Retinoid cream associated with death in clinical trial, but relationship does not appear causal

Patients using a cream containing tretinoin, a retinoid commonly used to treat acne and other conditions, appeared more likely to die than those using a placebo in a clinical trial that was halted early as a result, according to a report in the January issue of Archives of Dermatology, one of the JAMA/Archives journals. However, evidence does not suggest these excess deaths were caused by the therapy.

"The potential of retinoid compounds to prevent cutaneous malignant lesions [skin cancers] has been of considerable interest, and some are effective for this purpose," the authors write as background information in the article. In 1998, the Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) Trial was launched to assess whether high-dose therapy with a cream containing one such retinoid, tretinoin, could prevent cancer. A total of 1,131 veterans (97 percent men, average age 71) were randomly assigned to apply either a cream containing 0.1 percent tretinoin or an unmedicated cream daily to their face and ears. They were then examined by a dermatologist every six months, with a planned study end date of Nov. 15, 2004.

A report prepared for one of the study's several oversight committees in 2004 identified a statistically significant increase in the number of deaths among study participants in the group using tretinoin. The trial was therefore halted six months early, in May 2004. Martin A. Weinstock, M.D., Ph.D., of the VA Medical Center and Brown University, Providence, R.I., and colleagues assessed the data collected during the study to assess the relation of the medication to death risk.

Because death was not an end point in the original study, additional efforts were made to identify study participants who had died and gather more information about cause of death, including accessing the VA master death file. Through these records and original study data, researchers identified 108 patients in the tretinoin group and 76 in the control group who died before the end of the intervention period and an additional 14 in each group who died before the end of the study period (November 2004). After considering other factors that might increase the risk of death—including smoking, age and co-occurring illnesses—there was still a significantly higher risk of death in the treatment group.

However, additional analyses did not support tretinoin as a cause of death. For example, there was no clear association between the number of tubes of cream used and death. There was no consistency in the causes of death among participants. However, in the treatment group, 15 patients died of non-small cell lung cancer, 12 of vascular disorders and 15 of respiratory and other chest disorders—causes associated with smoking, which some previous studies have suggested interacts with compounds in some ways similar to tretinoin, but administered systemically, to produce additional health risks. Participants were asked whether they smoked, but their smoking status was not verified, potentially affecting the detected associations.

"The biological implausibility, lack of specificity of causes of death, inconsistency with previous experience, weakness of other supportive evidence in our data and weak statistical signal cast doubt on a potential causal association of topical tretinoin with death in the VATTC Trial," the authors write. "We do not conclude that this trial provides appropriate grounds for hesitating to use topical tretinoin in clinical practice in the absence of additional evidence."

(Arch Dermatol. 2009;145[1]:18-24. Available pre-embargo to the media at www.jamamedia.org.)
Editor's Note: This study was supported by the Cooperative Studies Program (CSP) of the Office of Research and Development, U.S. Department of Veterans Affairs, and the American Cancer Society. OrthoNeutrogena, a division of Ortho-McNeil Pharmaceutical Inc., provided the tretinoin, 0.1 percent, and the vehicle creams. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Physicians Should Discuss Results With Patients

"Public health ideally uses the precautionary principle—that possible harm should be avoided before harmful effects are unquestionably proven," write Lisa M. Schilling, M.D., M.S.P.H., and Robert P. Dellavalle, M.D., Ph.D., M.S.P.H, of the Department of Veterans Affairs Medical Center, Denver, in an accompanying editorial.

"At a minimum, this principle should cause prescribing physicians to discuss the results of the VATTC with elderly men using topical tretinoin," they write. "More circumspect practitioners may wish to discuss the results of the VATTC with all patients using topical tretinoin. This dialogue should include that the results of the VATTC may have been due to chance, but also that the outcome of death was not initially anticipated, and owing to the ad hoc analysis, various important risk factors, such as smoking status, might not have been completely ascertained. These discussions provide an opportunity for all health care providers prescribing tretinoin to emphasize tobacco prevention and cessation with their patients."

(Arch Dermatol. 2009;145[1]:76. Available pre-embargo to the media at www.jamamedia.org.)
Editor's Note: This study was supported in part by Colorado Health Informatics Collaboration Academic Enrichment Funds from the University of Colorado Denver School of Medicine and a Cancer Prevention and Control Career Development Award grant. Please see the article for additional information, including author contributions and affiliations, financial disclosures, funding and support, etc.

Victims of intimate partner violence display distinct patterns of facial injury

Women who are victims of intimate partner violence tend to have different patterns of facial injury than women who experience facial trauma from other causes, according to a report in the January/February issue of Archives of Facial Plastic Surgery, one of the JAMA/Archives journals. This information, and other key characteristics such as a delay before visiting a health care facility, could help surgeons and other physicians recognize patients who are victims of this type of abuse.

Intimate partner violence—abuse by a spouse or significant other—affects approximately 25 percent to 33 percent of women in the United States, according to background information in the article. Between 88 percent and 94 percent of intimate partner violence victims seek medical attention for injuries to the head and neck, and 56 percent of those have facial fractures. "Because intimate partner violence accounts for 34 percent to 73 percent of facial injuries in women, facial plastic surgeons and other health care providers who treat patients with maxillofacial injuries are in a unique position to identify these victims and refer them to local domestic violence service programs for safety planning, information and referrals, support services and advocacy, depending on the victims' needs and choices," the authors write.

Oneida A. Arosarena, M.D., of the Temple University School of Medicine, Philadelphia, and colleagues reviewed the medical and dental records of 326 women (average age 35 years) treated for facial trauma at one university medical center between 1998 and 2004. Of the 45 patients (13.8 percent) who were assault victims, 18 were documented victims of intimate partner violence, while 24 of the remaining 26 assault victims could not or did not identify their assailant. Other common causes of injury included motor vehicle crashes (139 patients, or 42.6 percent), falls (70 patients, or 21.5 percent) and unknown or undocumented causes (35 patients, or 10.7 percent).

Overall, assault was associated with mandible (jaw) fractures, zygomatic complex fractures (complicated breaks in the cheekbones), orbital blow-out fractures (cracks or breaks in bones surrounding the eye) and intracranial (brain) injury. "Specifically, higher than expected numbers of zygomatic complex fractures, orbital blow-out fractures and intracranial injuries were found in intimate partner violence victims," the authors write. "Victims assaulted by unknown or unidentified assailants were more likely to have mandible fractures than were other assault victims."

Results of the study indicate that about one in four women at risk for ongoing intimate partner violence was referred for protective service as required by state law and hospital policy. "Underreporting of intimate partner violence remains a hindrance to appropriate social intervention for many victims," the authors write. "While our study was limited to facial trauma victims, it demonstrates that universal screening and examination of the patterns of presentation, including patterns of injury, can assist medical professionals in identifying these patients and initiating appropriate medical and social intervention."

(Arch Facial Plast Surg. 2009;11[1]:48-52. Available pre-embargo to the media at www.jamamedia.org.)

Motor skill learning may be enhanced by mild brain stimulation

People who received a mild electrical current to a motor control area of the brain were significantly better able to learn and perform a complex motor task than those in control groups. The findings could hold promise for enhancing rehabilitation for people with traumatic brain injury, stroke and other conditions.

The study is presented in the January 20, 2009 early online edition of the Proceedings of the National Academy of Sciences, and was conducted by researchers at the National Institutes of Health (NIH). The research team from NIH's National Institute of Neurological Disorders and Stroke (NINDS) worked in collaboration with investigators at Columbia University in New York City and Johns Hopkins University in Baltimore.

Motor skills, which are used for activities from typing and driving, to sports, require practice and learning over a prolonged period of time. During practice, the brain encodes information about how to perform the task, but even during periods of rest, the brain is still at work strengthening the memory of doing the task. This process is known as consolidation.

Subjects in this study were presented with a novel and challenging motor task, which involved squeezing a "joy stick" to play a targeting game on a computer monitor, which they practiced over five consecutive days. During practice, one group received 20 minutes of transcranial direct current stimulation (tDCS) and the other group received only a 30 second "sham" stimulation. tDCS involves mild electrical stimulation applied through surface electrodes on the head, and works by modulating the excitability, or activity, of cells in the brain's outermost layers. In this study, Dr. Cohen and his team directed tDCS to the primary motor cortex, the part of the brain that controls movement.

Over the five-day training period, the skill of the tDCS group improved significantly more that that of the control (sham) group, apparently through an effect on consolidation. During the three month follow-up period,

the two groups forgot the skill at about the same rate, but the tDCS group continued to perform better because they had learned the skill better by the end of training.

Leonardo Cohen, M.D., of NINDS Human Cortical Physiology and Stroke Neurorehabilitation Section is available for comment, and can address how this technique potentially could be used to help people with brain injuries relearn or acquire motor skills.

Language driven by culture, not biology

Language in humans has evolved culturally rather than genetically, according to a study by UCL (University College London) and US researchers. By modelling the ways in which genes for language might have evolved alongside language itself, the study showed that genetic adaptation to language would be highly unlikely, as cultural conventions change much more rapidly than genes. Thus, the biological machinery upon which human language is built appears to predate the emergence of language.

According to a phenomenon known as the Baldwin effect, characteristics that are learned or developed over a lifespan may become gradually encoded in the genome over many generations, because organisms with a stronger predisposition to acquire a trait have a selective advantage. Over generations, the amount of environmental exposure required to develop the trait decreases, and eventually no environmental exposure may be needed - the trait is genetically encoded. An example of the Baldwin effect is the development of calluses on the keels and sterna of ostriches. The calluses may initially have developed in response to abrasion where the keel and sterna touch the ground during sitting. Natural selection then favored individuals that could develop calluses more rapidly, until callus development became triggered within the embryo and could occur without environmental stimulation. The PNAS paper explored circumstances under which a similar evolutionary mechanism could genetically assimilate properties of language – a theory that has been widely favoured by those arguing for the existence of 'language genes'.

