient efficacy and cost-effectiveness data to help inform policy on this drug in the United States," Turakhia said.

An estimated 2.3 million Americans have atrial fibrillation, a disorder during which the heart's two upper chambers fail to beat effectively. The irregular beating can cause pools of blood to form, and if a clot escapes from the heart and blocks an artery in the brain, a stroke occurs.

Atrial fibrillation is responsible for about 15 percent of the 700,000 strokes per year in the United States. Many patients are prescribed the anticoagulant warfarin as a preventive measure. Although warfarin is effective at reducing a patient's stroke risk, it is a less-than-perfect therapy: The dosage has to be just right (too little and it could fail to prevent stroke, too much and it could lead to serious or fatal hemorrhage), and patients on the drug face constant blood testing and dose adjustment.

"Among my patients, I get asked about alternatives to warfarin a dozen times a week," said Turakhia, who specializes in the treatment and research of atrial fibrillation. "Many of them are just unhappy with the need for regular, often lifelong blood testing."

Much research has focused on developing a suitable replacement for warfarin, which has been in clinical use for 65 years. Dabigatran, an oral anti-clotting drug that requires no blood testing, emerged as one promising alternative. In a large, multicenter study published in the New England Journal of Medicine last year, the drug was about as effective as warfarin in preventing strokes but less likely to cause intracranial hemorrhages. Patients on the new drug, though, did have a slightly increased risk of heart attack.

"It looked like we may have a therapy that is at least as effective and maybe even more effective than warfarin," said Freeman. But the question remained whether dabigatran would be cost-effective. "We were very interested in answering this question," he said.

For this study, the researchers developed a mathematical model to compare outcomes and costs of warfarin, low-dose (110 mg twice daily) dabigatran and high-dose (150 mg twice daily) dabigatran. The drug isn't yet priced for the U.S. market, but the researchers used pricing from the United Kingdom, where the drug is approved for prevention of venous thromboembolism, to estimate costs of $13 per day for high-dose dabigatran. (Warfarin costs just over $1 per day.)

The team's model simulated 10,000 patients aged 65 and older with atrial fibrillation and risk factors for stroke. They determined that high-dose dabigatran prevented 1,000 more intracranial hemorrhages and 600 more strokes than warfarin was calculated to prevent, though dabigatran resulted in 400 additional heart attacks. They also determined that total lifetime costs were $143,193 for warfarin, and $168,398 for high-dose dabigatran. (Though warfarin is much less expensive than dabigatran, the costs of lifelong monitoring and adverse effects boosted its total costs.)

When taking into consideration adverse outcomes and costs, the researchers calculated that high-dose dabigatran yielded an additional 0.56 quality-adjusted-life-year — a common metric that takes into account quality of life as well as length of survival — when compared with conventional therapy with warfarin. Offering half a year of quality-adjusted life to a patient is "a fairly significant benefit," the researchers noted.

The analysis also showed that the high-dose drug came at an incremental cost over warfarin of $45,372 per quality-adjusted-life-year — well below the commonly accepted cost-effective threshold of $50,000. "That's why this is exciting," Turakhia said of the findings. Not only does the new drug "represent a breakthrough in patient convenience," but it may also make economic sense to use it, depending on how it is priced.

The researchers pointed out that their findings are dependent on the drug's price: The drug, which is marketed as Pradaxa by the Germany company Boehringer Ingelheim, would be less cost-effective if it was more expensive than the researchers' estimate. (If it were $13.70 a day, for example, its cost per quality-adjusted-life-year would exceed $50,000.) "We wanted to show what pricing range made sense," said Freeman.

In terms of study limitations, scientists and physicians are looking for ways to more efficiently determine the proper dose of warfarin, and advances in that area could also alter the comparative cost benefits. The researchers also noted that their data on efficacy came from the one large clinical trial — and that the findings needed to be validated in clinical practice. ("A lot needs to be determined outside of clinical trials, in the real world," noted Turakhia.) But "if the drug continues to perform as well as it did in studies, it could be significant competition to warfarin over the long term," said Freeman.

Other Stanford authors on the study were medical student Ruo Zhu; Douglas K. Owens, MD, an investigator at the VA and professor of medicine and of health research and policy at the medical school; Alan Garber, MD, PhD, professor of medicine; and Paul Wang, MD, professor of medicine. None of the authors have financial ties to Boehringer Ingelheim.

Funding for the study came from an American Heart Association-Pharmaceutical Roundtable Outcomes Research Award, a VA Health Services Research & Development Career Development Award and an American Heart Association National Scientist Development Grant. More information about the Department of Medicine, which also supported the research, is available at http://medicine.stanford.edu/.

http://www.eurekalert.org/pub_releases/2010-11/sumc-ndm102810.php

Fox Chase researchers identify risk factors for the spread of breast cancer to lymph nodes

SAN DIEGO, CA (November 1, 2010)—Breast cancer, one of the most prevalent cancers in women, afflicts an additional 200,000 women each year and causes about 40,000 deaths annually. The disease often extends to neighboring lymph nodes, in part, through lymphovascular invasion (LVI)—a process in which cancer cells invade blood vessels or the lymphatic system—and can often translate into a poor prognosis for patients. Some scientists argue that evidence of LVI does not necessarily mean that the disease will recur in the lymph nodes after radiation to the breast alone, but research from Fox Chase Cancer Center now shows that the appearance of LVI in the breast tissue does in fact predict recurrence of breast in the regional lymph nodes.

By carefully examining recurrence patterns of thousands of women with breast cancer from records spanning more than 30 years, Wilhelm Lubbe, M.D.,Ph.D., chief resident in Fox Chase's Radiation Oncology Department, and his colleagues have now shown that the appearance of LVI in breast tissue predicts the future recurrence of cancer to nearby lymph nodes. "The microscopic diagnosis of LVI is challenging which highlights the importance of excellent pathologists," says Lubbe, who will present the results this week at the Annual Meeting of the American Society for Radiation Oncology.

Knowing that the disease is going to extend to neighboring lymph nodes, such as those in the armpit, is important prognostically. But it has still been unclear whether supplementary radiation therapy targeting these areas improves outcomes.

"There still is a lot of debate as to whether additional radiation to the regional lymph nodes is needed in a woman with LVI," Lubbe says.

In the study, Lubbe's team analyzed an extensive database of 3,082 breast cancer patients who underwent whole-breast radiation or minimal surgical resection of breast tissue between 1970 and 2009. This dataset, at least twice as large as many others of its kind, provided enough statistical power for the investigators to detect a subtle, yet significant trend.

"Luckily, at Fox Chase, we had the resources to maintain this huge database by meticulously following a large number of patients over the course of decades," Lubbe says.

The team searched for factors aside from LVI that determine outcomes. The disease was more likely to invade lymph nodes in women younger than 35. Also, additional radiation therapy under the armpit via a technique called a posterior axillary boost (PAB) lead to fewer breast cancer recurrences in these women's regional lymph nodes. Ironically, this extra procedure led to less regional recurrence even though the women were of higher risk than other treatment groups. Overall, the 10-year recurrence rate was only 1.4%. But it was 4% for women treated with radiation above the collar bone alone, compared to 0.5% for those who also received a PAB - the posterior boost of radiation under the armpits.

"Our data suggest that patients who are at higher risk of their cancer spreading can potentially benefit from additional radiation by a technique called a posterior axillary boost," Lubbe says. "But the recommendation to add radiation, and what technique is used, is very patient-specific, because with any intervention there's additional risk."

In the future, Lubbe would like to identify other objective biological markers, such as proteins or genes, which predict recurrence rates and patient outcomes. "Ultimately, we'd like to find a faster and more accurate process for assessing the risk of cancer spread to regional lymph nodes and the rest of the body," Lubbe says.

Co-investigators include Tianyu Li, Penny Anderson, Lori Goldstein, Crystal Denlinger, Holly Dushkin, Ramona Swaby, Richard Bleicher, Elin Sigurdson and Gary Freedman.

http://www.eurekalert.org/pub_releases/2010-11/fccc-fcr110110.php

Fish show unique parenting skills

By Victoria Gill Science and nature reporter, BBC News

Discus fish are surprisingly attentive parents, scientists have found.

The colourful little creatures are known to feed their offspring with a nutritious mucus on their skin.

Now a study has suggested that the tropical fish actually wean their fry, "encouraging" them to forage for themselves, and that when it comes to looking after their young, discus fish have more in common with mammals. Researchers describe their behaviour in the Journal of Experimental Biology.

This nurturing in discus fish is a well recognised behaviour, but this is the first time it has been studied in detail.

Intensive caring

Mr Jonathan Buckley from the University of Plymouth, UK, was a member of the team that carried out the study.

Along with his supervisor, Dr Katherine Sloman, and colleagues in Brazil, he found that, when it comes to looking after their young, discus fish have more in common with mammals than with most other fish.

He explained: "For the first couple of weeks - when the fry first hatch - the parents take amazingly good care of them."

Both parents' skin is covered in the mucus; the offspring surround the parent and constantly nibble on it.

At this stage, the tiny, vulnerable fry are never on their own. The male and female even share parental responsibility - "flicking" the young from one parent to the other when they need a break from feeding them.

Mr Buckley likened this to mammals suckling their young.

He and his team have now documented some even more striking similarities between the way these fish take care of their fry and the way mammals nurture and feed their babies.

DISCUS FISH

The fish are native to the Amazon

Because of their beauty and popularity with tropical fish enthusiasts, they are often referred to as the "King of the aquarium"

Each parenting pair will co-ordinate their own individual "flicking" action to transfer their offspring to the other parent

He told BBC News that, after the first two weeks, the parents appeared to deliberately wean their young.

"In week three there's a change - the parents are constantly swimming away," he explained. "We think this is the beginning of the weaning period - they're trying to make it more energetically efficient for the fry to forage rather than feed."

When the researchers studied the mucus itself, they found that it contained antibodies - immune system-bolstering substances. "This transfer of antibodies to offspring is primarily a staple of mammalian parental care and [previously] unseen in fish," he said. These findings show, Mr Buckley added, just how much fish are underestimated in terms of the complexity of their behaviour. The work could also show how the fish might be affected by pollution in their Amazon habitat.

Pollutants, particularly from mining, run into the waters and the scientists think that these could be absorbed into the mucus and, subsequently fed to the fry.

"The capture and sale of this species generates a significant amount of money for the people who live in that part of Brazil," Mr Buckley said. "So it's important to understand how the fish are affected by changes in their environment."

Dr Sloman collaborated with Adalberto Val from the Laboratory of Ecophysiology and Molecular Evolution in Manaus, Brazil, to set up the colony of breeding discus fish that were used in this study.

http://news.bbc.co.uk/earth/hi/earth_news/newsid_9139000/9139756.stm

Doctors told to cut anti-psychotic drugs for dementia

The use of anti-psychotic drugs for dementia patients must be cut by two-thirds by November 2011, the minister responsible has warned doctors.

Care Services Minister Paul Burstow sets out limits for use of anti-psychotics in dementia sufferers. Care Services Minister Paul Burstow told Panorama that GPs must "take responsibility" and drastically reduce the amount of drugs being prescribed. Evidence suggests the drugs - used to control aggressive behaviour - have dangerous side effects. A leading GP said most doctors agree that their use needs to be curtailed.

Mr Burstow said the evidence for cutting their use is compelling: "It kills people. It cuts their lives short. It reduces the quality of their lives. It is now time for those responsible for prescribing to take responsibility and cut the prescribing, and make sure we improve the quality of life for people with dementia."

'Chemical cosh'

A study commissioned for the government reported in 2009 that anti-psychotics are being prescribed to 180,000 patients and their side effects, including increased risk of stroke, mean that the deaths of 1,800 people a year are attributable to their use.

Mr Burstow, the Liberal Democrat minister, campaigned in opposition on behalf of dementia patients and their families to reduce the reliance on the drugs both for patients being cared for at home and those in care facilities.

Most of the drugs were developed in the 1950s for the treatment of psychosis and are not licensed for long term use with dementia. They are prescribed "off label" for dementia patients because of their strong sedative effects and doctors have turned to them to deal with the behavioural symptoms of dementia patients.