The study modelled ways in which genes encoding language-specific properties could have coevolved with language itself. The key finding was that genes for language could have coevolved only in a highly stable linguistic environment; a rapidly changing linguistic environment would not provide a stable target for natural selection. Thus, a biological endowment could not coevolve with properties of language that began as learned cultural conventions, because cultural conventions change much more rapidly than genes.

The authors conclude that it is unlikely that humans possess a genetic 'language module' which has evolved by natural selection. The genetic basis of human language appears to primarily predate the emergence of language.

The conclusion is reinforced by the observation that had such adaptation occurred in the human lineage, these processes would have operated independently on modern human populations as they spread throughout Africa and the rest of the world over the last 100,000 years. If this were so, genetic populations should have coevolved with their own language groups, leading to divergent and mutually incompatible language modules. Linguists have found no evidence of this, however; for example, native Australasian populations have been largely isolated for 50,000 years but learn European languages readily.

Professor Nick Chater, UCL Cognitive, Perceptual and Brain Sciences, says: "Language is uniquely human. But does this uniqueness stem from biology or culture? This question is central to our understanding of what it is to be human, and has fundamental implications for the relationship between genes and culture. Our paper uncovers a paradox at the heart of theories about the evolutionary origin and genetic basis of human language – although we have appear to have a genetic predisposition towards language, human language has evolved far more quickly than our genes could keep up with, suggesting that language is shaped and driven by culture rather than biology.

"The linguistic environment is continually changing; indeed, linguistic change is vastly more rapid than genetic change. For example, the entire Indo-European language group has diverged in less than 10,000 years. Our simulations show the evolutionary impact of such rapid linguistic change: genes cannot evolve fast enough to keep up with this 'moving target'.

"Of course, co-evolution between genes and culture can occur. For example, lactose tolerance appears to have co-evolved with dairying. But dairying involves a stable change to the nutritional environment, positively selecting the gene for lactose tolerance, unlike the fast-changing linguistic environment. Our simulations show that this kind of co-evolution can only occur when language change is offset by very strong genetic pressure. Under these conditions of extreme pressure, language rapidly evolves to reflect pre-existing biases, whether the genes are subject to natural selection or not. Thus, co-evolution only occurs when the language is already almost entirely genetically encoded. We conclude that slow-changing genes can drive the structure of a fast-changing language, but not the reverse.

"But if universal grammar did not evolve by natural selection, how could it have arisen? Our findings suggest that language must be a culturally evolved system, not a product of biological adaption. This is consistent with current theories that language arose from the unique human capacity for social intelligence."

The more promiscuous the female, the speedier the sperm

Researchers use fish to settle a sperm competition debate

Female promiscuity appears to have triggered changes in the type of sperm a male produces, according to new research on fish from central Africa.

The study, published in the Proceedings of the National Academy of Sciences of the USA, examines how competition for reproduction influences the sperm of many species of African cichlids. These fish have extremely diverse mating behaviours, ranging from strict monogamy to species where females mate with many males in quick succession.

"In promiscuous species we found that males produced larger and faster sperm than in closely related species that were monogamous," says Sigal Balshine, associate professor in the department of Psychology, Neuroscience & Behaviour at McMaster University, and senior author on the study. "This research offers some of the first evidence that sperm has evolved to become more competitive in response to females mating with multiple males."

Female promiscuity is a major problem for males because the sperm from rival suitors will compete in the race to procreate, explains Balshine. While the idea that sperm would evolve to become more competitive when males compete for fertilization seems obvious, to date there has been little evidence to support this theory.

For the study, researchers collected males from 29 closely related species found off the Zambian shores of Lake Tanganyika (Africa). After examining the relationship between promiscuity and sperm quality the researchers used computer simulations to assess how sperm evolved in these fish.

"Our analysis confirmed that sperm became more competitive only after a species shifted their mating behaviours to become more promiscuous," says John Fitzpatrick, lead author of the study and a biology graduate student from McMaster University, now with the University of Western Australia. "The first step in producing more competitive sperm was by influencing how much energy the sperm can produce. Just like a mechanic could make a car drive faster by installing a better engine, evolution appears to act first on the engine that drives sperm movement."

Funding for the study was provided by NSERC, Canada Fund for Innovation and Ontario Innovation Trust. McMaster University, one of four Canadian universities listed among the Top 100 universities in the world, is renowned for its innovation in both learning and discovery. It has a student population of 23,000, and more than 140,000 alumni in 128 countries.

Penn study: Breast cancer survivors call for more 'survivorship care' from primary care physicians

Findings illustrate need for more coordinated care to protect long-term cancer survivors

(PHILADELPHIA) – As the nation's growing population of breast cancer survivors ages, many patients will likely develop common chronic illnesses like diabetes and heart disease, and they'll need specialized care to balance those problems with the late effects of cancer therapies they received. They'll also need screenings and advice about new strategies for preventing recurrences of their disease.

But many patients give low marks to the post-cancer care they receive from their primary care physicians, who generally serve as a patient's main health care provider after they're released from active treatment with their oncologists, according to a new study from the University of Pennsylvania's Abramson Cancer Center published in the Journal of Clinical Oncology.

"Getting primary care physicians involved in a comprehensive survivorship care plan is critical to delivering high quality, accessible care to diverse groups of cancer survivors," says Jun J. Mao, MD, MSCE, the lead author of the study and an assistant professor of Family Medicine and Community Health who leads integrative medicine efforts at Penn's Abramson Cancer Center. "Currently, however, lack of communication between oncologists and primary care physicians is felt by survivors to be a major limitation of our existing system, so treatment summaries or survivorship plans may serve as important tools to bridge the communication gap and improve care delivery by primary care physicians."

In a study of 300 breast cancer survivors cared for at the Abramson Cancer Center's Rowan Breast Center, the Penn researchers found that patients offered mixed reviews of the survivorship care they received from their primary care physicians. While most patients said they were happy with the general care, psychosocial support and health promotion information they received, they reported being less satisfied by their physicians' knowledge of late effects of cancer therapies and ways to treat symptoms related to their disease or its treatment. Only 28 percent of patients felt that their primary care physicians and oncologists communicated well together – a partnership that the Penn researchers say will be a key way to create survivorship plans in the future.

Most patients surveyed felt that educational interventions to strengthen survivorship care in the primary care setting would be valuable, with 72 percent saying they felt it was important to teach themselves in order to create a cohesive care plan with both types of doctors. Seventy percent of patients endorsed the idea of developing a primary care clinic specifically for breast cancer survivors – a group that is two million strong, the largest group of all cancer survivors in the United States.

Penn's "Living Well After Cancer" Program Offers Model for Primary Care Involvement in Survivorship

As a nationally recognized leader in the field of cancer survivorship, the Abramson Cancer Center is uniquely positioned to create models of survivorship care and tools to help cancer survivors of all kinds. Penn's Living Well After Cancer Program, for adult and childhood cancer survivors, is a LIVESTRONG Survivorship Center of Excellence. This designation, awarded by the Lance Armstrong Foundation, reflects excellence in clinical care, research and education. Within the Living Well After Cancer Program, the same nurse practitioners who care for patients during their diagnosis and treatment help them develop an individualized survivorship care plan at the end of their treatment that guides patients if and when they transition back to their primary care or specialty provider for follow-up care.

And through the Abramson Cancer Center's OncoLink (www.oncolink.org), the Internet's first multimedia cancer information resource, individual survivorship care plans are now available – in both English and Spanish - to millions of cancer survivors worldwide. The Penn researchers say that expanding programs like these to more cancer patients may help boost their satisfaction with survivorship care delivered via primary care physicians.

"Our goal is to provide optimal care and guidance to patients from diagnosis through the post-treatment survivorship period. Providers at Penn recognize that cancer patients require specialized care even as they begin new lives as survivors," says study co-author Linda A. Jacobs, PhD, RN, Director of the Abramson Cancer Center's LIVESTRONG Survivorship Center of Excellence. "Developing treatment summaries and care plans for all patients at the end of cancer treatment will guide patients and providers in appropriate surveillance and follow-up care throughout their lives."

Inherited traits may explain differences in 'identical' twins

* 15:43 19 January 2009 by **Ewen Callaway**

Forget nature versus nurture, new research on twins hints at a crack in the conventional view that environment and genes combine to influence our traits.

"Environment makes twins different – that's part of our traditional paradigm that is pretty well known," says Art Petronis, a geneticist at the University of Toronto, who led the new study. "Unfortunately, most of the attempts to identify what specific environmental factors make twins different failed."

Instead, inherited chemical adornments to DNA letters might play a substantial role in shaping individual differences between all people.

Petronis' team found that "identical" twins, who by definition share DNA, exhibit considerably different patterns of one kind of chemical modification across their genomes. These modifications, known as methylations, can affect gene activation, as well as DNA replication and recombination.

Functional variations

Dubbed the epigenome, scientists have found increasing evidence that such changes underlie susceptibility to cancer, mental illness and, in mice, coat colour.

Researchers, including Petronis, have noticed individual genes and swathes of DNA that seem to differ between identical twins, but this is the first effort to look across the entire human genome.

Using DNA microarrays designed to measure methylation, Petronis' team compared the patterns in tissues belonging to 57 pairs of identical twins. This method interrogated just 1 or 2% of the total genome, but at sites peppered across the 22 non-sex chromosomes.

"We detected that epigenetic differences are a universal phenomenon. We see them in various locations across the entire genome," he says.