They are supposed to be used as a last resort and only prescribed for short periods and one at a time.

Professor Tim Kendall, who wrote the current guidelines on when and how anti-psychotics should be used, is critical of how much they are being relied upon. "By far and away the most common use is to control people's behaviours. It's nothing more than a chemical cosh," he said.

The government currently spends more than £80m on anti-psychotic drugs for dementia patients a year - and spends £8.2bn overall in the treatment of dementia.

"I don't think we're spending that £8.2 billion at all well. If we were spending it well we wouldn't have this unacceptable level of prescribing anti-psychotics in the system," Mr Burstow said.

'Virtually comatose'

Professor Steve Field, chairman of the Royal College of General Practitioners, said reliance on the drugs is part of a wider problem in the system and most GPs agree that their use needs to be reduced.

"This isn't just about prescribing, this is about the whole system. It needs to change the system is a disgrace as it is at the moment and we all need to do better."

Glynne Thompson has been attempted to wean her husband Ken, who she cares for at home, off the anti-psychotics that he was prescribed in order to control his behaviour as his dementia worsened.

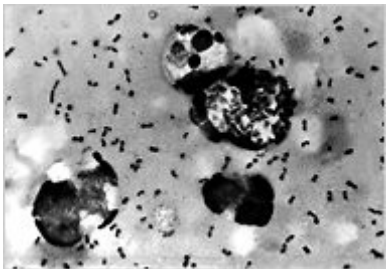
"He was virtually comatose is the only way to explain it - constantly dribbling, it was like being confronted with a baby that couldn't do anything for themselves," Mrs Thompson said of the side effects of the drugs.

http://www.bbc.co.uk/news/uk-11645889

Europe's Plagues Came From China, Study Finds

By NICHOLAS WADE

The great waves of plague that twice devastated Europe and changed the course of history had their origins in China, a team of medical geneticists reported Sunday, as did a third plague outbreak that struck less harmfully in the 19th century.



A bubonic plague smear, prepared from a lymph removed from an adenopathic lymph node, or bubo, of a plague patient, demonstrates the presence of the Yersinia pestis bacteria that causes the plague. **Centers for Disease Control and Prevention, via Getty Images**

And in separate research, a team of biologists reported conclusively this month that the causative agent of the most deadly plague, the Black Death, was the bacterium known as Yersinia pestis. This agent had always been the favored cause, but a vigorous minority of biologists and historians have argued the Black Death differed from modern cases of plague studied in India, and therefore must have had a different cause.

The Black Death began in Europe in 1347 and carried off an estimated 30 percent or more of the population of Europe. For centuries the epidemic continued to strike every 10 years or so, its last major outbreak being the Great Plague of London from 1665 to 1666. The disease is spread by rats and transmitted to people by fleas or, in some cases, directly by breathing.

One team of biologists, led by Barbara Bramanti of the Institut Pasteur in Paris and Stephanie Haensch of Johannes Gutenberg University in Germany, analyzed ancient DNA and proteins from plague pits, the mass burial grounds across Europe in which the dead were interred. Writing in the journal PLoS Pathogens this month, they say their findings put beyond doubt that the Black Death was brought about by Yersinia pestis.

Dr. Bramanti's team was able to distinguish two strains of the Black Death plague bacterium, which differ both from each other and from the three principal strains in the world today. They infer that medieval Europe must have been invaded by two different sources of Yersinia pestis. One strain reached the port of Marseilles

on France's southern coast in 1347, spread rapidly across France and by 1349 had reached Hereford, a busy English market town and pilgrimage center near the Welsh border.

The strain of bacterium analyzed from the bones and teeth of a Hereford plague pit dug in 1349 is identical to that from a plague pit of 1348 in southern France, suggesting a direct route of travel. But a plague pit in the Dutch town of Bergen op Zoom has bacteria of a different strain, which the researchers infer arrived from Norway.

The Black Death is the middle of three great waves of plague that have hit in historical times. The first appeared in the 6th century during the reign of the Byzantine emperor Justinian, reaching his capital, Constantinople, on grain ships from Egypt. The Justinian plague, as historians call it, is thought to have killed perhaps half the population of Europe and to have eased the Arab takeover of Byzantine provinces in the Near East and Africa.

The third great wave of plague began in China's Yunnan province in 1894, emerged in Hong Kong and then spread via shipping routes throughout the world. It reached the United States through a plague ship from Hong Kong that docked at Hawaii, where plague broke out in December 1899, and then San Francisco, whose plague epidemic began in March 1900.

The three plague waves have now been tied together in common family tree by a team of medical geneticists led by Mark Achtman of University College Cork in Ireland. By looking at genetic variations in living strains of Yersinia pestis, Dr. Achtman's team has reconstructed a family tree of the bacterium. By counting the number of genetic changes, which clock up at a generally steady rate, they have dated the branch points of the tree, which enables the major branches to be correlated with historical events.

In the issue of Nature Genetics published online Sunday, they conclude that all three of the great waves of plague originated from China, where the root of their tree is situated. Plague would have reached Europe across the Silk Road, they say. An epidemic of plague that reached East Africa was probably spread by the voyages of the Chinese admiral Zheng He who led a fleet of 300 ships to Africa in 1409.

"What's exciting is that we are able to reconstruct the historical routes of bacterial disease over centuries," Dr. Achtman said.

Lester K. Little, an expert on the Justinian plague at Smith College, said in an interview from Bergamo, Italy, that the epidemic was first reported by the Byzantine historian Procopius in 541 A.D. from the ancient port of Pelusium, near Suez in Egypt. Historians had assumed it arrived there from the Red Sea or Africa, but the Chinese origin now suggested by the geneticists is possible, Dr. Little said.

The geneticists' work is "immensely impressive," Dr. Little said, and adds a third leg to the studies of plague by historians and by archaeologists.

The likely origin of the plague in China has nothing to do with its people or crowded cities, Dr. Achtman said. The bacterium has no interest in people, whom it slaughters by accident. Its natural hosts are various species of rodent such as marmots and voles, which are found throughout China.

http://www.nytimes.com/2010/11/01/health/01plague.html

Kuiper Belt Objects Don Coats of Many Colors

By Jennifer Ouellette | Mon Nov 1, 2010 12:19 PM ET

All those objects in the Kuiper Belt circling around the sun might have been partially responsible for the demotion of Pluto from its former planetary status, earning them the enmity of a certain segment of the public, but there's some fascinating science yet to be discovered about these mysterious icy bodies.

Last week scientists at NASA's Goddard Space Flight Center announced that around 1000 of these objects come in hues of red, white and blue.

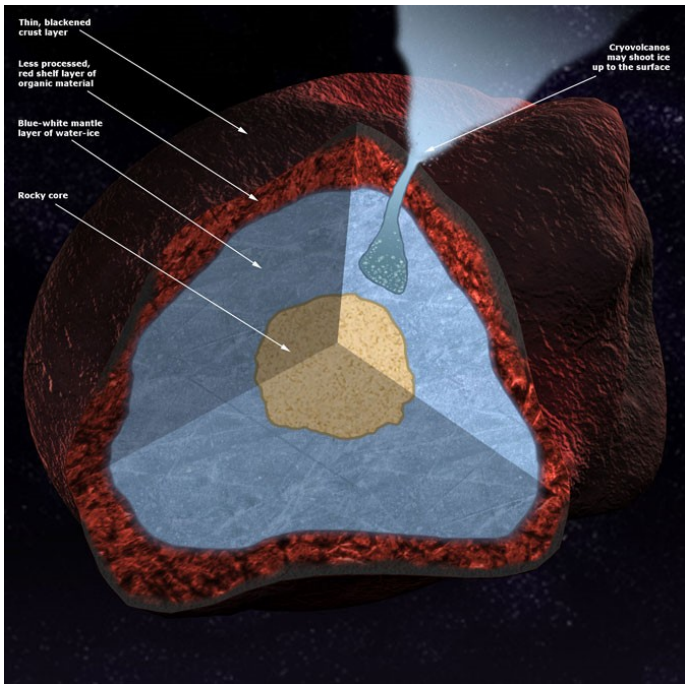
That's surprising, because like comets, Kuiper Belt objects don't have atmospheres, which means their surfaces should be black -- charred to soot by radiation from the sun. They're largely made of hydrocarbons and water ice, which tend to turn dark and tar-like in terrestrial lab experiments. Something more complex must be happening for the Kuiper Belt objects to show so many colors. And a new computer model offers some tantalizing clues.

Led by John Cooper, the NASA scientists compiled data collected by the Voyager mission, which is limited, but sufficient to produce a multi-layered model to explain the red, white and blue colors. The idea is that the incoming radiation causes changes at different layered depths, depending on the chemical composition. And the chemical composition of those various layers, combined with possible dynamic processes, accounts for the changing colors.

The different orbits might be a factor too: one class of Kuiper Belt objects, so-called Cold Classical objects, move in circular orbits and have a reddish hue, while those that move in elliptical orbits show up as blue or white.

So why aren't all of them cooked to inky blackness by radiation? It might be location, location, location. Cooper and his cohorts suggest that, for instance, the Cold Classical objects may have formed in a "sweet spot" where the incoming plasma ions aren't energetic enough to turn the surface layers black. Instead, there is more of a sandblasting effect: the radiation chips away at the surface layer (ion sputtering), eroding it gradually. The effect could be heightened by dust particles from collisions of other larger objects nearby hitting the object's surface.

The redness comes from the now-exposed second "shelf" layer, which contains water ice, carbon, methane, nitrogen and ammonia -- all substances that can be "cooked" into organic molecules via prolonged exposure to a less intense form of radiation from the Sun. Too little radiation, and the object would be bright white; too much, and you would get the deep black that we see in comets. Just like in the Goldilocks fairy tale, the amount of radiation that hits these reddish objects is just right.



NASA/Conceptual Image Lab/Tyler Chase

Once you have the possibility of organic molecules occurring naturally in the universe by radiating just the right mix of materials -- well, it inches science further toward the possibility that biological materials like amino acids might also occur naturally.

"We're not saying that life is produced in the Kuiper Belt," Cooper is quick to emphasize. "But the basic chemistry may start there, as could also happen in similar Kuiper Belt environments elsewhere in the universe and that is a natural path which could lead toward the chemical evolution of life."

That shelf layer isn't the end of the story, either, when it comes to the white-hued objects. Underneath that could be a deep mantle layer that periodically erupts, bringing patches of white ice to the surface. In other words, those Kuiper Belt objects that appear to be white -- most notably Eris (pictured here) -- are dynamic, possibly volcanically active.

And when NASA's New Horizons mission passes through the Kuiper Belt on its way to Pluto (and its moon, Charon) in 2014, Cooper and his colleagues should get even more data to confirm which materials are present in these icy bodies, and further refine their models.

http://news.discovery.com/space/kuiper-belt-objects-don-coats-of-many-colors.html

Black raspberries may prevent colon cancer, study finds

Black raspberries are highly effective in preventing colorectal tumors in two mouse models of the disease, according to a University of Illinois at Chicago study. The findings are published in the November issue of Cancer Prevention Research. Colorectal cancer is the third most common cancer and the second leading cause of cancer-related death in both men and women in the U.S., according to the National Cancer Institute.

Building on previous research that found black raspberries have antioxidant, anti-cancer, anti-neurodegenerative and anti-inflammatory properties, the researchers looked at the fruit's ability to prevent colon cancer.

"We saw the black raspberry as a natural product, very powerful, and easy to access," said Dr. Wancai Yang, assistant professor of pathology at the UIC College of Medicine and senior author of the study, whose research focuses on the interactions of genetic and nutritional factors in the development of intestinal cancer and tumor prevention.

The researchers used two strains of mice, Apc1638 and Muc2, which each have a specific gene knocked out, causing the mice to develop either intestinal tumors (in the case of Apc1638) or colitis in the case of Muc2. Colitis is an inflammation of the large intestine that can contribute to the development of colorectal cancer.

Both mouse strains were randomized to be fed either a Western-style, high-risk diet (high in fat and low in calcium and vitamin D) or the same diet supplemented with 10 percent freeze-dried black raspberry powder for 12 weeks.

The researchers found that in both mouse strains the black raspberry-supplemented diet produced a broad range of protective effects in the intestine, colon and rectum and inhibited tumor formation.

In the Apc1638 mice, tumor incidence was reduced by 45 percent and the number of tumors by 60 percent. The researchers found that black raspberries inhibited tumor development by suppressing a protein, known as beta-catenin, which binds to the APC gene.

In the Muc2 mice, tumor incidence and the number of tumors were both reduced by 50 percent, and black raspberries inhibited tumor development by reducing chronic inflammation associated with colitis.

The researchers now hope to obtain funding to begin clinical trials in humans, said Yang. Because black raspberries not only prevent cancer but also inflammation, they may also protect against other diseases, such as heart disease.

DHA 'fish oil' supplements do not seem to slow cognitive, functional decline in Alzheimer's disease

Patients with mild to moderate Alzheimer's disease (AD) who received supplementation with the omega-3 fatty acid docosahexaenoic acid (DHA), believed to possibly reduce the risk of AD, did not experience a reduction in the rate of cognitive and functional decline, compared to patients who received placebo, according to a study in the November 3 issue of JAMA, a theme issue on aging.

Joseph F. Quinn, M.D., of Oregon Health and Science University and the Portland VA Medical Center, Portland, Ore., presented the findings of the study at a JAMA media briefing at the National Press Club.

"Several studies have found that consumption of fish, the primary dietary source of omega-3 fatty acids, is associated with a reduced risk of cognitive decline or dementia. Some studies have found that consumption of DHA, but not other omega-3 fatty acids, is associated with a reduced risk of Alzheimer disease," the authors write. However, those studies were observational and did not control who received DHA. Animal studies that used DHA showed reductions in Alzheimer-like brain pathology.

Dr. Quinn and colleagues conducted a randomized, controlled trial to examine whether DHA supplementation would slow the rate of cognitive and functional decline in individuals with Alzheimer's disease. The study, which was conducted between November 2007 and May 2009 at 51 U.S. clinical research sites, included 402 individuals with mild to moderate Alzheimer's disease. Participants were randomly assigned to DHA at a dose of 2 grams/day or to identical placebo (60 percent were assigned to DHA and 40 percent were assigned to placebo). Duration of treatment was 18 months. Changes in cognitive and functional abilities were assessed with the Alzheimer's Disease Assessment Scale

(ADAS-cog) and the Clinical Dementia Rating (CDR) sum of boxes. Rate of brain atrophy was also determined by volumetric magnetic resonance imaging (MRI) in a subsample of participants.

A total of 295 participants completed the trial while taking study medication (DHA: 171; placebo: 124). The researchers found that supplementation with DHA had no beneficial effect on rate of change on ADAS-cog score, with the rate of average change in the score over 18 months being 8.27 points for the placebo group and 7.98 points for the DHA group. The rate of points change on CDR sum of boxes over 18 months was 2.93 for the placebo group compared with 2.87 for the DHA group.

Among the individuals participating in the MRI substudy (102 had MRIs at the beginning of the study and at 18 months [DHA group: 53; placebo group: 49]), an analysis showed no effect of DHA treatment on total brain volume change during 18 months.

"In summary, these results indicate that DHA supplementation is not useful for the population of individuals with mild to moderate Alzheimer disease," the authors write.

The researchers add that "because part of the rationale for the trial was epidemiological evidence that DHA use before disease onset modifies the risk of Alzheimer disease, it remains possible that an intervention with DHA might be more effective if initiated earlier in the course of the disease in patients who do not have overt dementia."

(JAMA. 2010;304[17]:1903-1911. Available pre-embargo to the media at www.jamamedia.org)

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

Please Note: For this study, there will be multimedia content available, including the JAMA Report video, embedded and downloadable video, audio files, text, documents, and related links. This content will be available at 10 a.m. ET Tuesday, November 2 at www.digitalnewsrelease.com/?q=jama_3763.

Editorial: Treatment of Alzheimer Disease and Prognosis of Dementia

In an accompanying editorial, Kristine Yaffe, M.D., of the University of California, San Francisco and Veterans Affairs Medical Center, San Francisco, comments on the findings of this study.

"This trial adds to a growing literature that treatment with DHA does not improve symptoms of AD. Although several observational studies reported that diets rich in fish or supplements with omega-3 fatty acids were associated with reduced risk

of developing AD, most randomized clinical trials for treatment of AD or mild cognitive impairment or in healthy elderly individuals have not found a beneficial effect."

(JAMA. 2010;304[17]:1952-1953. Available pre-embargo to the media at www.jamamedia.org)

http://www.eurekalert.org/pub_releases/2010-11/jaaj-do102810.php

Severely injured should go directly to trauma center: Research

Risk of dying is 24 percent greater if a patient first stops at a non-trauma center

TORONTO, Ont., Nov. 2, 2010-Severely injured patients should be transported directly from the scene of an accident to a trauma center, even if it means bypassing a closer hospital, according to new research that shows this results in a nearly 25 per cent lower death rate.

However, even though 80 to 85 per cent of people in North America live within a one-hour drive or flight of a trauma center, 30 to 60 per cent of severely injured patients are still taken to the nearest hospital.

Researchers led by Dr. Avery Nathens, trauma director at St. Michael's Hospital in Toronto, identified 11,398 patients who were severely injured in Ontario between 2002 and 2007. Of those, 66 per cent were transported directly to one of Ontario's nine adult trauma centres and 30 per cent were transferred to trauma centres after being assessed at the closest hospital.

Overall, 18 per cent of the patients died, or 2,065 people. Four per cent of patients died before they could be transferred to a trauma centre - or 22 per cent of all deaths. Previous studies have not included those patients, so doctors have assumed the death rate is the same for people taken directly to trauma centres and those who are transferred after first being assessed at a non-trauma centre.

By considering the outcome of all patients, Nathens found the risk of dying is 24 per cent greater if a patient first stops at a non-trauma centre. His study will appear in the December issue of the Journal of the American College of Surgeons and is available on-line.

About half of the patients died more than 2-1/2 hours after arriving at a non-trauma centre, suggesting that ways to identify these patients earlier and having more rapid access to ambulance service to transfer them might make a difference.

"Trauma centres save lives," Nathens said. "We acknowledge that access to these trauma centres can be a challenge, given Ontario's geography. So we have to find innovative ways to make sure that hospitals and providers who receive these patients are equipped with the highest level of skills and resources to provide to provide optimal care and a means to transfer them ASAP."

http://www.eurekalert.org/pub_releases/2010-11/smh-sis110210.php

Study shows how ancient plants and soil fungi turned the Earth green

A new breakthrough by scientists at the University of Sheffield has shed light on how the Earth's first plants began to colonise the land over 470 million years ago by forming a partnership with soil fungi.

The research, which was published today (2 November 2010) in Nature Communications, has provided essential missing evidence showing that an ancient plant group worked together with soil-dwelling fungi to 'green' the Earth in the early Palaeozoic era, nearly half a billion years ago.

The research, which also involved experts from the Royal Botanic Gardens, Kew, Imperial College London and the University of Sydney, has provided new insights into our understanding of the evolving dynamic behaviour of the Earth's land plants and fungi.

Scientists have long-suspected that soil fungi formed mutually beneficial relationships with early land plants to play an essential role in assisting their initial colonisation of terrestrial environments. However, until now there has been a lack of evidence demonstrating if and how the earliest ancient land plants, from the early Palaeozoic era (over 470 million years ago), might have cooperated with fungi for mutual benefit.

The team studied a thalloid liverwort plant, which is a member of the most ancient group of land plants that still exists and still shares many of the original features of its ancestors. They used controlled-environment growth rooms to simulate a CO2-rich atmosphere, similar to that of the Palaeozoic era when these plants originated. This environment significantly amplified the benefits of the fungi for the plant's growth and so favoured the early formation of the association between the plant and its fungal partner.

The team found that when the thalloid liverwort was colonised by the fungi, it significantly enhanced photosynthetic carbon uptake, growth and asexual reproduction, factors that had a beneficial impact on plant fitness. The plants grow and reproduce better when colonised by symbiotic fungi because the fungi provide essential soil nutrients. In return, the fungi also benefit by receiving carbon from the plants. The research found that each plant was supporting fungi that had an area of 1-2 times that of a tennis court.

Professor David Beerling, from the Department of Animal and Plant Sciences at the University of Sheffield, said: "By studying these ancient plants we open a window on the past to investigate how the earliest land plants evolved. Our results support the idea that the 'greening' of the Earth was promoted by a symbiosis between

plants and fungi. It shows that plants didn't get a toe-hold on land without teaming up with fungi – this has long been suspected, but until now not investigated. It will require us to think again about the crucial role of cooperation between organisms that drove fundamental changes in the ecology of our planet."

Martin Bidartondo from the Jodrell Laboratory at the Royal Botanic Gardens, Kew, said: "Fungi are present in every type of habitat throughout the world and are essential for many plants to grow. It is exciting that we are now beginning to discover the fungi associated with 'lower' plants, and that many more still remain to be investigated."

Notes for Editors: Citation: 'Mutualistic mycorrhiza-like symbiosis in the most ancient group of land plants' Claire P. Humphreys , Peter J. Franks , Mark Rees, Martin I. Bidartondo, Jonathan R. Leake & David J. Beerling.

http://www.eurekalert.org/pub_releases/2010-11/uos-ssh110210.php

Nostrums: Caution Urged on Cholesterol-Lowering Supplement

By RONI CARYN RABIN

Americans trying to avoid cholesterol-lowering drugs are spending tens of millions of dollars each year on Chinese red yeast rice, a supplement found to lower LDL, or "bad," cholesterol. But the amount of the active ingredient in the supplement varies widely from one brand to another and possibly from batch to batch, a new study has found. And one in three tested products contained a substance that may be toxic to the kidneys.

For the study, published Monday in Archives of Internal Medicine, scientists analyzed samples from a dozen red yeast rice products. While some capsules contained as little as 0.1 milligram of the active ingredient, known as monacolins, others contained 11.15 milligrams.

Four tested samples contained citrinin, a fungus that causes kidney failure in animals.

Earlier studies by the same authors had reported that red yeast rice did effectively lower LDL cholesterol. Now the authors are urging caution, noting that as supplements, the products are not regulated by the Food and Drug Administration and are not standardized. The F.D.A. has warned consumers not to use red yeast rice products that claim to lower cholesterol.

"Our take on it is that red yeast rice, unlike a lot of unproven herbal products, really works," said the lead author, Dr. Ram Y. Gordon, a cardiologist at Chestnut Hill Hospital, part of the University of Pennsylvania Health System. "But because of what we found, there are inherent problems in saying that this is good for people."

http://www.nytimes.com/2010/11/02/health/research/02nostrums.html

Virus breakthrough raises hope over ending common cold

Scientists say they have made a landmark discovery which could pave the way for new drugs to beat illnesses like the common cold.

Until now experts had thought that antibodies could only tackle viral infections by blocking or attacking viruses outside cells. But work done by the Medical Research Council shows antibodies can pass into cells and fight viruses from within. PNAS journal said the finding held promise for a new antiviral drugs.

The Cambridge scientists stressed that it would take years of work and testing to find new therapies, and said that the pathway they had discovered would not work on all viruses.

Fighting viruses

Some antiviral drugs are already available to help treat certain conditions, like HIV.

But viruses remain mankind's biggest killer, responsible for twice as many deaths each year as cancer, and are among the hardest of all diseases to treat.

The new discovery by Dr Leo James and colleagues transforms the previous scientific understanding of our immunity to viral diseases like the common cold, 'winter vomiting' and gastroenteritis.

It shows that antibodies can enter cells and that once inside, they then trigger a response, led by a protein called TRIM21. This protein pulls the virus into a disposal system used by the cell to get rid of unwanted material.

The researchers found this process happens quickly, usually before most viruses have chance to harm the cell. And they discovered that increasing the amount of TRIM21 protein in cells makes this process even more effective, suggesting new ways of making better antiviral drugs.

Dr James said: "Doctors have plenty of antibiotics to fight bacterial infections but few antiviral drugs.

"Although these are early days, and we don't yet know whether all viruses are cleared by this mechanism, we are excited that our discoveries may open multiple avenues for developing new antiviral drugs."