What's more, twins spawned from fertilised eggs that separated after just a few cell divisions differed more than twins who split days later. This suggests that some epigenetic divergence occurs very early in embryo development, Petronis says.

Fraternal or non-identical twins share even fewer methylations than identical twins, Petronis' team found. He theorises that these epigenetic variations are vestiges of methylation patterns initially present in sperm or egg cells.

Developmental differences

His team did not examine the result of these epigenetic changes, but other scientists have little doubt they contribute to traits such as disease susceptibility. "Some fraction of them I'm sure will lead to functional differences," says Andrew Chess, a biologist at Harvard Medical School.

Randy Jirtle, a geneticist at Duke University Medical Center in Durham, North Carolina, thinks meeting twins in person offers ample proof of the epigenome at work. "Behaviourally they are a little different, but not so much in the way they look," he says.

The importance of epigenetic changes doesn't stop with twins. Jirtle speculates that developmental differences between organisms lies principally in epigenetic modifications, not DNA sequences: "If we had the same epigenome as a mouse, we'd have a snout and a long tail."

Journal reference: Nature Genetics (DOI: 10.1038/ng.286)

Were Mercury and Mars separated at birth?

* 19 January 2009

LINE up Mercury, Venus, Earth and Mars according to their distance from the sun and you'll see their size distribution is close to symmetrical, with the two largest planets between the two smallest. That would be no coincidence - if the pattern emerged from a debris ring around the sun.

When the four terrestrial planets - Mercury, Venus, Earth and Mars - are placed side by side, it's clear their size distribution is close to symmetrical, with the two largest lying between the two smallest **(Illustration: NASA)**

Brad Hansen of the University of California, Los Angeles, built a numerical simulation to explore how a ring of rocky material in the early solar system could have evolved into the planets. He found that two larger planets typically form near the inner and outer edges of the ring, corresponding to Venus and Earth. A number of smaller bodies also form within the ring. These are typically scattered away by the larger two, but if they experience collisions on the way, they can end up in stable orbits similar to those of Mercury and Mars. Once beyond the ring, they cannot acquire mass and so remain pint-sized.

"This is nicely consistent with various properties of Mercury and Mars," says Hansen, who presented the work at the American Astronomical Society meeting in Long Beach, California. Both small planets have features that could have been caused by giant impacts. In one run of Hansen's simulation, Earth received a smash, too, much like the one thought to have created the Moon. *Issue 2691 of New Scientist magazine*

Cheap paint could protect against super-fast wireless

* 17:33 19 January 2009 **by Colin Barras**

As wireless communications become faster, it's not just older, slower devices that are left behind. The shielding that protects sensitive electronic equipment like that used in hospitals is becoming increasingly obsolete as new, higher frequencies are used to send data.

Now Japanese researchers have come to the rescue with a new metal-rich coating designed to protect newly vulnerable devices. The development is timely: while the latest wireless communications use electromagnetic waves with a frequency of over 100 gigahertz, the best wave absorbers commercially available are effective only up to around half that.

The 120 GHz band, for example, can send data at up to 10 gigabits per second. That's fast enough for the real-time transmission of uncompressed video in high-definition TV format, and rivals the speed of the fastest wired local area networks.

Iron constitution

The ability to block electromagnetic (EM) waves comes about when a material's magnetic field resonates at the same frequency as the wave. Wave absorbers are usually made from iron-rich oxides, but higher-frequency transmissions outstrip the power of iron to absorb electromagnetic waves.

However, the standard oxide coating – which contains barium as well as iron – has a maximum resonance frequency that is outstripped at 48 GHz.

Shin-ichi Ohkoshi's team at the University of Tokyo in Japan has just identified a new aluminium-iron oxide able to block waves with a frequency almost four times higher.

The team used a sensitive magnetometer to confirm that a powder of the new oxide can absorb EM waves of up to 182 GHz at room temperature.

Protective paint

The composition of the new material somehow distorts the bonds between iron and oxygen from their usual shape, which the team believes explains the material's magnetic properties. Learning more about this effect may make it possible to identify new metal oxides that can absorb EM waves at even higher frequencies.

Particles of the new material could be incorporated in a paint to shield sensitive equipment in medical areas, labs, or aeroplanes from the effects of high-speed wireless communications, says Ohkoshi, who adds that the paint would be relatively cheap to make because aluminium and iron are abundant materials.

"We collaborated with DOWA Electronics, a Japanese industrial company [to make a 100-kilogram sample order]," says Ohkoshi. "The manufacturing cost is very cheap – around £10 ($14) per kg."

Journal reference: Journal of the American Chemical Society (DOI: 10.1021/ja807943v)

Baffling the body into accepting transplants

An unexpected discovery made by a Sydney scientist has potential to alter the body's response to anything it perceives as not 'self', such as a tissue or organ transplant.

Stacey Walters, an immunology researcher at the Garvan Institute of Medical Research, has found that by greatly boosting the levels of the hormone BAFF in mice, it is possible to alter their immune systems so that they will accept tissue transplants without the need for any immunosuppression.

The findings have just been published in the Journal of Immunology.

Specifically, Stacey has found that mice genetically engineered to produce large amounts of BAFF (B cell activating factor), don't reject transplants.

She has shown that increased numbers of B cells (caused by boosted BAFF levels) in turn stimulate the production of T regulatory cells, which then control T cells, the body's killer cells.

The surprising thing about the results is that B cells, which make antibodies, were not known to have any role in the production of T regulatory cells. Nor would it have been thought possible for them to influence the body's response to a transplant, which has been considered a function of T cells only.

"In normal situations, something has to turn the immune system off once your body's fought an invader, such as a virus. It's the T regulatory cells that come in and say 'enough's enough'," Stacey explained.

Just to make sure it was the B cells that were provoking the changes, Stacey repeated her experiments on a mouse in which B cells were genetically knocked out, but high BAFF levels preserved. She found that when there are no B cells, normal allograft rejection occurs.

Stacey's results give us insight into previously unknown interrelationships between various classes of immune cells. Manipulating these relationships may offer a way of preserving organ grafts in the future without the need for toxic immunosuppressive drugs.

Acupuncture stops headaches, but 'faked' treatments work almost as well

Headache sufferers can benefit from acupuncture, even though how and where acupuncture needles are inserted may not be important. Two separate systematic reviews by Cochrane Researchers show that acupuncture is an effective treatment for prevention of headaches and migraines. But the results also suggest that faked procedures, in which needles are incorrectly inserted, can be just as effective.

"Much of the clinical benefit of acupuncture might be due to non-specific needling effects and powerful placebo effects, meaning selection of specific needle points may be less important than many practitioners have traditionally argued," says lead researcher of both studies, Klaus Linde, who works at the Centre for Complementary Medicine Research at the Technical University of Munich, Germany.

In each study, the researchers tried to establish whether acupuncture could reduce the occurrence of headaches. One study focused on mild to moderate but frequent 'tension-type' headaches, whilst the other focused on more severe but less frequent headaches usually termed migraines. Together the two studies included 33 trials, involving a total of 6,736 patients.

Overall, following a course of at least eight weeks, patients treated with acupuncture suffered fewer headaches compared to those who were given only pain killers. In the migraine study, acupuncture was superior to proven prophylactic drug treatments, but faked treatments were no less effective. In the tension headache study, true acupuncture was actually slightly more effective than faked treatments.

The results indicate that acupuncture could be a used as an alternative for those patients who prefer not to use drug treatments, and additionally may result in fewer side effects. However, Linde says more research is still required, "Doctors need to know how long improvements associated with acupuncture will last and whether better trained acupuncturists really achieve better results than those with basic training only."

Stop traffic crashes: Switch on the lights

Street lighting provides a simple, low cost means of stemming the global epidemic of road traffic death and injury. Low income countries should consider installing more lights, and high income countries should think carefully before turning any off to reduce carbon emissions, is the advice from a new Cochrane Review.

Street lighting may be considered an obvious means of preventing road traffic crashes, but the scientific evidence for this has been uncertain and many studies are decades out of date. Some even suggest that drivers 'feel' safer on better lit roads and may speed up as a result. But a systematic review by Cochrane Researchers now shows that street lighting does indeed reduce crashes and injuries on the roads.

The World Health Organization estimates that 1 million people die each year on the world's roads and up to an additional 50 million are injured, causing an estimated global bill of $578 billion.

"Road traffic crashes are not just the unfortunate culmination of chance, but are events that can be analysed so that the risk factors are identified and then addressed. Darkness is a risk factor – street lighting is therefore a valuable tool," said lead researcher, Fiona Beyer, of the Institute of Health and Society at the University of Newcastle in the UK.

The researchers reached their conclusions by pooling data from 14 studies on the effects of street lighting on road safety. They found that street lighting reduced total crashes by between 32% and 55%, and fatal injury crashes by 77%.

Without intervention, the number of deaths due to road traffic crashes is expected to reach 2.3 million by 2020. It is thought that nine out of ten deaths will occur in low and middle income countries. But Beyer says the results may also have implications for policy makers who plan to reduce public street lighting under the premise of cutting carbon emissions and costs.

"In the UK, an increasing number of local councils are looking to turn off some public street lighting in a move to reduce costs and carbon emissions. The potential adverse road safety impact of such a policy should be carefully considered in light of our findings," said Beyer.

Preterm birth: Magnesium sulphate cuts cerebral palsy risk

Magnesium sulphate protects very premature babies from cerebral palsy, a new study shows. The findings of this Cochrane Review could help reduce incidence of the disabling condition, which currently affects around one in every 500 newborn babies overall, but up to one-in-ten very premature babies (< 28 weeks of gestation).