Sir Greg Winter, deputy director of the MRC Laboratory of Molecular Biology, said: "This research is not only a leap in our understanding of how and where antibodies work, but more generally in our understanding of immunity and infection."

http://www.bbc.co.uk/news/health-11673034

Vampire Moth Discovered -- Evolution at Work

John Roach for National Geographic News

A previously unknown population of vampire moths has been found in Siberia. And in a twist worthy of a Halloween horror movie, entomologists say the bloodsuckers may have evolved from a purely fruit-eating species.

Only slight variations in wing patterns distinguish the Russian population from a widely distributed moth species, Calyptra thalictri, in central and southern Europe known to feed only on fruit.

When the Russian moths were experimentally offered human hands this summer, the insects drilled their hook-and-barb-lined tongues under the skin and sucked blood.

A vampire moth in Siberia sucks blood from a researcher's hand. **Photograph by Sharon Hill**

Entomologist Jennifer Zaspel at the University of Florida in Gainesville said the discovery suggests the moth population could be on an "evolutionary trajectory" away from other C. thalictri populations. This is the second population of vampire moths Zaspel and her team have found. They discovered the first in Russia in 2006.

Next January, she will compare the Russian population's DNA to that of other populations and other species to confirm her suspicions.

"Based on geography, based on behavior, and based on a phenotypic variation we saw in the wing pattern, we can speculate that this represents something different, something new," Zaspel said.

"But it is really difficult to say without knowing genetic differences between individuals in that population, and among individuals from other populations, how different this group is going to be."

(Zaspel's research is funded in part by a grant from the National Geographic Society's Committee for Research and Exploration. National Geographic owns National Geographic News.)

Blood Feeding

If it turns out that Zaspel has indeed caught a fruit-eating moth evolving blood-feeding behavior, it could provide clues as to how some moths develop a taste for blood.

Some researchers, she noted, hypothesize that blood-feeding in insects and animals evolved from behaviors such as feeding on tears, dung, and pus-filled wounds.

"We see a progression from nectar feeding and licking or lapping at fruit juices to different kinds of piercing behaviors of fruits and then finally culminating in this skin piercing and blood-feeding," she said.

Chris Nice, a biologist who studies butterfly evolution at Texas State University in San Marcos, said few butterfly and moth species are equipped with the hook-and-barb-lined tongues needed to pierce fruit.

"The fruit-piercing stage in the first place sets the stage, in a morphological sense, for further transitions into, in this case, the blood-feeding," he said.

Nice added that genetic research such as Zaspel's is the only way to test ideas on how certain behaviors evolve.

Sexual Gift?

The next question is why this Russian population of C. thalictri appears to have evolved blood-feeding behavior, Zaspel said. Only male moths exhibit blood-feeding, she noted, raising the possibility that as in some species of butterflies and other moths, the Russian moths do it to pass on salt to females during copulation.

"There is no evidence it prolongs the life of the male, or anything like that," she said. "So we suspect that it is probably going to the female."

The sexual gift, she said, would provide a nutritional boost to young larvae that feed on leaf-rich, but sodium-poor, diets. If salt is otherwise limited in the environment the sexual gift theory "would make sense," Nice added.

http://news.nationalgeographic.com/news/2008/10/081027-vampire-moth-evolution-halloween-missions.html

A sweet discovery raises hope for treating Ebola, Lassa, Marburg and other fast-acting *viruses*

New research published in the Journal of Leukocyte Biology suggests that a purified form of a product modified from simple sugar molecules can eradicate killer viruses by mobilizing white blood cells

When a team of European researchers sought to discover how a class of antiviral drugs worked, they looked in an unlikely place: the sugar dish. A new research report appearing in the Journal of Leukocyte Biology (http://www.jleukbio.org) suggests that a purified and modified form of a simple sugar chain may stop fast-acting and deadly viruses, such as Ebola, Lassa, or Marburg viruses, in their tracks. This compound, called

chlorite-oxidized oxyamylose or COAM, could be a very attractive therapeutic option because not only did this compound enhance the early-stage immune defenses in mice, but because of sugar's abundance, it is derived from easily obtainable sources.

"We modified and purified a safe drug from natural sources and discovered how it can protect against deadly virus infections," said Ghislain Opdenakker, M.D., a researcher involved in the study from the Laboratory of Immunobiology at the Rega Institute for Medical Research and the University of Leuven in Belgium.

To make this discovery, researchers infected mice with a virus that kills in less than a week. When one group of these infected mice was treated with an unpurified version of the compound, about half of the infected mice were protected from the effects of the virus. Researchers then purified the compound and treated another group of infected mice. In that group, more than 90 percent survived the deadly infection. These results suggest that the purified compound almost completely blocked the killer virus by speeding the response of the body's fast-acting immune cells, called white blood cells or leukocytes, at the early stage of infection.

"This is an exciting discovery because it offers hope that we will finally be able to really do something about some of the world's deadliest viruses – rapidly mobilizing antiviral immune cells is critical in the race between these killer viruses and the host," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology. "The fact that this compound comes from something as abundant as sugar just sweetens the findings."

Details: *Sandra Li, Sofie Starckx, Erik Martens, Chris Dillen, Nathalie Lamerant-Fayel, Nele Berghmans, Mieke Gouwy, Melissa van Pel, Hubertine Heremans, Claudine Kieda, Willem E. Fibbe, Alfons Billiau, Jo Van Damme, and Ghislain Opdenakker. Myeloid cells are tunable by a polyanionic polysaccharide derivative and co-determine host rescue from lethal virus infection. J Leukoc Biol November 2010 88:1017-1029; doi:10.1189/jlb.1109724 ; http://www.jleukbio.org/content/88/5/1017.abstract*

http://www.eurekalert.org/pub_releases/2010-11/foas-asd110310.php

Asthma drug prevents spread of breast cancer: study

TORONTO, Ont. — November 1, 2010 — A drug commonly used in Japan and Korea to treat asthma has been found to stop the spread of breast cancer cells traditionally resistant to chemotherapy, according to a new study led by St. Michael's pathologist Dr. Gerald Prud'homme.

"Tranilast, a drug approved for use in Japan and South Korea, and not in use in Canada or the U.S., has been used for more than two decades to treat asthma and other allergic disorders including allergic rhinitis and atopic dermatitis," Dr. Prud'homme says. "Now, our study is the first to discover it not only stops breast cancer from spreading but how the drug targets breast cancer cells."

Researchers grew breast cancer stem cells, which give rise to other cancer cells, in culture. The cells were injected into two groups of mice, including one group, which was also treated with tranilast. Dr. Prud'homme and his colleagues found the drug reduced growth of the primary cancerous tumour by 50 per cent and prevented the spread of the cancer to the lungs. Researchers also identified a molecule in the cancer cell that binds to tranilast and appears to be responsible for this anti-cancer effect.

Tranilast binds to a molecule known as the aryl hydrocarbon receptor (AHR), which regulates cell growth and some aspects of immunity. This makes the drug beneficial in treating allergies, inflammatory diseases and cancer.

"For the first time, we were able to show that tranilast shows promise for breast cancer treatment in levels commonly well-tolerated by patients who use the drug for other medical conditions," Dr. Prud'homme said. "These results are very encouraging and we are expanding our studies. Further studies are necessary to determine if the drug is effective against different types of breast and other cancers, and its interaction with anti-cancer drugs.

Dr. Prud'homme says clinical trials in cancer patients may be possible within a few years. The study is published today in the journal PLoS ONE.

http://www.eurekalert.org/pub_releases/2010-11/smh-adp110210.php

Levels of coumarin in cassia cinnamon vary greatly even in bark from the same tree

A "huge" variation exists in the amounts of coumarin in bark samples of cassia cinnamon from trees growing in Indonesia, scientists are reporting in a new study. That natural ingredient in the spice may carry a theoretical risk of causing liver damage in a small number of sensitive people who consume large amounts of cinnamon. The report appears in ACS' bi-weekly Journal of Agricultural and Food Chemistry.

Friederike Woehrlin and colleagues note that cinnamon is the second most popular spice, next to black pepper, in the United States and Europe. Cinnamon, which comes from the bark of trees, is sold as solid sticks and powder with the country of origin rarely declared on the package label. There are two main types: Ceylon cinnamon (also known as "true" cinnamon) and cassia cinnamon. Ceylon grows in Sri Lanka (formerly Ceylon), the Seychelles, and Madagascar. Cassia generally comes from China and Indonesia. Both types can

contain coumarin, a natural flavoring found in plants. Studies have linked high coumarin intake to liver damage in a small number of sensitive people.

The scientists analyzed 91 cinnamon samples purchased from stores in Germany. They found that coumarin levels varied widely among different bark samples of Cassia cinnamon. Therefore they analyzed cassia bark samples of five trees received directly from Indonesia and found a huge variation even among samples collected from a single tree. The study confirmed that cassia cinnamon has the highest levels of coumarin, while Ceylon had the lowest levels. On average, cassia cinnamon powder contained up to 63 times more coumarin than Ceylon cinnamon powder and cassia cinnamon sticks contained 18 times more coumarin than Ceylon sticks. "Further research is necessary to identify factors influencing the coumarin levels in cassia cinnamon and to possibly allow the harvesting of cassia cinnamon with low coumarin levels in the future," the report notes.

Health officials say it is almost impossible for consumers to distinguish between Ceylon and cassia in cinnamon powder. Cinnamon sticks, however, do look different. Cassia cinnamon sticks consist of a thick layer of rolled bark, while Ceylon cinnamon sticks have thin layers of bark rolled up into a stick.

ARTICLE FOR IMMEDIATE RELEASE "Quantification of Flavoring Constituents in Cinnamon: High Variation of Coumarin in Cassia Bark from the German Retail Market and in Authentic Samples from Indonesia"
http://www.eurekalert.org/pub_releases/2010-11/acs-loc110310.php

Specific changes in the brain associated with sleep deprivation described in new study

Discovery of novel genes and brain areas associated with sleep deprivation may have implications for improved management of brain function

SEATTLE, Wash. Researchers at the Allen Institute for Brain Science and SRI International have published the most systematic study to date of the effects of sleep deprivation on gene expression in the brain. The findings have implications for improving the understanding and management of the adverse effects of sleep deprivation on brain function.

The study, available in Frontiers in Neuroscience, has created an extensive and detailed map of gene activity, known as gene expression, in the mouse brain across five behavioral conditions including sleeping, waking and sleep deprivation. Activity of approximately 220 genes responding to these conditions was examined in detail, down to the cellular level, throughout the brain. Additionally, seven brain areas were examined by DNA microarray analysis, which reports the expression levels of tens of thousands of genes and allows a genome-wide analysis of the consequences of sleep deprivation.

"Although most people experience occasional sleep deprivation and recognize its impact on their mood and behavior, there is little scientific understanding of how sleep loss actually affects brain function," said Thomas Kilduff, Ph.D., senior director of the Center for Neuroscience at SRI International. "This pioneering study documents how extending wakefulness affects gene expression in specific brain regions and describes a 'molecular anatomical signature' of sleep deprivation. Our findings may contribute to treatments that will help improve sleep quality and reduce problems arising from sleep deprivation."

By comparing which genes were turned on and where in the brain across the different conditions, the researchers discovered that the majority of the neurons in the forebrain were affected in diverse ways by sleep deprivation, painting a dynamic picture of the molecular consequences of sleep deprivation on higher cognitive functions. Affected forebrain regions include the neocortex, amygdala and hippocampus, which mediate cognitive, emotional and memory functions that are impaired by sleep deprivation.

Detailed analysis of 209 brain areas revealed a novel set of genes not previously associated with sleep deprivation, including genes associated with the stress response, cell-cell signaling, and the regulation of other genes. One gene, neurotensin, has been implicated in schizophrenia and is similarly induced by antipsychotic drugs. These genes may provide potential targets for therapeutic intervention to alleviate the effects of sleep deprivation.

"These data illustrate the complex and dynamic relationship between sleep and sleep deprivation, neuroanatomical pathways and gene expression," said Ed Lein, Ph.D., senior director of neuroscience at the Allen Institute for Brain Science and senior author of the study. "The breadth and level of detail provided by these data will be a unique resource for the scientific community, and to that end we have made the data set publicly available online in its entirety."