The neuroprotective function of magnesium in preterm babies was first suggested in the early nineties. Cochrane Researchers who carried out a systematic review of the available evidence say this role is now established. Magnesium sulphate is usually given as a slow infusion through a vein, but can also be given as an injection into the muscle.

"There is now enough evidence to support giving magnesium sulphate to women at risk of very preterm birth as a protective agent against cerebral palsy for their baby," said lead researcher, Lex Doyle, who works at the Department of Obstetrics and Gynaecology at the Royal Women's Hospital and the University of Melbourne in Australia.

Exactly how magnesium protects the brain is not certain, but it is essential for many processes that keep cells working normally, it may protect against harmful molecules that can damage or kill cells, and it improves blood flow under some circumstances.

The researchers reviewed data from five trials of antenatal magnesium sulphate therapy, which together included 6,145 babies. Overall 63 women at risk of very preterm birth had to be given magnesium sulphate to prevent one case of cerebral palsy in the baby.

Side effects of the treatment include flushing, sweating, nausea, vomiting, headaches and palpitations. However, the researchers found no increase in major complications in mothers due to magnesium therapy.

Low-carbohydrate diet burns more excess liver fat than low-calorie diet, study finds

DALLAS - People on low-carbohydrate diets are more dependent on the oxidation of fat in the liver for energy than those on a low-calorie diet, researchers at UT Southwestern Medical Center have found in a small clinical study. The findings, published in the journal Hepatology, could have implications for treating obesity and related diseases such as diabetes, insulin resistance and nonalcoholic fatty liver disease, said Dr. Jeffrey Browning, assistant professor in the UT Southwestern Advanced Imaging Research Center and of internal medicine at the medical center.

“Instead of looking at drugs to combat obesity and the diseases that stem from it, maybe optimizing diet can not only manage and treat these diseases, but also prevent them,” said Dr. Browning, the study’s lead author.

Although the study was not designed to determine which diet was more effective for losing weight, the average weight loss for the low-calorie dieters was about 5 pounds after two weeks, while the low-carbohydrate dieters lost about 9½ pounds on average.

Glucose, a form of sugar, and fat are both sources of energy that are metabolized in the liver and used as energy in the body. Glucose can be formed from lactate, amino acids or glycerol.

In order to determine how diet affects glucose production and utilization in the liver, the researchers randomly assigned 14 obese or overweight adults to either a low-carbohydrate or low-calorie diet and monitored seven lean subjects on a regular diet.

After two weeks, researchers used advanced imaging techniques to analyze the different methods, or biochemical pathways, the subjects used to make glucose. “We saw a dramatic change in where and how the liver was producing glucose, depending on diet,” said Dr. Browning.

Researchers found that participants on a low-carbohydrate diet produced more glucose from lactate or amino acids than those on a low-calorie diet.

“Understanding how the liver makes glucose under different dietary conditions may help us better regulate metabolic disorders with diet,” Dr. Browning said.

The different diets produced other differences in glucose metabolism. For example, people on a low-calorie diet got about 40 percent of their glucose from glycogen, which is comes from ingested carbohydrates and is stored in the liver until the body needs it.

The low-carbohydrate dieters, however, got only 20 percent of their glucose from glycogen. Instead of dipping into their reserve of glycogen, these subjects burned liver fat for energy.

The findings are significant because the accumulation of excess fat in the liver - primarily a form of fat called triglycerides - can result in nonalcoholic fatty liver disease, or NAFLD. The condition is the most common form of liver disease in Western countries, and its incidence is growing. Dr. Browning has previously shown that NAFLD may affect as many as one-third of U.S. adults. The disease is associated with metabolic disorders such as insulin resistance, diabetes and obesity, and it can lead to liver inflammation, cirrhosis and liver cancer.

“Energy production is expensive for the liver,” Dr. Browning said. “It appears that for the people on a low-carbohydrate diet, in order to meet that expense, their livers have to burn excess fat.”

Results indicate that patients on the low-carbohydrate diet increased fat burning throughout the entire body.

Dr. Browning and his colleagues will next study whether the changes that occur in liver metabolism as a result of carbohydrate restriction could help people with nonalcoholic fatty liver disease. Previous research has shown a correlation between carbohydrate intake and NAFLD.

Other researchers from the Advanced Imaging Research Center involved with the study were Dr. Matthew Merritt, assistant professor of radiology; Dr. Craig Malloy, professor of radiology and internal medicine; and Dr. Shawn Burgess, assistant professor of pharmacology. Other UT Southwestern researchers involved were Jeannie Davis, clinical research coordinator; and Santhosh Satapati, graduate student. A researcher from Texas Tech University Health Sciences Center also contributed.

Mayo Clinic Researchers Find Experimental Therapy Turns on Tumor Suppressor Gene in Cancer Cells

JACKSONVILLE, Fla. - Researchers at Mayo Clinic have found that the experimental drug they are testing to treat a deadly form of thyroid cancer turns on a powerful tumor suppressor capable of halting cell growth. Few other cancer drugs have this property, they say.

In the Feb. 15 issue of Cancer Research (available online Jan. 20), they report that RS5444, being tested in a Phase 1/2 clinical trial to treat anaplastic thyroid cancer, might be useful for treating other cancers. The agent is also known as CS-7017.

From previous research, the investigators knew that RS5444 binds to a protein known as PPAR-gamma, a transcriptional factor that increases the expression of many genes. They had found that human anaplastic thyroid tumor cells treated with RS5444 expressed a protein known as p21, which inhibited cell replication and tumor growth. But they did not understand how. They have now discovered that the agent actually forces PPAR-gamma to turn on the RhoB tumor suppressor gene, which in turn induces p21 expression.

"This is very unusual," says the study's lead investigator, John Copland, Ph.D., a cancer biologist at the Mayo Clinic campus at Jacksonville. "Drugs typically target genes and proteins that are over-expressed and turn them off. We found that RS5444 turns on a valuable tumor suppressor gene. We rarely find a drug that can take a suppressed gene and cause it to be re-expressed."

This finding suggests that other cancers in which RhoB is deactivated might respond to RS5444 or to similar drugs, says co-author Robert Smallridge, M.D., who treats thyroid cancer patients at Mayo Clinic in Jacksonville.

"This study provides a hint that this class of drugs could have a significant effect on cancer biology because of its action on this tumor suppressor gene," says Dr. Smallridge.

According to Dr. Copland, "RS5444 and other so-called PPAR-gamma drugs, which were originally created to treat diabetes because they help regulate glucose metabolism, are in development or being tested as cancer therapies. Taken orally, RS5444 requires 1,000-fold less dosage than current Food and Drug Administration-approved drugs in this class of compounds to inhibit tumor growth."

The researchers have been seeking to identify and characterize the molecular mechanisms underlying the cause and progression of human anaplastic thyroid carcinoma. Their goal is to develop effective molecular targeted therapies.

This cancer is extremely rare - fewer than 600 cases are diagnosed in the U.S. annually — but may be better known of late because it may have been the type of thyroid cancer that led to the death of William Rehnquist, chief justice of the United States. "It is also one of the most aggressive and deadliest known cancers, since it doesn't respond to any known treatment," says Dr. Smallridge. "The rate of survival hasn't changed in 25 years. Eighty-five percent of patients die within a year of diagnosis."

In previous work, the investigators identified a combination of drugs that reduced tumor size in animal models, strongly implicating that this regimen might benefit patients with the cancer. RS5444, developed by Daiichi Sankyo, Co., Ltd., in Japan, was one agent tested in combination with chemotherapy. Sankyo researchers discovered RS5444 in a screen for antitumor activity and then sought help from Mayo Clinic Cancer Center to further study its properties. Their encouraging findings in preclinical studies led to the launch of a multicenter Phase 1/2 clinical trial, testing use of RS5444 and paclitaxel chemotherapy in patients with the cancer. The study, led by Dr. Smallridge, is being conducted at Mayo Clinic campuses in Jacksonville and Rochester, Minn. and at eight other sites nationally.

Clinical Trial Information

This study was designed to look at the specific signaling pathways within anaplastic thyroid cancer cells that are disrupted by RS5444. Researchers had thought that because PPAR-gamma was mutated in a subset of thyroid cancers, PPAR-gamma might be acting as a tumor suppressor gene, and that turning it back on restored that function. This hypothesis made sense, because PPAR-gamma is a powerful nuclear receptor that activates genes involved in such cellular processes as differentiation, apoptosis, cell-cycle control, carcinogenesis, and inflammation.

But they found that PPAR-gamma regulates transcription of the RhoB gene. "Within several hours of administering the drug, we can see that it binds to the PPAR-gamma protein in cancer cells and activates RhoB transcription, causing expression of RhoB messenger RNA that is translated into protein. By a yet-to-be-identified mechanism, RhoB then induces the transcription of p21, thereby shutting down the cell cycle and blocking tumor growth," Dr. Copland says. "That shows us that turning RhoB back on may be a key mechanism for regulating growth of this cancer," he says.

For proof, the researchers then turned off expression of RhoB in cells that were treated with the drug, and demonstrated that p21 could not be activated. "That shows RhoB is required for p21 transcription," Dr. Copland says. "RhoB acts as a tumor suppressor, and it is turned off in anaplastic thyroid cancers. Turning this gene back on may lead to an effective molecular targeted chemotherapy regimen to fight this cancer," he says.

Dr. Smallridge adds, "Hitting this pathway inhibits tumor growth up to fourfold in laboratory cells and in animal experiments, and we are optimistic that it could be one cancer pathway capable of manipulation in patients. We hope there are other cancers in which RhoB is silenced, such as head and neck, brain, and lung cancers, that could benefit as well where RhoB has been shown to be down-regulated in patient tumor tissues."

Co-authors included researchers from Daiichi Sankyo, Co., Ltd., Eastern Virginia Medical School, and Mayo Clinic.
The study was funded by grants from the National Institutes of Health, Mayo Clinic Research Committee, the Florida Department of Health Bankhead Coley grant, and a grant for Rare Cancers from Dr. Ellis and Dona Brunton. Funding from the company is being used to conduct the clinical trial. Drs. Copland and Smallridge have a patent application pending on the use of molecular markers to confirm response to PPAR-gamma drugs.

FISH OUT OF WATER

New Species of Climbing Fish from Remote Venezuela Shakes the Catfish Family Tree

A new species of fish from tropical South America is confirming suspected roots to the loricariid catfish family tree. Lithogenes wahari shares traits with two different families of fish: the bony armor that protects its head and tail, and a grasping pelvic fin that allows it to climb vertical surfaces. The discovery of both of these characteristics in Lithogenes suggests to ichthyologists Scott Schaefer of the American Museum of Natural History and Francisco Provenzano of the Universidad Central de Venezuela that the common ancestor of the Loricariidae and Astroblepidae probably could grasp and climb rocks with its tail and mouth.

Lithogenes wahari New catfish species Lithogenes wahari found in the Río Cuao **Photo: S. Schaefer/AMNH.**

The unusual catfish caught the team's attention twenty years ago in Caracas. An anthropologist working in the remote state of Amazonas collected samples of local foods and brought them to the Instituto de Zoologíca for identification. "The fish was so strange in morphology that it did not fit into any taxonomic category that we were aware of," recalls Schaefer, a curator in the Division of Vertebrate Zoology at the Museum. "But it looked like it was run over by a truck. We needed better specimens." It took years to pin down where the fish was found, but the team collected L. wahari after several trips further and further into the headwaters of the Río Cuao, a tributary of the Río Orinoco. They literally picked 84 specimens off of rocks.

The new samples of L. wahari confirmed that the species is a member of a group that bridges two catfish families. Bony plates on both its head and tail, plus other features, link the species to the Loricariidae, a widespread and successful family of fully armored catfishes. But L. wahari also has a specialized pelvic fin that decouples from its body and moves backward and forward independently. This feature—used in combination with a grasping mouth to move like an inchworm up rocks—is otherwise found only in a family of climbing catfish restricted to the Andes, the Astroblepidae.

Schaefer and Provenzano propose that L. wahari is the third known species in the subfamily Lithogeninae, and that the specialized features shared among the three species confirms their placement within the family Loricariidae at the base of this large radiation of catfishes. This phylogenetic arrangement suggests that the common ancestor to both families probably inhabited upland, rather than lowland, streams of the Amazon and Orinoco river basins, where most of the family diversity is currently found.

"We see new fish species all the time, but when you also get new information about the biological history of a group, it's the most fun," says Schaefer. "The question is whether the grasping pelvis and climbing behavior evolved once or if it was independently acquired in these groups. I don't think it evolved twice, although there are slight anatomical differences—so the jury is still out."

The paper is published in American Museum Novitates. Research was supported by the Constantine S. Niarchos Scientific Expedition Fund and the National Science Foundation.

Orphaned elephants forced to forge new bonds decades after ivory ban

An African elephant never forgets – especially when it comes to the loss of its kin, according to researchers at the University of Washington. Their findings, published online in the journal, Molecular Ecology, reveal that the negative effects of poaching persist for decades after the killing has ended.

"Our study shows that it takes a long time – upwards of 20 years – for a family who has lost its kin to rebuild," said lead researcher Kathleen Gobush, Ph.D., a research ecologist for the National Oceanic and Atmospheric Agency and a former doctoral student at the University of Washington Center for Conservation Biology.

African elephants rely heavily on matriarchs to lead groups and keep families together. Before the 1989 ban on ivory trade, nearly 75 percent of all elephants in Tanzania's Mikumi National Park were killed. Poachers targeted those with the largest tusks – particularly older matriarchs. "A lot of these females lost their sisters and mothers, and were left living a solitary existence," said Sam Wasser, Ph.D., director of the Center for Conservation Biology at the University of Washington. "So the question became, what are the long-term impacts on the genetic relatedness of groups?"

In search of an answer, the scientists tracked more than 100 groups of elephants living in Mikumi National Park. They assessed the lasting effects of poaching on group size, relatedness, and social bonding by comparing information about each group with previous reports of protected populations.

The researchers found that elephants in Mikumi formed unusually small groups, with nearly a third of the females living alone. Interestingly, some of the elephants chose to forge new bonds with unrelated groups after their own kin had perished.

"When we saw the solitary females, we initially thought that some lucky elephants still had their families, while other elephants had lost it all," Gobush said. "But we actually saw a flexibility in their behavior. Some elephants were able to find their way and create new bonds with unrelated female elephants, while others did not."

The researchers say it is unclear how long the effects will persist, especially in light of the recent increase in illegal ivory trade. But one thing is certain: Poaching continues to introduce major disruptions in the African elephant's family tree at a substantial cost.

"Elephants are very long-lived animals. They are extremely social, and there's a tremendous amount of group integrity and competitive ability," Wasser said. "It's been nearly 20 years since the ivory ban and there are still incredibly persistent impacts of illegal culling on these populations."

Notes: The article, "Genetic relatedness and disrupted social structure in a poached population of African elephants" (by Kathleen Gobush, Ben Kerr and Samuel Wasser, Department of Biology, University of Washington, Washington, USA) is published online this week in Molecular Ecology, and will be included in the full Issue 18:4 http://www3.interscience.wiley.com/journal/119878204/issue DOI: 10.1111/j.1365-294X.2008.04043.x*

1. Molecular Ecology is published by Wiley-Blackwell and can be accessed online at http://www3.interscience.wiley.com/journal/119878204/issue

2. Wiley-Blackwell was formed in February 2007 as a result of the merger between Blackwell Publishing Ltd. and Wiley's Scientific, Technical, and Medical business. Together, the companies have created a global publishing business with deep strength in every major academic and professional field. Wiley-Blackwell publishes approximately 1,250 scholarly peer-reviewed journals and an extensive collection of books with global appeal. For more information on Wiley-Blackwell, please visit http://eu.wiley.com/WileyCDA/Brand/id-35.html

Frogs are being eaten to extinction: new study

The global trade in frog legs for human consumption is threatening their extinction, according to a new study by an international team including University of Adelaide researchers.

The researchers say the global pattern of harvesting and decline of wild populations of frogs appears to be following the same path set by overexploitation of the seas and subsequent "chain reaction" of fisheries collapses around the world. The researchers have called for mandatory certification of frog harvests to improve monitoring and help the development of sustainable harvest strategies.

University of Adelaide ecologist Associate Professor Corey Bradshaw says frogs legs are not just a French delicacy.

"Frogs legs are on the menu at school cafeterias in Europe, market stalls and dinner tables across Asia to high end restaurants throughout the world," says Associate Professor Bradshaw, from the University's School of Earth and Environmental Sciences and also employed as a Senior Scientist by the South Australian Research and Development Institute (SARDI).

"Amphibians are already the most threatened animal group yet assessed because of disease, habitat loss and climate change - man's massive appetite for their legs is not helping."

The annual global trade in frogs for human consumption has increased over the past 20 years with at least 200 million and maybe over 1 billion frogs consumed every year. Only a fraction of the total trade is assessed in world trade figures. Indonesia is the largest exporter of frogs by far and its domestic market is 2-7 times that.

"The frogs' legs global market has shifted from seasonal harvest for local consumption to year-round international trade," says Associate Professor Bradshaw. "But harvesting seems to be following the same pattern for frogs as with marine fisheries - initial local collapses in Europe and North America followed by population declines in India and Bangladesh and now potentially in Indonesia.

"Absence of essential data to monitor and manage the wild harvest is a large concern."

The study team also includes researchers from the Memorial University of Newfoundland in Canada, the National University of Singapore and Harvard University. A paper about the study is soon to be published online in the journal Conservation Biology.

Lottery wins no guarantee of health or long-term wealth

* 15:42 20 January 2009 **by Jim Giles**

Ever daydreamed about winning the lottery? You probably imagined a life of financial comfort and good health. But research suggests that such fantasies are often just that. Real lottery winners are not guaranteed either better health or even long-term financial security, say the economists behind two new studies. And amongst UK lottery winners, the problem seems to originate in the pub.

Andrew Clark and Bénédicte Apouey of the Paris School of Economics analysed the British Household Panel Survey, which includes data on around 8000 people who won the lottery between 1994 and 2005.

They found that those who won more money received a bigger boost to their mental well-being, but overall health did not improve.

That may be because winners smoked and drank more after receiving their prize. "Lottery wins might not be good for your physical health," says Clark, who is preparing his findings for publication. "You party too much."

Cash cow

If a win does not help physical health, it might at least be expected to ensure financial well-being. But a study of the Florida lottery suggests this is not always the case.

Scott Hankins of the University of Kentucky, Lexington, and colleagues compared (pdf format) big winners – prizes in the range $50,000 to $150,000 – with those who won less than $10,000.

Bankruptcy rates amongst the big winners were 50% lower than average in the two years after the prize. After that, however, rates jumped up. Averaged over the five years following the prize, roughly 5% of winners in both groups went bankrupt.

It is notable that the prizes were usually greater than the debts that eventually sunk the winners, says Hankins. The average prize was $65,000 – over $10,000 more than the average amount owed by the winners who went bankrupt.

Some economists have used similar results to argue against using one-off payments such as tax rebates to improve people's well-being. But, of course, many lottery winners do become rich, even if, for some, it's only temporary.

James Hanley, an epidemiologist at McGill University in Montreal, Canada, notes that the lives of the rich are unusual and so might not tell us much about the rest of us.