The resulting open data resource is one of a growing collection of public online resources provided by the Allen Institute, which was founded by philanthropist Paul G. Allen to advance brain research.

Sleep deprivation leads to a range of cognitive, attention and emotional deficits, including irritability and impaired memory, coordination, and concentration. These effects, which can compromise health, performance and safety, are common among those who work extended hours, including military and medical personnel, and

others suffering from chronic sleep loss. Sleep deficits have also been linked to the development of some chronic diseases and disorders, including diabetes, depression, obesity and cardiovascular disease.

The control of sleeping and waking and the consequences of sleep deprivation are believed to be associated with gene activity changes in brain regions involved in sleep regulation and higher level functions. Understanding these changes in gene activity is a critical step toward advances in the treatment of sleep disorders and mitigation of the effects of sleep deprivation.

The data in this study are publicly available via the ALLEN Brain Atlas data portal (www.brain-map.org) as the "Sleep Study". This online dataset comprises a substantial collection of data detailing where specific genes are expressed, or "turned on", throughout the mouse brain for five conditions of sleeping and waking. Specifically, it includes searchable image-based gene expression data for approximately 220 sleep-related genes, genome-wide microarray data for seven sleep-associated brain areas, and a 3D viewing tool for visualizing changes in gene expression across different conditions.

This public resource is a unique resource for sleep researchers worldwide and holds promise for accelerating progress toward understanding and effective treatment of sleep disorders.

***Citation**: C.L. Thompson et al. (2010) Molecular and anatomical signatures of sleep deprivation in the mouse brain. Frontiers in Neuroscience, Vol. 4, Article 165, doi: 10.3389/fnins.2010.00165.*

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http://www.eurekalert.org/pub_releases/2010-11/aifb-sci110310.php

Stone Age humans needed more brain power to make big leap in tool design

Stone Age humans were only able to develop relatively advanced tools after their brains evolved a greater capacity for complex thought

Stone Age humans were only able to develop relatively advanced tools after their brains evolved a greater capacity for complex thought, according to a new study that investigates why it took early humans almost two million years to move from razor-sharp stones to a hand-held stone axe.

Researchers used computer modelling and tiny sensors embedded in gloves to assess the complex hand skills that early humans needed in order to make two types of tools during the Lower Palaeolithic period, which began around 2.5 million years ago. The cross-disciplinary team, involving researchers from Imperial College London, employed a craftsperson called a flintnapper to faithfully replicate ancient tool-making techniques.

The team say that comparing the manufacturing techniques used for both Stone Age tools provides evidence of how the human brain and human behaviour evolved during the Lower Palaeolithic period.

Neuroscientist Dr Aldo Faisal, the lead author of the study from the Departments of Bioengineering and Computing at Imperial College London, says: "The advance from crude stone tools to elegant hand-held axes was a massive technological leap for our early human ancestors. Hand-held axes were a more useful tool for defence, hunting and routine work. Interestingly, our study reinforces the idea that tool making and language evolved together as both required more complex thought, making the end of the Lower Palaeolithic a pivotal time in our history. After this period, early humans left Africa and began to colonise other parts of the world."

Prior to today's study, researchers have had different theories about why it took early humans more than 2 million years to develop stone axes. Some have suggested that early humans may have had underdeveloped motor skills or abilities, while others have suggested that it took human brains this time to develop more complex thoughts, in order to dream up better tool designs or think about better manufacturing techniques.

The researchers behind today's study say that their evidence, from studying both tool-making techniques, confirms that the evolution of the early human brain was behind the development of the hand-held axe. Furthermore, the team suggest that the advancement of hand-held axe production may have also coincided with the development of language, as these functions overlap in the same regions of the modern and early human brains.

The flintnapper who participated in today's study created two types tools including the razor-sharp flakes and hand-held axes. He wore a data glove with sensors enmeshed into its fabric to record hand and arm movements during the production of these tools.

After analysing this data, the researchers discovered that both flake and hand-held axe manufacturing techniques were equally complex, requiring the same kind of hand and arm dexterity. This enabled the scientists to rule out motor skills as the principal factor for holding up stone tool development.

The team deduced from their results that the axe-tool required a high level of brain processing in overlapping areas of the brain that are responsible for a range of different functions including vocal cords and complex hand gestures.

This is the first time that neuroscientists, archaeologists, anthropologists and flintnappers have teamed together, using cutting edge technology including data glove sensors and advanced modelling, to develop a deeper understanding of early human evolution.

In the future, the team plan to use their technology to compare tools made by Neanderthals, an extinct ancestor of humans, to glean insights into their brain development.

The study also included researchers from the Department of Anthropology, from Emory University; Department of Archaeology and Osteology, Gotland University College; and the Department of Archaeology, Exeter University.

http://www.eurekalert.org/pub_releases/2010-11/icl-sah110310.php

Do holes make moles?

Surprising first ancestor of bizarre marsupial moles

(PhysOrg.com) -- The mysterious origins of Australia's bizarre and secretive marsupial moles have been cast in a whole new and unexpected light with the first discovery in the fossil record of one of their ancestors.

Marsupial mole emerging from hole to eat a lizard. Photo copyright: Mike Gillam/Auscape

The find reveals a remarkable journey through time, place and lifestyle: living marsupial moles are blind, earless and live underground in the deserts of the Northern Territory, Western Australia and South Australia, yet their ancestors lived in lush rainforest far away in north Queensland.

In the journal Proceedings of the Royal Society B, a team led by Professor Mike Archer, of the University of New South Wales (UNSW), reports the discovery of the remarkable 20 million-year-old fossil at the Riversleigh World Heritage fossil site.

Although related to kangaroos, koalas and other marsupials, living marsupial moles far more closely resemble Cape golden moles, which burrow through the desert sands of Africa. The two golden-furred animals not only look indistinguishable when seen side by side but share many other similarities in their teeth and skeletons that reflect their subterranean lifestyles.

Yet the Cape golden mole is a placental mammal - the group that includes rats, bats, elephants and humans – and these two very different branches of the mammal family evolved from a common ancestor at least 125 million years ago, says Professor Archer. Having diverged in ancestry, however, their similar lifestyles have meant that they have converged in anatomy.

"This fossil discovery came as a real shock," he says. "Until now, we had always assumed that marsupial moles must have evolved in an unknown ancient Australian desert because, like Cape golden moles, the living marsupial moles survive only in deserts.

"Yet this ancestral Australian mole, which is not as specialised as the living form, has been discovered in ancient rainforest deposits—not deserts. The fossils suggest that they became mole-like while burrowing through the mossy floors of those ancient forests."

This missing link has solved a second mystery about how the highly specialised V-shaped teeth of the living marsupial mole evolved. Although they are almost identical to the teeth of their African counterparts, it is now clear that they went down a completely different evolutionary pathway to get there, says co-author Dr Robin Beck of the American Museum of Natural History.

"This ancient link makes it clear that marsupials followed a completely different path from placentals but ended up with almost identical-looking teeth."

Co-author UNSW Associate Professor Suzanne Hand said: "It goes to the heart of global debates about relationship versus convergence - whether animals are similar because they are closely related or similar because they have had to adapt to related challenges. It's also exciting because it so beautifully demonstrates just how adaptive Australian marsupials can be when given the right evolutionary challenges and enough time to meet them." *Provided by University of New South Wales*

http://www.physorg.com/news/2010-11-holes-moles-ancestor-bizarre-marsupial.html

Gustav Klimt's mysterious embryos

Amy Maxmen, contributor

Zeus covertly impregnated Danaë, the legendary princess of Argos, by disguising himself as golden coins, which streamed into the princess's locked chamber and ran down her thighs like raindrops as she slept. Danaë's father had imprisoned the princess to shield her from men because of a prediction that his future grandson would one day kill him. The disguised Zeus gave Danaë a son, and destiny took its course.

Despite the richness of this entire myth, the erotic moment of Zeus's conquest has been a favourite among artists for centuries, as it symbolises the victory of passion and creativity over repression - or perhaps just because it's the steamiest scene.

Austrian painter Gustav Klimt's 1907 depiction, however, differs from the others in that it mirrors Zeus's stream of golden coins with another stream of circular forms that have eluded art historians for decades.

It took the eyes of developmental biologist Scott Gilbert at Swarthmore College in Pennsylvania to identify these shapes as early embryonic forms drifting down the right side of Klimt's Danaë, over the naked, supine princess.

(Image: Gustav Klimt)

Art historians have called the circles "ovaloid shapes", "ornaments" and "gold filagree disks". Two analyses related them to biological forms, but oddly identified them as "chromosome-like" and "gilded spermatozoa". But the moment Gilbert laid eyes upon a reproduction of Danaë in an art book, he saw spheres of embryonic cells: blastocysts.

A blastocyst consists of a layer of cells surrounding a cavity that hovers above a lump of cells - the source of embryonic stem cells that will eventually divide to form the fetal anatomy. Comparisons of any textbook blastocyst with the painting's circular forms are likely to convince art historians of Gilbert's interpretation.

What really shocked Gilbert wasn't just that nobody had identified these blastocysts before, but that Klimt had painted the obscure objects in the first place.

In a manuscript currently in press for an art journal, Gilbert and Sabine Brauckmann, a historian of science at Tartu University Library in Estonia, discuss the use of fertilization and embryos in the art of Gustav Klimt, Diego Rivera and Frida Kahlo. They say these artists painted biological images to symbolize creation.

To find out where Klimt acquired such knowledge, Brauckmann sifted through the Viennese archives and concluded that Klimt had soaked up embryology at soirees held by a leading anatomist in Vienna, Emil Zuckerkandl, and his wife Bertha.

Bertha, a writer with a passion for the arts, would invite her talented circle of friends over in the evenings for scientific lectures accompanied by slides of blood vessels, brain cells and other microscopic wonders. Klimt was among the artists, musicians, writers and scientists in attendance.

"In these salons, there was this high level of integration between science and the arts that you just don't have today," says Gilbert. "And I think that high art today not only goes away from that, but almost rebels against science."

Each field offered the other new ways of seeing. Just as the language of embryology (symmetry, formation, rhythm, choreography) was largely borrowed from artistic discourse, Gilbert says, science once gave artists metaphorical bulbs from which to blossom.

"At certain times in history, science was a part of the artistic vocabulary," Gilbert says. "Cell biology was being used as an emblem. Diego Rivera paints cells in a mechanized context to show how technology might eventually regulate our biological proclivities, including reproduction. Frida Kahlo used fertilization to depict the creation of something new."

Artists found beauty in science, and then made science beautiful.

http://www.newscientist.com/blogs/culturelab/2010/11/gustav-klimts-mysterious-embryos.html

Pompeiians Flash-Heated to Death—"No Time to Suffocate"

Victims' lifelike poses among clues that ash was not the key killer, study says.

Maria Cristina Valsecchi in Rome for National Geographic News

The famous lifelike poses of many victims at Pompeii—seated with face in hands, crawling, kneeling on a mother's lap—are helping to lead scientists toward a new interpretation of how these ancient Romans died in the A.D. 79 eruptions of Italy's Mount Vesuvius.

Until now it's been widely assumed that most of the victims were asphyxiated by volcanic ash and gas. But a recent study says most died instantly of extreme heat, with many casualties shocked into a sort of instant rigor mortis.

Volcanologist Giuseppe Mastrolorenzo and colleagues began by analyzing layers of buried volcanic ash and rock, then fed the data into a computer simulation of the Mount Vesuvius eruption.

Plaster cast of a Pompeiian volcano victim, made from a centuries-old hollow in solidified ash. **Photograph by Hans Madej/laif/Redux**

They concluded that the volcano, some six miles (ten kilometers) from Pompeii, produced six different pyroclastic surges—fast-moving, ground-hugging waves of hot, toxic gases and ash (aerial picture of Pompeii ruins).

Most of the hundreds of fatalities occurred during the fourth surge—the first to reach Pompeii—even though that surge was relatively slow and ash-poor.

Ash-deposit analysis and computer simulations of the surges suggest that Pompeii was at the edge of the flows' reach. That would mean the fourth surge "was too weak to wreck buildings," Mastrolorenzo, of the Italian National Institute for Geophysics and Volcanology, told National Geographic News.