He suggests looking for natural experiments in which ordinary people were gradually given more money – previous examples of which have linked income boosts to improved health.

Journal reference: Journal of the American Medical Association (vol 290, p2023)

Starving bacteria bumped up early Earth's oxygen

* 21 January 2009 **by Devin Powell**

HUNGRY nickel-grabbing bacteria could be to thank for the surge in atmospheric oxygen 2.5 billion years ago that made Earth hospitable to life.

Stefan Lalonde of the University of Alberta in Edmonton, Canada, and colleagues measured the concentration of nickel deposited in layered sedimentary rocks, or "banded iron formations". They found that levels had dropped by two-thirds in the 200 million years prior to the "Great Oxygenation Event".

The team speculate that this drop in nickel starved primordial ocean-dwelling bacteria called methanogens that used dissolved nickel in seawater to help turn food into energy and methane. As methane reacts with oxygen to remove it from the atmosphere, a decline in the methane produced by bacteria would have led to a build-up of oxygen.

Though it is not clear quite how much the ancient bacteria relied on the metal, "growing modern methanogens in the lab requires extremely high concentrations of nickel", says Stephen Zinder at Cornell University in Ithaca, New York.

So what could have caused the nickel shortage? A surge in the number of magma plumes just before the nickel decline removed a large amount of heat from Earth's core, say the team. In these cooler conditions, more oceanic crust was created relative to continental crust. This contains less of the nickel that the bacteria can use. The work was presented at the American Geophysical Union meeting in December.

"This study is one of the first to look at hard data about metal concentrations, which is an important new idea," says Timothy Lyons of the University of California, Riverside. But he suspects the oxygenation effect may be less than the team thinks, because the bacterial famine could have enabled other atmospheric reactions that used up oxygen.

NEJM study: Americans owe 5 months of their lives to cleaner air

BYU/Harvard SPH research shows reducing air pollution brings measureable health gains

A new study by researchers at Brigham Young University and Harvard School of Public Health shows that average life expectancy in 51 U.S. cities increased nearly three years over recent decades, and approximately five months of that increase came thanks to cleaner air.

"Such a significant increase in life expectancy attributable to reducing air pollution is remarkable," said C. Arden Pope III, a BYU epidemiologist and lead author on the study in the Jan. 22 issue of the New England Journal of Medicine. "We find that we're getting a substantial return on our investments in improving our air quality. Not only are we getting cleaner air that improves our environment, but it is improving our public health."

The research matched two sets of data from 51 cities across the nation: changes in air pollution between about 1980 and about 2000; and residents' life expectancies during those years. The scientists applied advanced statistical models to account for other factors that could affect average life spans, such as changes in population, income, education, migration, demographics and cigarette smoking.

In cities that had previously been the most polluted and cleaned up the most, the cleaner air added approximately 10 months to the average resident's life. On average, Americans were living 2.72 years longer at the end of the two-decade study period; up to five months, or 15 percent, of that increase came because of reduced air pollution. Other studies show that these gains are likely coming from reductions in the cardiovascular and cardiopulmonary disease that typically accompany air pollution.

"There is an important positive message here that the efforts to reduce particulate air pollution concentrations in the United States over the past 20 years have led to substantial and measurable improvements in life expectancy," said study co-author Douglas Dockery, chair of the Department of Environmental Health at Harvard School of Public Health.

Pope and Dockery have teamed with other researchers on landmark studies published in the early 1990s that revealed the negative health effects of particulate air pollution known as "PM2.5" – tiny pollutants smaller than 2.5 microns in diameter, smaller than 4/100 the width of a human hair. The Environmental Protection Agency used those and related studies as the basis for tightening air pollution standards in 1997.

The latest study evaluated the impact of resulting decreases in particulate pollution on average life spans in cities for which air pollution data were available. In fact, researchers had to build life expectancy data for the 214 counties that are part of the study's 51 metropolitan areas.

"Life expectancy is the single most comprehensive summary of how people's longevity is affected by factors like air pollution that cause early death," said co-author Majid Ezzati, associate professor of international health at Harvard School of Public Health. "We were able to use routine mortality statistics to track longevity in all cities over a long period of time and analyze how it has been influenced by changes in air pollution."

The analysis found that for every decrease of 10 micrograms per cubic meter of particulate pollution in a city, its residents' average life expectancy increased by more than seven months. During the 1980s and 1990s the average PM2.5 levels in the 51 U.S. cities studied dropped from 21 to 14 micrograms per cubic meter. In cities such as Pittsburgh and Buffalo, the decrease was closer to 14 micrograms per cubic meter.

The research also observed gains in life expectancy even in cities that initially had relatively clean air but had further improvements in air quality, suggesting the continuing benefits to ongoing efforts to reduce air pollution.

The researchers emphasized that there are other important and often overlapping factors that influence life expectancy, but this study demonstrated that improvements in air quality can contribute to significant and measurable improvements in life expectancy.

The study was funded by the Centers for Disease Control and Prevention, the Association of Schools of Public Health, the Environmental Protection Agency, the National Institute of Environmental Health Sciences, and the Mary Lou Fulton Professorship at BYU.

Topical treatment wipes out herpes with RNAi

BOSTON, Mass. - condoms or abstinence, most efforts to prevent sexually transmitted diseases have a common logic: keep the pathogen out of your body altogether. While this approach is certainly reasonable enough, it doesn't help the countless people worldwide who, for a number of reasons, are not in a position to control their sexual circumstances.

Now, Harvard Medical School professor of pediatrics Judy Lieberman, who is also a senior investigator at the Immune Disease Institute, has overseen the development of a topical treatment that, in mice, disables key genes necessary for herpesvirus transmission. Using a laboratory method called RNA interference, or RNAi, the treatment cripples the virus in a molecular two-punch knockout, simultaneously disabling its ability to replicate, as well as the host cell's ability to take up the virus.

What's more, the treatment is just as effective when applied anywhere from one week prior to a few hours after exposure to the virus. In that sense, the basic biology of this prophylactic enables a real-world utility.

"People have been trying to make a topical agent that can prevent transmission, a microbicide, for many years," says Lieberman. "But one of the main obstacles for this is compliance. One of the attractive features of the compound we developed is that it creates in the tissue a state that's resistant to infection, even if applied up to a week before sexual exposure. This aspect has a real practicality to it. If we can reproduce these results in people, this could have a powerful impact on preventing transmission."

These findings will be published in the January 22 issue of Cell Host and Microbe.

The World Health Organization estimates that approximately 536 million people worldwide are infected with herpes simplex virus type 2 (HSV-2), the most common strain of this sexually transmitted disease. Women are disproportionately affected. This is especially serious, since the virus can easily be passed from mother to child during birth, and untreated infants face risks of brain damage and death. While HSV-2 alone isn't life-threatening in adults, infection does increase a person's vulnerability to other viruses such as HIV.

In order for the herpesvirus to infect the host, two conditions must be met. First, the virus must be able to enter and take over host cells. Second, the virus must then reproduce itself. Lieberman's topical treatment uses RNAi to foil both these events.

RNAi, a biological process that was identified barely a decade ago, has transformed the field of biological research. A breakthrough that earned the Nobel Prize in 2006, RNAi is a natural cellular process that occurs in all cells of all multicellular organisms to regulate the translation of genetic information into proteins. This

natural process can be manipulated by researchers to switch off specific genes, and there is much research and development work to harness RNAi for therapeutics.

Many in the field think RNAi-based drugs may be the next important new class of drugs. By introducing tiny RNA molecules into cells, researchers can target a gene of interest and, in effect, throw a wrench into that gene's ability to build protein molecules. For all intents and purposes, that gene is now disabled.

While RNAi has profoundly accelerated the ability of scientists to probe and interrogate cells in the Petri dish, therapeutic breakthroughs have proved far more problematic. Researchers have had a difficult time delivering these tiny RNA molecules and ensuring that they actually penetrate the desired cells and tissues in a living organism.

Modifying a delivery technique that Lieberman developed in 2005, she and postdoctoral fellow Yichao Wu and junior researcher Deborah Palliser (who now heads her own laboratory at Albert Einstein College of Medicine) treated mice with strands of RNA that were fused to cholesterol molecules, which made it possible for the molecules to pass through the cell membranes. When applied in the form of a topical solution, these RNA molecules could then be fully absorbed into the vaginal tissue, protecting the mice against a lethal dose of administered virus.

One RNA molecule in the topical solution targeted a herpes gene called UL29, which the virus needs to replicate. Knocking out UL29 inactivates the virus.

Another RNA molecule targeted Nectin-1, a surface protein found on cells in the vaginal tissue. Nectin-1 acts as a kind of host gatekeeper to which the virus binds to pass into the cell. Without Nectin-1, the virus simply can't infect cells.

Either RNA molecule delivered by itself would be sufficient to block the virus, but together in this RNAi cocktail, the host tissue becomes like a fortress that pulls up the drawbridge to block the enemy's entrance, and also has a full-fledged battle plan to slaughter the enemy if they make it through.

"As far as we could tell, the treatment caused no adverse effects, such as inflammation or any kind of autoimmune response," says Lieberman. "And while knocking out a host gene can certainly be risky, we didn't see any indication that temporarily disabling Nectin-1 interfered with normal cellular function."

Lieberman was recently awarded a grant from the Massachusetts Life Science Center to collaborate with a corporate partner to build on these results to develop a topical microbicide that might be suitable for human use.

In addition, she's investigating how this same approach might be used to treat HIV in a multi-institutional program funded by the National Institutes of Health that includes researchers at the Tulane National Primate Research Center, St. George's Hospital in London, and Alnylam Pharmaceuticals in Cambridge. The research was supported by the National Institutes of Health. ***Full citation***

Cell Host & Microbe, January 22, 2009, Vol 5 No. 1 "Durable Protection from Herpes Simplex Virus-2 Transmission Following Intravaginal Application of siRNAs Targeting Both a Viral and Host Gene"

Yichao Wu,1 Francisco Navarro,1 Ashish Lal,1 Emre Basar,1 Rajendra K. Pandey,2 Muthiah Manoharan,2 Yang Feng,3 Sandra J. Lee,3 Judy Lieberman,1, and Deborah Palliser1,4

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Did the Moon's far side once face Earth?

* 21 January 2009 **by Richard Fisher**

BILLIONS of years ago, the man in the moon may have performed the ultimate about-face, when an asteroid flipped the moon around.

The far side of the moon never faces us, because the moon rotates once for every orbit it makes of the Earth. Yet an analysis of impact craters shows the far side may once have pointed our way.

Mark Wieczorek and Matthieu Le Feuvre at the Paris Institute of Earth Physics in France studied the relative age and distribution of 46 known craters, gouged out by impacts from debris originating in the solar system's asteroid belt.

According to earlier computer simulations, the moon's western hemisphere as viewed from Earth should have about 30 per cent more craters than the eastern hemisphere. That's because the west always faces in the direction in which the moon orbits, which makes it more likely to be hit by debris, for the same reason that more raindrops strike a moving car's front windshield than its rear.

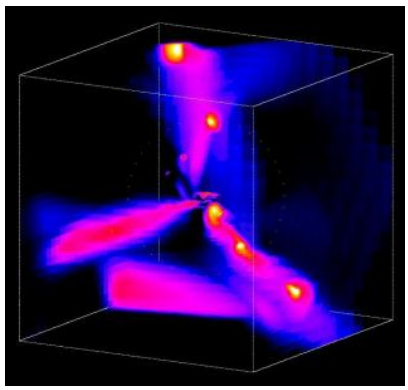
The western hemisphere of the Moon, as seen by the Galileo spacecraft (Image: Johnson Space Center Collection / NASA)

However, when Wieczorek and Le Feuvre compared the relative ages of the craters, using data about the sequence in which ejected material was deposited on the surface, they found the opposite to be true. Although the youngest impact basins were concentrated in the western hemisphere, as expected, the older craters were mostly congregated in the east. This suggests that the eastern face had once been bombarded more than the western face (Icarus, DOI: 10.1016/j.icarus.2008.12.017).

This could be explained if a large asteroid impact had set the moon turning. Such an impact would have put the satellite's rotation rate out of whack, so that for tens of thousands of years it would have appeared to slowly turn as viewed from Earth. Eventually, it would have settled into the current position.

The handful of lunar-rock debris collected from craters formed by a big enough smash suggest that the moon turned to face the other way more than 3.9 billion years ago, says Wieczorek. Asian probes currently circling the moon could reveal additional craters that would support the about-face idea.

New understanding of the origin of galaxies advanced



Jerusalem– A new theory as to how galaxies were formed in the Universe billions of years ago has been formulated by Hebrew University of Jerusalem cosmologists. The theory takes issue with the prevailing view on how the galaxies came to exist.

The new theory, motivated by advanced astronomical observations and based on state-of-the-art computer simulations, maintains that the galaxies primarily formed as a result of intensive cosmic streams of cold gas (mostly hydrogen) and not, as current theory contends, due primarily to galactic mergers. The researchers show that these mergers had only limited influence on the cosmological makeup of the universe as we know it.

Computer simulation of galaxy formation shows matter flowing into the center of a galaxy through three cold gas streams. Such pictures provide the basis for the new theory of galaxy formation via these streams. **The Hebrew University of Jerusalem**

The results of the cosmology research group, led by Prof. Avishai Dekel, who holds the Andre Aisenstadt Chair of Theoretical Physics at the Racah Institute of Physics of the Hebrew University, appear in the current issue of the journal Nature.

The galaxies are the building blocks of the Universe. Each of them comprises some hundred billion radiant stars, such as our sun, which extend across about 50,000 light years. Every galaxy is embedded in a spherical halo made of dark matter that cannot be seen but is detected through its massive gravitational attraction. The exact nature of this matter is still unknown.

The galaxies are composed into two major types: spiral and elliptical. The spiral galaxies, such as our Milky Way, are rotating disks, rich in hydrogen gas, and are constantly forming new stars. The young stars give the spiral galaxies a blue tint. In contrast, the elliptical galaxies have bodies with a larger, more rounded shape, and are made of old, red stars that are devoid of gas. They are therefore referred to as red and dead.

The attempt to understand the way in which these two types of galaxies form is the primarily challenge facing modern cosmological researchers. The formation of galaxies is an essential stage in the cosmological process that leads to the formation of life.

The accepted model until now has as its basis the idea of spherical gas infall into a central disk, followed by mergers between disks. The assumption is that the stars formed slowly within the gaseous disks, and that the disks converted into globes when they merged. In such a merger, the colliding gas clouds produce a big burst of new stars at a rate of hundreds of solar masses per year.

This model has lately been put to question as a result of astronomical observations using new and more powerful telescopes which enable observations at greater depth into the Universe, making it possible thus to examine what happened in the galaxies some ten billion years ago (about three billion years after the Big Bang which first established the Universe). "The large galaxies, as they appear in this early stage, indeed created stars at a very rapid rate, but this does not appear to be at all a result of galactic mergers," says Prof. Dekel. The astronomical observations were led by researchers in Garching, Germany, headed by Prof. Reinhard Genzel of the Max Planck Institute, whose group is collaborating with the Hebrew University researchers.

The question that emerged was how these galaxies were able to form stars so quickly and in large quantities at such an early stage without massive galactic mergers.

In the article published in Nature, Prof. Dekel and his Hebrew University and French associates, pose their new theoretical model, which explains these observed phenomena. Their findings are based on computer simulations carried out by the French researchers headed by Prof. Romain Teyssier. The simulations, using one

of the most powerful supercomputers in Europe, made it possible in an unprecedented manner to carry out a detailed investigation of how galaxies formed in the early Universe.

The picture that emerges is of galaxy-building that results from a continuous flow of cold gas along a few narrow streams rather than by mergers. These gas streams follow the filaments of the "cosmic web" that defines the large-scale structure of matter in the Universe, filaments that feed the dark-matter halos in the first place. These cold gas streams penetrate through the dark-matter halo of each galaxy and the hot gas that fills it and reach the center, where they become a rotating disk. These disks, each subject to its own, local, gravitational forces, break into a few giant clumps in which the gas converts into stars very efficiently.

In their calculations, Dekel and his group show that the rate of star formation, as predicted by this theory, is compatible with the observed rate. The researchers refer to these massive star formers in the early universe as Stream-Fed Galaxies (SFG). The galaxy merger phenomenon, in this view, was not the primary factor as maintained in current theory.

Prof. Dekel and his Hebrew University associates, Prof. Re'em Sari and Dr. Daniel Ceverino, worked out a simple physical theory that explains the formation of giant clumps in the early massive disks, and how they are driven by the cosmic streams. They predict that the migration of these clumps to the disk centers led to the formation of elliptical galaxies already in the early Universe, independent of galaxy mergers. They are thus making the revolutionary proposal that the role of cosmic gas streams is not limited only to the formation of star-forming disks, but that these streams are also responsible for the subsequent formation of the red-and-dead elliptical galaxies. New state-of-the-art simulations confirm this theory.

Research exposes the risk to infants from the chemicals used in liquid medicines

Study reveals importance of researching medicines for children

A team of medical scientists from the University of Leicester has published research which looks into the harmful substances in liquid medicines that premature babies are being exposed to.

Research published today (Jan 20) ahead of print in the Fetal & Neonatal Edition of Archives of Disease in Childhood documents the non-drug ingredients (excipients) present in liquid medicines given to premature infants as part of their medical care.

The study led by Dr Hitesh Pandya, Senior Lecturer in Child Health in the Department of Infection, Immunity and Inflammation at the University of Leicester and Consultant Paediatrician at the University Hospitals of Leicester NHS Trust, revealed that the chemicals added to medicines to improve their taste, absorption and to prolong their shelf-life could be potentially harmful to very small babies. The chemicals generally used are ethanol, sorbitol and Ponceaau 4R (a colouring agent). The study revealed that premature babies are exposed to these potentially harmful excipients in amounts equivalent to over three pints of beer per week.

Dr Pandya said: "This study documents a worldwide problem. It shows that the collection of medicines given to babies may ultimately lead to them being exposed to harmful chemicals with the potential for short and long-term toxic effects. Our research highlighted this, and we are planning further studies on the chemicals to understand exactly what these effects might be. What our study hasn't done is find any direct evidence on the cause and effect of these chemicals and the medical problems that these babies might be being treated for."

Dr Andrew Currie, Consultant at the University Hospitals of Leicester NHS Trust who was also part of the research team said "Parents should not panic about these findings. These chemicals can be found in foods all around the world. What the study highlighted is that we have a greater understanding of the side-effects of the drugs than we do of the chemicals that many of these drugs are mixed with; there just simply hasn't been enough research done. It is often necessary that these chemicals are added to medications, and in the majority of cases it improves the way the drugs work, but we should be taking more of an interest in them and their effects. It is great news that Dr Pandya and his team will continue their research."

Dr Pandya added: "Babies and older children are often given medicines that have only received formal testing on adults, which means we estimate amounts that should be given to children and babies. There are numerous reasons for this, such as the practical problems in performing studies in very small babies, worries their parents may have about involving their child in drug trials and drug manufacturer's reluctance to tackle the problem. Our study showed that more work needs to be done to tackle this problem and to improve our understanding."