The surge also carried relatively little ash, leaving behind a sediment layer only about an inch (three centimeters) deep, previous sediment measurements have shown.

But during the surge "temperatures outdoors—and indoors—rose up to 300°C [570°F] and more, enough to kill hundreds of people in a fraction of a second," said Mastrolorenzo, who led the study, published in the June 2010 issue of the journal PLoS ONE.

Among the evidence for such fatal temperatures are the team's bone studies. In a lab the researchers heated bone samples of freshly dead modern-day humans and horses, then compared the results to those seen in bones of Pompeiian victims of Vesuvius. Specific patterns of color and cracking in the ancient bones, among other features, "proved they were exposed to extreme heat," he said.

In addition, other reports have cited the melting of Pompeiian lead-tin silverware, which occurs at about 480°F [250°C], and the telltale charring of wood objects and food as proof of the temperatures during the disaster, according to the new study.

And then there are those death postures. About three-quarters of the known Pompeii victims are "frozen in suspended actions" and show evidence of sudden muscle contractions, such as curled toes, the study says.

"Heretofore archaeologists misinterpreted them as people struggling to breathe and believed they died suffocated by ashes," Mastrolorenzo said. "Now we know that couldn't be."

Because of the extreme heat, "when the pyroclastic surge hit Pompeii, there was no time to suffocate," he said. "The contorted postures are not the effects of a long agony, but of the cadaveric spasm, a consequence of heat shock on corpses."

http://news.nationalgeographic.com/news/2010/11/101102/pompeii-mount-vesuvius-science-died-instantly-heat-bodies/

Americans less healthy than English, but live as long or longer, study finds

Older Americans are less healthy than their English counterparts, but they live as long or even longer than their English peers, according to a new study by researchers from the RAND Corporation and the Institute for Fiscal Studies in London.

Researchers found that while Americans aged 55 to 64 have higher rates of chronic diseases than their peers in England, they died at about the same rate. And Americans age 65 and older -- while still sicker than their English peers -- had a lower death rate than similar people in England, according to findings published in the journal Demography.

The paper was co-authored by James Banks and Alastair Muriel of the Institute for Fiscal Studies and James P. Smith, distinguished chair in labor markets and demographic studies at RAND.

"If you get sick at older ages, you will die sooner in England than in the United States," Smith said. "It appears that at least in terms of survival at older ages with chronic disease, the medical system in the United States may be better than the system in England."

The study expands upon an earlier analysis by Banks and Smith that found that Americans aged 55 to 64 suffered from diseases such as diabetes at rates up to twice those seen among similarly aged people in England. The trend was observed across all socioeconomic groups.

Researchers analyzed information from two comparable surveys of people age 50 and over in the United States and England -- the Health and Retirement Survey and the English Longitudinal Survey of Ageing -- funded by the National Institute on Aging in the United States.

In the new study, researchers examined the prevalence of illness among those 55 to 64 and 70 to 80. They also looked for the first time at the onset of new illnesses in those age groups in the United States and England during the years spanning 2002 to 2006. Finally, researchers examined trends in death rates in each country.

The findings showed that both disease prevalence and the onset of new disease were higher among Americans for the illnesses studied -- diabetes, high-blood pressure, heart disease, heart attack, stroke, chronic lung diseases and cancer. Researchers found that the higher prevalence of illness among Americans compared to the English that they previously found for those aged 55 to 64 was also apparent for those in their 70s. Diabetes rates were almost twice as high in the United States as in England (17.2 percent versus 10.4 percent) and cancer prevalence was more than twice as high in the United States (17.9 percent compared to 7.8 percent) for people in their 70s.

In spite of both higher prevalence and incidence of disease in America, death rates among Americans were about the same in the younger ages in this period of life and actually lower at older ages compared to the English. Researchers say there are two possible explanations why death rates are higher for English after age 65 as compared to Americans. One is that the illnesses studied result in higher mortality in England than in the United States. The second is that the English are diagnosed at a later stage in the disease process than Americans. "Both of these explanations imply that there is higher-quality medical care in the United States than in England, at least in the sense that these chronic illnesses are less likely to cause death among people living in the United States," Smith said.

"The United States' health problem is not fundamentally a health care or insurance problem, at least at older ages," Banks said. "It is a problem of excess illness and the solution to that problem may lie outside the health care delivery system. The solution may be to alter lifestyles or other behaviors."

The study also investigated the relationship between the financial resources of individuals in both countries and how soon they would they would die in the future.

While poorer people are more likely to die sooner than their more well-off counterparts, researchers say their finding supports the view that the primary pathway between health and wealth is that poor health leads to a depletion of household wealth, rather than being poor causes one's health to decline. Researchers found that the substantial changes in wealth that occurred in the years 1992 and 2002 in the United States through increases in stock prices and housing prices did not alter the probability of subsequent death.

The research was supported by grants from the U.S. National Institute on Aging and the U.K. Economic and Social Research Council. The study was conducted through the Institute for Fiscal Studies in London and RAND Labor and Population, which examines issues involving U.S. labor markets, the demographics of families and children, social welfare policy, the social and economic functioning of the elderly, and economic and social change in developing countries.

http://www.eurekalert.org/pub_releases/2010-11/rc-alh110110.php

Genetic deletion discovered as risk factor for autism and schizophrenia

Researchers have identified the deletion of a genomic region on chromosome 17 as a significant risk factor for autism spectrum disorders (ASD) and schizophrenia. A mutation of one of the genes in the deleted interval already is a known cause of renal cysts and diabetes syndrome (RCAD).

The research, by an international collaboration of scientists led by Emory University, will be published in the American Journal of Human Genetics. Lead author of the study is Daniel Moreno-De-Luca, MD, MSc, Emory postdoctoral fellow in the Department of Human Genetics. Senior authors at Emory include David H. Ledbetter, PhD and Christa L. Martin, PhD.

Scientists have known that autism and schizophrenia are strongly influenced by genetic mutations. Although they have shown that rare copy number variations – insertions or deletions of genomic material – play a common and overlapping role in the two disorders, they had not previously identified this specific copy number variation (CNV), which confers very high risk.

The research team performed cytogenetic array analysis in patients with neurodevelopmental disorders referred for clinical testing. They detected a recurrent deletion at 17q12 in 24 patients out of more than 23,000 patients with ASD, developmental delay, intellectual disability, or schizophrenia. This deletion was not present in any of 52,448 control individuals.

"We calculate a minimum odds ratio of 13.58 for this sample," says Ledbetter, "meaning that someone with this deletion is at least 13.58 times more likely to develop ASD or schizophrenia than is someone lacking this CNV."

The deleted 17q12 region contains 15 genes, including HNF1B, the gene associated with RCAD. A number of the ASD patients in the study were found to have kidney disease and/or diabetes as well. RCAD patients, as opposed to what was initially believed, also often have neurodevelopmental disorders.

"We have uncovered a copy number variation that confers a very high risk for ASD, schizophrenia, and neurodevelopmental disorders," says Moreno-De-Luca. "This is significant, because the 17q12 deletion is among the 10 most frequent pathogenic recurrent genomic deletions identified in children with unexplained neurodevelopment impairments. We believe it also may increase risk for other psychiatric conditions such as bipolar disorder."

http://www.eurekalert.org/pub_releases/2010-11/eu-gdd110210.php

Obesity rate will reach at least 42 percent, say models of social contagion

Projections suggest obesity among American adults may not plateau until 2050

CAMBRIDGE, Mass. -- Researchers at Harvard University say America's obesity epidemic won't plateau until at least 42 percent of adults are obese, an estimate derived by applying mathematical modeling to 40 years of Framingham Heart Study data.

Their work, published this week in the journal PLoS Computational Biology, runs counter to recent assertions by some experts that the obesity rate, which has been at 34 percent for the past five years, may have peaked. An additional 34 percent of American adults are overweight but not obese, according to the federal government's Centers for Disease Control and Prevention.

The Harvard scientists say that their modeling shows that the proliferation of obesity among American adults in recent decades owes in large part to its accelerating spread via social networks.

"Our analysis suggests that while people have gotten better at gaining weight since 1971, they haven't gotten any better at losing weight," says lead author Alison L. Hill, a graduate student in Harvard's Program for Evolutionary Dynamics, Biophysics Program, and at the Harvard-MIT Division of Health Sciences and Technology. "Specifically, the rate of weight gain due to social transmission has grown quite rapidly."

The projections by Hill and colleagues are a best-case scenario, meaning that America's obesity rate could rise above 42 percent of adults. One silver lining is that their model suggests the U.S. population may not reach this level for another 40 years, making the future rate of increase much more gradual than over the past 40 years. Only 14 percent of Framingham Heart Study participants were obese in 1971.

Along with co-authors David G. Rand, Martin A. Nowak, and Nicholas A. Christakis, Hill broke down the spread of obesity into three components:

* the rate at which obesity has spread through social networks, via transfer from person to person;
* the rate of non-social transmission of obesity, such as through easier access to unhealthy foods or increasingly sedentary lifestyles;
* the rate of "recovery" from obesity, defined as weight loss sufficient to push body mass index (BMI) back below 30.

"We find that while non-social transmission of obesity remains the most important component in its spread, social transmission of obesity has grown much faster in the last four decades," says Rand, a research scientist in the Program for Evolutionary Dynamics and a fellow in Harvard's Department of Psychology and Berkman Center for Internet & Society.

Hill, Rand, and colleagues found that a non-obese American adult has a 2 percent chance of becoming obese in any given year -- a figure that has risen in recent decades -- and that this number rises by 0.4 percentage points with each obese social contact, meaning that five obese contacts doubles the risk of becoming obese.

By comparison, an obese adult has a 4 percent chance of losing enough weight to fall back to merely "overweight" in any given year. This figure has remained essentially constant since 1971.

"These results suggest that social norms are changing the propensity for becoming obese by non-social mechanisms, and also magnifying the effect that obese individuals have on their non-obese contacts," the scientists write in PLoS Computational Biology.

Hill, Rand, Nowak, and Christakis' work was funded by the National Institute on Aging, the John Templeton Foundation, the Bill and Melinda Gates Foundation, the National Science Foundation/National Institutes of Health Joint Program in

Mathematical Biology, and graduate fellowships from the National Science Foundation and the Canadian Natural Sciences and Engineering Research Council.

http://www.eurekalert.org/pub_releases/2010-11/hu-orw110210.php

Study: Brain 'energy crisis' may spark Parkinson's

WASHINGTON (AP) — Parkinson's disease may stem from an energy crisis in the brain, years before symptoms appear.

If the research pans out, it points to a possible new approach for Parkinson's: Giving a boost to a key power switch inside brain cells in hopes of slowing the disease's inevitable march instead of just treating symptoms.

"This is an extremely important and interesting observation that opens up new therapeutic targets," says Dr. Flint Beal of New York's Weill Cornell Medical College, who wasn't involved with the new study.

Beal said scientists already are planning first-stage tests to see if a drug now used for diabetes might help Parkinson's, too, by targeting one of the implicated energy genes.

At issue are little power factories inside cells, called mitochondria. Increasingly, scientists suspect that malfunctioning mitochondria play some role in a list of degenerative brain diseases.

After all, brain cells are energy hogs, making up about 2% of body weight yet consuming about 20% of the body's energy. So a power drain could trigger some serious long-term consequences.

"It could be a root cause" of Parkinson's, says Dr. Clemens Scherzer of Boston's Brigham and Women's Hospital and Harvard University.

About 5 million people worldwide, and 1.5 million in the U.S., have Parkinson's, characterized by increasingly severe tremors and periodically stiff or frozen limbs. Patients gradually lose brain cells that produce dopamine, a chemical key to the circuitry that controls muscle movement. There is no cure, although dopamine-boosting medication and an implanted device called deep brain stimulation can help some symptoms.

No one knows what causes Parkinson's. To find genetic clues, Scherzer gathered an international team of researchers to comb studies of more than 300 samples of brain tissue — from diagnosed Parkinson's patients, from symptom-free people whose brains showed early Parkinson's damage was brewing, and from people whose brains appeared normal. They even used a laser beam to cut out individual dopamine-producing neurons in the most ravaged brain region, the substantia nigra, and examine gene activity.

The team found 10 sets of genes that work at abnormally low levels in Parkinson's patients, genes that turned out to play various roles in the mitochondria's energy production, Scherzer recently reported in the journal Science Translational Medicine. Especially compelling, the genes also were sluggish in people with presymptomatic, simmering Parkinson's.

And all the gene sets are controlled by what Scherzer calls a master regulator gene named PGC-1alpha — responsible for activating many other genes that maintain and repair those mitochondrial power factories.

So might revving up PGC-1alpha in turn boost underperforming mitochondrial genes and protect the brain? To see, the researchers tested dopamine-producing neurons from rats that were treated in ways known to cause Parkinson's-like damage. Sure enough, boosting the power switch prevented that damage.

This genetic evidence supports years of tantalizing hints that mitochondria are culprits in Parkinson's, says Dr. Timothy Greenamyre of the University of Pittsburgh Medical Center.

He ticks off the clues: A rare, inherited form of Parkinson's is caused by a mutated gene involved with mitochondrial function. A pesticide named rotenone that can kill dopamine cells and trigger Parkinson's symptoms in animals also is toxic to mitochondria. So is another Parkinson's-triggering chemical named MPTP.

Now with Scherzer's study, "it's going to be harder and harder for people to think that mitochondria are just a late player or an incidental player in Parkinson's disease," Greenamyre says.

The crux of all that complicated neurogenetics: A diabetes drug named Actos is among the compounds known to activate part of that PGC-1alpha pathway, and Weill Cornell's Beal says it's poised for an initial small trial in Parkinson's.

Separately, a nutrient named Coenzyme Q10 is believed important in mitochondrial energy production, and Beal is leading a study to see if high doses might help Parkinson's. Results are due in 2012.

But Scherzer issues a caution: The average Parkinson's patient has lost about 70% of his or her dopamine-producing neurons by the time of diagnosis. So if blocking a brain energy drain is going to do any good, scientists may have to find ways to spot brewing Parkinson's much earlier.

"I don't think you can turn back the clock," he says.

http://www.usatoday.com/yourlife/health/medical/2010-11-03-parkinsons-brain_N.htm

Vitamin E linked to increased risk of some strokes

Taking vitamin E could slightly increase the risk of a particular type of stroke, a study says.

The British Medical Journal study found that for every 1,250 people there is the chance of one extra haemorrhagic stroke - bleeding in the brain. Researchers from France, Germany and the US studied nine previous trials and nearly 119,000 people. But the level at which vitamin E becomes harmful is still unknown, experts say. The study was carried out at Harvard Medical School, Boston, and INSERM in Paris.

Haemorrhagic strokes are the least common type and occur when a weakened blood vessel supplying the brain ruptures and causes brain damage.

Researchers found that vitamin E increased the risk of this kind of stroke by 22%. The study also found that vitamin E could actually cut the risk of ischaemic strokes - the most common type of stroke - by 10%. Ischaemic strokes account for 70% of all cases and happen when a blood clot prevents blood reaching the brain.

Experts found vitamin E could cut the risk, equivalent to one ischaemic stroke prevented per 476 people taking the vitamin.

Lifestyle check

However, they warned that keeping to a healthy lifestyle and maintaining low blood pressure and low cholesterol have a far bigger effect on cutting the risk of ischaemic stroke than taking vitamin E.

More than 111,000 people have a stroke every year and they are the third biggest cause of death in the UK.

Those who survive are frequently left with disability.

While none of the trials suggested that taking vitamin E increased the risk for total stroke, the differences were notable for the two individual types of strokes.

The authors concluded: "Given the relatively small risk reduction of ischaemic stroke and the generally more severe outcome of haemorrhagic stroke, indiscriminate widespread use of vitamin E should be cautioned against."

Previous studies have suggested that taking vitamin E can protect the heart from coronary heart disease, but some have also found that the vitamin could increase the risk of death if taken in high doses.

Dr Peter Coleman, deputy director of research at The Stroke Association, said: "This is a very interesting study that shows that the risk of haemorrhagic stroke can be slightly increased by high levels of orally taken Vitamin E, although what is a high level has not clearly been ascertained. "More research is required to discover the mechanism of action and the level at which Vitamin E can become harmful.

"We urge people to maintain a lifestyle of a balanced diet, regular exercise and monitoring their blood pressure to reduce their risk of a stroke but would be very interested in seeing further research into this study," he said.

http://www.bbc.co.uk/news/health-11696677

New statistical model moves human evolution back 3 million years

Evolutionary divergence of humans from chimpanzees likely occurred some 8 million years ago rather than the 5 million year estimate widely accepted by scientists, a new statistical model suggests.

The revised estimate of when the human species parted ways from its closest primate relatives should enable scientists to better interpret the history of human evolution, said Robert D. Martin, curator of biological anthropology at the Field Museum, and a co-author of the new study appearing in the journal Systematic Biology. ***Here is a link to the article***

http://sysbio.oxfordjournals.org/content/early/2010/11/04/sysbio.syq054.full.html?ijkey=CaQif1LgTAd7xOD&keytype=ref

Working with mathematicians, anthropologists and molecular biologists, Martin has long sought to integrate evolutionary information derived from genetic material in various species with the fossil record to get a more complete picture.

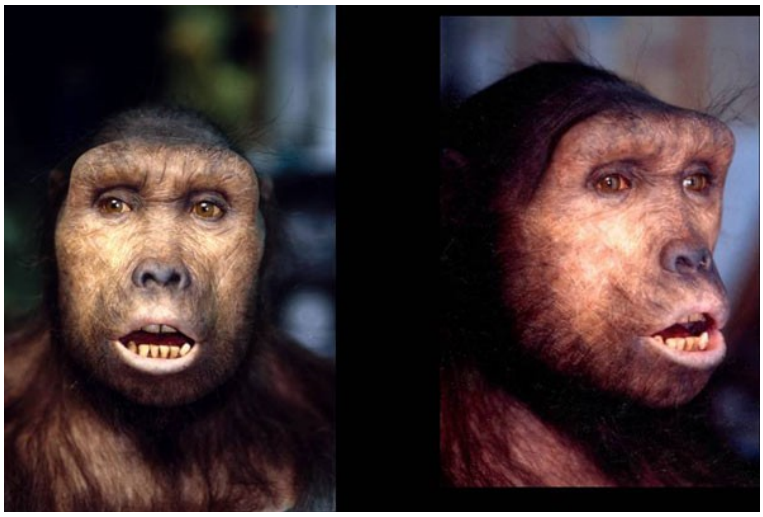
Comparing DNA among related animals can provide a clear picture of how their shared genes evolved over time, giving rise to new and separate species, Martin said. But such molecular information doesn't yield a timetable showing when the genetic divergence occurred.

Fossil evidence is the only direct source of information about long-extinct species and their evolution, Martin and his colleagues said, but large gaps in the fossil record can make such information difficult to interpret. For a generation, paleontologists have estimated human origins at 5 million to 6 million years ago.

But that estimate rests on a thin fossil record. By looking at all of today's primate species, all of the known fossil primates and using DNA evidence, computer models suggest a longer evolutionary timetable. The new analysis described in the Systematic Biology paper takes into account gaps in the fossil record and fills in those gaps statistically.

Such modeling techniques, which are widely used in science and commerce, take into account more overall information than earlier processes used to estimate evolutionary history using just a few individual fossil dates, Martin said. It can give scientists a broader perspective for interpreting data.

One example is a skull fossil discovered in Chad (central Africa) earlier in this decade. The fossil, named Sahelanthropus tchadensis and nicknamed Toumaï (which means "hope of life" in the local Goran language), raised great interest because it has many human characteristics. But consensus on how to classify the discovery has been elusive particularly because the fossil is about 7 million years old, well beyond the accepted time frame for human evolution. Under the new estimate, Toumaï would fall within the period after the human lineage split from chimpanzees, Martin said.



The new approach to dating evolutionary history builds on earlier work by Martin and colleagues. In 2002, they published a paper in Nature that argues the last common ancestor of today's primates lived some 85 million years ago.

This implies that for 20 million years before dinosaurs became extinct, early versions of primates also lived and evolved. It challenged the accepted theory that primates and other mammals didn't really thrive on the planet until dinosaurs were gone.

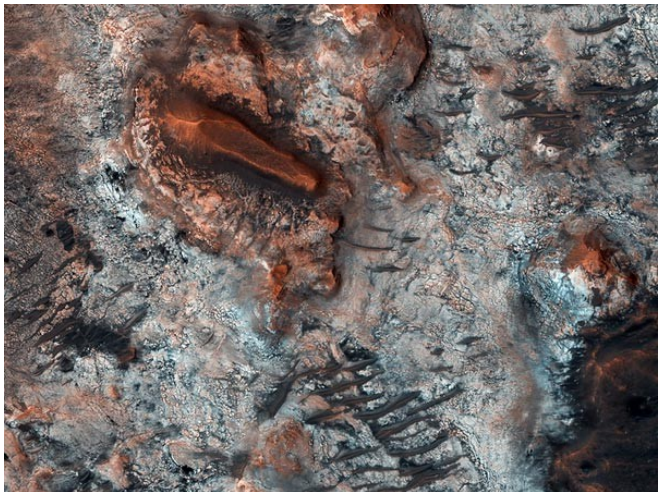
After that paper was published, Martin said he expected someone would apply the new statistical techniques to the question of human evolution, but when no one did, "We decided to do it ourselves."

http://www.eurekalert.org/pub_releases/2010-11/fm-nsm110510.php

Fossils Could Be Found by Next Mars Rover, Study Hints

Brian Handwerk for National Geographic News

A new theory for how oceans formed on ancient Mars also hints at the best spots for future fossil hunts on the red planet.



Based on the geology of Mars's northern plains, the new study suggests that bodies of water formed as groundwater slowly seeped through cracks in the crust. This process would have made oceans and lakes quickly—within just a few years—but also could have sustained the bodies of water over millennia.

However, even when Mars was supposedly wet, the planet likely didn't have a very thick atmosphere. Many scientists therefore think that if life as we know it evolved on Mars, the best places to look for it would be where liquid water would have been protected from extreme temperature changes and damaging ultraviolet radiation from the sun.

A satellite picture of Mars shows Mawrth Vallis, one of the possible landing sites for NASA's next rover.

To find life, "we have to look for regions on the planet where water would have been stable. In the case of Mars, this is in the subsurface," said study leader J. Alexis Palmero Rodriguez of the Planetary Science Institute in Arizona.

This presents a dilemma for fossil hunters, since digging deep to find potential traces of Martian life would involve time and equipment not available to the robotic rovers sent to explore the planet's surface.

But according to the new study, "the water upwelling [in northern Mars] would have been very ancient water trapped in the subsurface for billions of years. That's a very stable environment for organisms to form and evolve," Rodriguez said.

And that means some sediments left by those ancient seas—in surface deposits that would be accessible to rovers—may be hotbeds for Martian fossils.

Mars Water Pooled From Slow Seeps?

Mineral evidence on Mars suggests that surface water must have been present at some point in the past. In fact, several huge sediment deposits in the northern plains remind observers of the bottoms of Earth's oceans.

Previous theories had suggested Mars oceans formed due to massive, abrupt discharges of groundwater—but there's a hitch: "The channels thought to have been produced by this type of discharge are rare and only occur in a few regions of the planet," Rodriguez said.

What's more, "there are no obvious widespread channel systems extending from the highlands into the large Martian basins where oceans are thought to have once existed," he said. "What's the mechanism for the formation of these water bodies without widespread channels that can account for the amount of water required to form these lakes or oceans?"

In a region of northern Mars south of a scarp called Gemini Scopuli, sediments sit atop a basin that's highly fractured by tectonic processes and impact craters. Based on the rocks and minerals present—as seen via spectroscopy data from orbiting probes—groundwater appears to have come to the surface in this region for about two billion years, the study authors say.

The overall landscape suggests that, rather than abrupt gushes, pressurized groundwater could have escaped through the crust fractures in slow, long-lasting seeps, according to the new paper, published in this month's issue of the journal Icarus.

The study team thinks the water must have come from an extensive underground aquifer that reached from the plains to higher elevations.

A raised water table in the plains stopped surface water from sinking back into the soil, the team says. The upwelling water therefore pooled to form shallow oceans or systems of small lakes, similar to those seen when ground ice melts each spring on Alaska's northern slopes.

The new theory hints that oceans and lakes could have remained stable on Mars for perhaps thousands of years, undergoing seasonal cycles of freezing and thawing—as the Martian ice caps do today.

"The bodies of water would have remained stable for as long as groundwater emergence continued," Rodriguez said. "Highly saline lakes can remain liquid at freezing temperatures, and on Earth they have been observed to contain living organisms. The stability of ponded water would also increase if covered by ice," he said.

And stable lakes might have allowed any underground creatures brought to the surface to survive the difficult transition to an environment bombarded with UV radiation, Rodriguez said.

"We know that evolution and successful adaptations of life-forms to new environments are more likely to occur when there are geologically long periods of time available," he said. "So gradual and long-lived groundwater emergence would have increased the chances of successful adaptations to the surface and near-surface environments."

Don't Expect Mars Fossils to Be Familiar

Based on this theory, it's possible future robotic landers could find Martian fossils in deposits along exposed crater walls or surface fractures in the northern plains.

Even more tantalizing, the fractured basins, such as those seen near the north pole, are widespread across Mars, opening up a variety of sites where past slow-growing oceans—and potential fossils—may exist.

For example, NASA has yet to pick a landing site for the next big mission to the red planet, the Mars Science Laboratory. But one of the candidate sites, Mawrth Vallis, fits with the new study's ocean-formation model.

Overall, Rodriguez and colleagues "have put together an idea that ties together numerous diverse, otherwise anomalous phenomena—and one that's certainly a worthy idea to bring into the mix," said Victor Baker, a planetary scientist and geoscientist at the University of Arizona in Tucson who was not involved with the research.

Baker also agrees that Martian groundwater had the potential to support life. "There are subsurface environments on Mars, even today, which are undoubtedly not much different chemically, or [in terms of] temperatures and pressures, to subsurface environments on Earth that have life in them," he said.

But when dreaming of Martian fossils, Baker cautioned, don't expect to find the kinds most familiar to us on Earth. "Whatever is an indication of previous activities of living organisms can be a fossil. It doesn't have to be bones. It can be traces. It could be evidence of chemistry that one can tie back to a biological process," he said.

"To expect that Mars would have achieved something like the Cambrian explosion"—Earth's most intense burst of evolution—"would really be stretching it," he added. "But to expect that Mars might have [microorganisms] similar to what was characteristic life for most of Earth's very early history is not too great of a stretch."

http://news.nationalgeographic.com/news/2010/10/101103-science-space-mars-water-life-fossils-oceans/

Pregnancy problems could be from antibacterial agent

A chemical found in everything from antibacterial soaps and lotions to socks and toothpaste may disrupt an enzyme that plays an important role in pregnancy, University of Florida researchers say.

Thought to be harmless, triclosan gives many soaps and lotions their antibacterial oomph and is found in hundreds of popular products. But a team of UF researchers led by Margaret O. James has discovered that the

chemical hinders an enzyme linked to the metabolism of estrogen. The researchers' findings are reported in the November print issue of the journal Environment International.

In pregnancy, this enzyme, called estrogen sulfotransferase, helps metabolize estrogen and move it through the placenta into the developing fetus. There, the estrogen plays a crucial role in brain development and the regulation of genes.

"We suspect that makes this substance dangerous in pregnancy if enough of the triclosan gets through to the placenta to affect the enzyme," said James, a professor and chairwoman of medicinal chemistry in the UF College of Pharmacy. "We know for sure it is a very potent inhibitor. What we don't know is the kinds of levels you would have to be exposed to to see a negative effect.

"We know it is a problem, but we don't know how much of a problem. We need to move forward and do additional studies."

In pregnancy, the placenta basically serves as a developing baby's in-womb survival kit. Almost everything the fetus gets from its mother — namely food and oxygen — comes through the placenta. It also creates important hormones, such as progesterone and estrogen.

Aside from the role it plays in the fetus, estrogen also affects how much oxygen the baby gets from the mother, said Charles Wood, a professor and chairman of physiology and functional genomics in the UF College of Medicine and a co-author of the study. All of the oxygen a baby gets from its mother flows through the mother's uterine artery. Without enough estrogen, this artery can constrict, decreasing blood flow.

"If you don't make enough estrogen you can, we think, starve the baby of enough oxygen," Wood said.

Estrogen is also involved in signaling the uterus to contract during labor. But maintaining the right levels of the hormone during pregnancy is a delicate balance, Wood says. Too much estrogen could send the mother's body into premature labor. Too little could hinder the flow of oxygen. Both instances could affect how the baby's brain develops.

This is one of the reasons scientists are concerned about the pregnancy-related effects of chemicals such as triclosan. "Some of these (chemicals) can go and combine with estrogen receptors and mimic estrogen or keep estrogen off its receptors or change the metabolism of estrogen, which is what we are looking at with triclosan," Wood said.

In April 2010, the Food and Drug Administration decided to take a closer look at triclosan after several studies found links to problems with hormone regulation and other possible negative health effects. Other studies have shown that the chemical, which cannot be broken down by bacteria, stays in the environment long after it is used.

"Triclosan is a material that is present in the environment and everyone has low levels. If you use products with triclosan, you will likely have higher levels," said Bruce Hammock, a professor of entomology at the University of California-Davis who studies triclosan. "It has some real benefits but it is certainly not risk-free."

More studies are needed before researchers can conclude what effects triclosan really has on human health, James said.

"The triclosan is incorporated into household products because it inhibits bacterial growth," James said. "But the bad thing is it has this unexpected side effect of inhibiting this important enzyme in the body. At this point we don't know if the levels people are exposed to are high enough to cause an adverse effect."

http://www.physorg.com/news/2010-11-pregnancy-problems-antibacterial-agent.html

Most hysterectomies should be performed vaginally or laparoscopically

Recommendation of the AAGL advancing minimally invasive gynecology worldwide

Philadelphia, PA, November 7, 2010 – Approximately 600,000 hysterectomies are performed in the United States annually to treat benign disorders of the pelvis. More than two-thirds are performed through an abdominal incision. In an evidence-based position statement published online today in The Journal of Minimally Invasive Gynecology, the AAGL, a medical specialty society of over 5,000 gynecologic surgeons, advocates the practice of performing these procedures vaginally or laparoscopically in a minimally invasive manner, thus reducing morbidity and facilitating a faster recovery period.

Vaginal hysterectomy (VH) and laparoscopic hysterectomy (LH) are associated with low surgical risks and can be performed with a short hospital stay or in many instances as an outpatient procedure. Abdominal hysterectomy (AH) requires a relatively large abdominal incision and is associated with a number of disadvantages largely related to abdominal wound infections, relatively prolonged institutional stay, and delayed return to normal activities.

"When procedures are required to treat gynecologic disorders, the AAGL is committed to the principles of informed patient choice and provision of minimally invasive options," commented Franklin D. Loffer, MD, Executive Vice President/Medical Director of the AAGL. "When hysterectomy is necessary, the demonstrated

safety, efficacy, and cost-effectiveness of VH and LH mandate that they be the procedures of choice. When hysterectomy is performed without a laparotomy, early institutional discharge is feasible and safe, in many cases within the first 24 hours."

Clinical situations once considered as contraindications to LH are obesity and a previous cesarean section. However, evidence suggests that, aside from longer operative times, safety and efficacy are similar for obese and non-obese patients.

In conclusion the position statement asserts that "It is the position of the AAGL that most hysterectomies for benign disease should be performed either vaginally or laparoscopically and that continued efforts should be taken to facilitate these approaches. Surgeons without the requisite training and skills required for the safe performance of VH or LH should enlist the aid of colleagues who do or should refer patients requiring hysterectomy to such individuals for their surgical care."

The article is "Route of Hysterectomy to Treat Benign Uterine Disease," a position statement by the AAGL. Currently published as an Article in Press, it will appear in the Journal of Minimally Invasive Gynecology, Volume 18, Issue 1 (January/February 2011) published by Elsevier. doi:10.1016/j.jmig.2010.10.001

http://www.eurekalert.org/pub_releases/2010-11/ehs-mhs110410.php

Cellular 'alchemy' transforms skin into blood

Direct conversion of cell types could offer safer, simpler treatments than stem cells.

By Ewen Callaway

Human skin cells can be transformed into blood without first being sent through a primordial, stem-cell-like state, according to a ground-breaking study.

The breakthrough, published online today in Nature, follows work earlier this year showing that fibroblast cells from mouse skin, treated with the right cocktail of chemicals, can be transformed into neurons and heart muscle. However, it is the first study to accomplish this feat with human cells, and the first to create progenitor cells -- in this case for blood.

"It takes us a step along the line to believing that you can produce anything from almost anything," says Ian Wilmut, an embryologist and director of the MRC Centre for Regenerative Medicine in Edinburgh, UK. Such 'direct conversions' also offer a potentially safer, simpler tool for creating patient-specific cell therapies than is promised by adult cells reprogrammed to become stem cells (known as induced pluripotent stem cells, or iPS cells).

Mickie Bhatia, a stem-cell researcher at McMaster University in Hamilton, Canada, and his colleagues chose to make blood progenitors from skin cells because red blood cells created from stem cells do not make the adult form of haemoglobin. "Those cells, because they think they're embryonic, make embryonic and fetal blood," he says.

Creating a bloodline

To make blood progenitor cells, Bhatia and his team collected skin fibroblasts from several volunteers. They infected the cells with a virus that inserted the gene OCT4, and then grew them in a soup of immune-stimulating proteins called cytokines.

OCT4 is one of a handful of Yamanaka factors used to transform fibroblasts into iPS cells, but Bhatia's team found no evidence that the blood progenitor cells that they had made went through an embryonic state. The cells' gene-expression patterns never resembled those of embryonic stem cells, and the blood progenitor cells didn't cause mice to develop teratomas -- tumours that are characteristic of pluripotent cells.

"Everybody has their favourite cell type. There is a lot of this kind of alchemy going on."

The progenitors did, however, produce all three classes of blood cells -- white blood cells, red blood cells and platelets -- all of which seemed to function as they should, according to a battery of experiments. The red blood cells made adult haemoglobin, not the fetal form.

The ultimate test would be transplanting the cells into humans, says Bhatia, but that isn't on the cards -- at least not yet. "The clinical side is going to be a lot of work," he says. "At least from our estimation, this is the most encouraging result we've seen for using blood cells for cell-replacement therapy."

Sanguine about the possibilities

The potential for therapy is very much on the minds of Bhatia and other scientists who are converting cells directly. Because the progenitor cells bypass pluripotency, there is little risk of them forming tumours when implanted into patients, says Wilmut, who is working on creating other progenitor cells in his own lab.

Deepak Srivastava, a developmental biologist and director of the Gladstone Institute of Cardiovascular Disease in San Francisco, California, led the team responsible for making heart muscle from mouse fibroblasts3. He says that directly converted cells could also offer simpler treatments than iPS cells: the

fibroblasts that surround the heart could be transformed into new heart muscle using a stent that delivers drugs to reprogram the cells.

Converted cells aren't without their drawbacks, though. Unlike iPS and embryonic stem cells, they cannot easily multiply in the lab, so producing the large quantities needed for applications such as screening drugs could prove tough, says Wilmut.

Despite lab experiments establishing that the converted blood cells are indistinguishable from adult blood cells, it is still too early to tell whether they will be as good as the real thing once they are inside patients, says George Daley, a stem-cell biologist at Children's Hospital Boston in Massachusetts.

In particular, epigenetic modifications -- changes that modify gene expression without altering the DNA sequence -- could differ between blood cells produced naturally and those created by direct conversion. "The journey from a zygote to a specialized blood cell is very long. The journey from a fibroblast to a blood cell in a petri dish may take a very different route," says Daley.

Even with these caveats, direct conversion is gaining in popularity. "Everybody has their favourite cell type," says Daley. "There is a lot of this kind of alchemy going on."

http://www.scientificamerican.com/article.cfm?id=cellular-alchemy-transforms-sk