"Both the UK Government and the European Union have recently passed legislation to incentivise drug companies to develop better medicines for children. Our research team is planning to engage with parents to talk about how they can be encouraged to allow their children to participate in drug trials. We are also in close discussions with drug manufacturing companies about overcoming some of the practical hurdles that restrict performing drug trials in very small children. We are hopeful that this world-wide problem can be addressed for the benefit of future generations by highlighting the issue and through constructive engagement with interested parties."

Dr Pandya concluded by saying "Parents should begin to understand what chemicals are in the medicines being given to their children, but they should not be overly concerned. In many cases there may not be an alternative medicine, and the risk will be balanced in favour of using them in treatment. As a research team we do feel it is important that the [medicines regulators] not only ensure that all manufacturers provide detailed labelling of the excipient content of their products but all lead action to determine whether existing practice constitutes a risk, and if so, how this might be dealt with."

The authors point out that children's medicines have to cater for a wide age range, making it difficult for manufacturers to tailor their products for each age group. The inclusion of some excipients is also a necessity.

** The study was carried out by Amy Whittaker, Andrew E Currie, Mark Turner, David J Field, Hussain Mulla & Hitesh C Pandya*

Industrialization of China increases fragility of global food supply

Global grain markets are facing breaking point according to new research by the University of Leeds into the agricultural stability of China.

Experts predict that if China's recent urbanisation trends continue, and the country imports just 5% more of its grain, the entire world's grain export would be swallowed whole.

The knock-on effect on the food supply - and on prices - to developing nations could be huge.

Sustainability researchers have conducted a major study into the vulnerability of Chinese cropland to drought over the past 40 years, which has highlighted the growing fragility of global grain supply. Increased urban development in previously rich farming areas is a likely cause.

"China is a country undergoing a massive transformation, which is having a profound effect on land use," says Dr Elisabeth Simelton, research fellow at the Sustainability Research Institute at the University of Leeds, and lead author of the study. "Growing grain is a fundamentally low profit exercise, and is increasingly being carried out on low quality land with high vulnerability to drought."

The study looked at China's three main grain crops; rice, wheat and corn, to assess how socio-economic factors affect their vulnerability to drought. Researchers compared farming areas with a resilient crop yield with areas that have suffered large crop losses with only minor droughts. They found that traditionally wealthy coastal areas are just as susceptible to drought as areas with poor topography in the east of the country.

"Quality land is increasingly being used for high profit crops, such as vegetables and flowers. The impact of this on local and global economies is an issue that the newly created Centre for Climate Change, Economics and Policy (CCCEP) will address," explains Dr Simelton.

CCCEP is a partnership between the University of Leeds and the London School of Economics. Its main objectives include developing better climate change models and understanding how developing countries can adapt to climate change.

At the moment the Chinese government claims that China is 95% self sufficient in terms of grain supply. If China were to start importing just 5% of its grain (to make up a shortfall produced by low yields or change of land use to more profitable crops) the demand would hoover up the entire world's grain export.

The pressure on grain availability for international grain markets could, in turn, have a huge knock-on effect. Poorer countries are particularly vulnerable, as demonstrated by the 2007-2008 food crisis.

Published in the journal Environmental Science and Policy, the study used provincial statistics of harvests and rainfall together with qualitative case studies to establish the differences between land that is sensitive to drought and land that is not.

"One aim of this research is better understanding of the socio-economic responses to difficult conditions so that we can improve models of climate change" says Dr Simelton. "These trends of urbanisation are also happening in India, with the population predicted to keep on rising until at least 2050. Ultimately the limiting factor for grain production is land, and the quality of that land."

The research is part of the Quantifying and Understanding the Earth System (QUEST) project and has been funded by the Natural Environment Research Council (NERC). QUEST aims to look at global scale impacts of climate change across a range of areas including fisheries, agriculture, and epidemiology.

Measles Virus May Be Effective Prostate Cancer Treatment

Rochester, Minn. –A new study appearing in The Prostate has found that certain measles virus vaccine strain derivatives, including a strain known as MV-CEA, may prove to be an effective treatment for patients with advanced prostate cancer. The findings show that this type of treatment, called virotherapy, can effectively infect, replicate in and kill prostate cancer cells.

Prostate cancer is a leading cause death among males in the western world. It is currently the second most common cause of cancer-related deaths among American men with 186,320 new cases and 28,660 deaths expected to be recorded in 2008. A sizeable proportion of these patients ultimately relapse, with a 5-year failure

rate for treatment ranging from 14 to 34 percent. No curative therapy is currently available for locally advanced or metastatic prostate cancer.

The median survival time of MV-CEA-treated mice in the study almost doubled compared to the controls, and complete tumor regression was observed in one-fifth of treated animals.

"Based on our preclinical results as well as the safety of measles derivatives in clinical trials against other tumor types, these viral strains could represent excellent candidates for clinical testing against advanced prostate cancer, including androgen resistant tumors," says Evanthia Galanis, M.D., of the Mayo Clinic, senior author of the study. The study was supported by the Mayo Clinic Specialized Program of Research Excellence (SPORE) in prostate cancer.

These oncolytic strains of measles virus, represent a novel class of therapeutic agents against cancer that demonstrates no cross-resistance with existing treatment approaches, and can therefore be combined with conventional treatment methods.

Because primary tumor sites are easily accessible in prostate cancer, locally recurrent disease represents a promising target for virotherapy approaches. The virotherapy agent can easily be applied directly to the prostate tumor via ultrasound-guided needle injections and close monitoring of therapy can be achieved by non-invasive techniques including ultrasound and MRI.

The measles vaccine strains also have an excellent safety record with millions of vaccine doses having been safely administered in over 40 years of use. Repeated measurements of the marker CEA (carcinoembryonic antigen, produced when the virus replicates) following MV-CEA treatment can be performed via a simple blood test, and can potentially allow for optimization of dosing as well as the tailoring of individualized treatment. To date, no significant toxicity from MV-CEA treatment of patients with other tumor types has been observed.

Prior studies have demonstrated the therapeutic potency of MV-Edm derivatives against a variety of preclinical animal models including ovarian cancer, glioblastoma multiforme, breast cancer, multiple myeloma, lymphoma and hepatocellular carcinoma.

The promising results prompted the rapid translation of engineered MV-Edm strains in three clinical trials that are currently active. In the ovarian cancer trial, the furthest advanced; evidence of biologic activity has been noted in refractory ovarian cancer patients.

The results set the foundation for additional studies in preparation for using engineered measles strains in a clinical trial for the treatment of patients with advanced prostate cancer.

This study is published in The Prostate. Media wishing to receive a PDF of this article may contact medicalnews@bos.blackwellpublishing.net. To view the abstract for this article, please click here.

Researchers genetically link Lou Gehrig's disease in humans to dog disease

Discovery could help identify therapy for humans and dogs

COLUMBIA, Mo. –An incurable, paralyzing disease in humans is now genetically linked to a similar disease in dogs. Researchers from the University of Missouri and the Broad Institute have found that the genetic mutation responsible for degenerative myelopathy (DM) in dogs is the same mutation that causes amyotrophic lateral sclerosis (ALS), the human disease also known as Lou Gehrig's Disease. As a result of the discovery, which will be published in the Proceedings of the National Academy of Sciences this week, researchers can now use dogs with DM as animal models to help identify therapeutic interventions for curing the human disease, ALS.

"We uncovered the genetic mutation of degenerative myelopathy, which has been unknown for 30 years, and linked it to ALS, a human disease that has no cure," said Joan Coates, a veterinary neurologist and associate professor of veterinary medicine and surgery in the MU College of Veterinary Medicine. "Dogs with DM are likely to provide scientists with a more reliable animal model for ALS. Also, this discovery will pave the way for DNA tests that will aid dog breeders in avoiding DM in the future."

Previously, ALS research has relied heavily on transgenic rodents that expressed the mutant human gene SOD1, which causes ALS. Researchers found that dogs with DM also had mutations in their SOD1 gene. Many rodent models possess very high levels of the SOD1 protein that can produce pathologic processes distinct from those occurring in ALS patients. Since the SOD1 mutation is spontaneous in dogs, the clinical spectrum in dogs may represent more accurately that of human ALS.

"Compared with the rodent models for ALS, dogs with DM are more similar to people in size, structure and complexity of their nervous systems, and duration of the disease," said Gary Johnson, associate professor of veterinary pathobiology in the MU College of Veterinary Medicine. "The results from clinical trials conducted with DM-affected dogs may better predict the efficacies of therapeutic interventions for treating ALS in humans."

ALS causes progressive neurodegeneration, affecting both the central and peripheral nervous systems. The disease leads to advancing weakness and muscle atrophy, and culminates in paralysis and death. DM has been recognized for more than 35 years as a spontaneously occurring, spinal cord disorder in dogs. DM is reported most commonly in German Shepherds but also exists in other breeds, such as Cardigan and Pembroke Welsh Corgis, Rhodesian Ridgebacks, Chesapeake Bay Retrievers and Boxers. There are no treatments for ALS and DM that clearly have been shown to stop or slow progression of the diseases. Owners of dogs with DM usually elect euthanasia six months to a year after diagnosis when the dogs can no longer support their weight with their pelvic limbs, whereas people with ALS typically progress to the state of complete paralysis and succumb to respiratory failure.

The study, "Genome-wide association analysis reveals a SOD1 mutation in canine degenerative myelopathy which resembles amyotrophic lateral sclerosis," was published in the Proceedings of the National Academy of Sciences this week. This study was a collaborative project with MU researchers and Kerstin Lindbld-Toh and Claire Wade, researchers at the Broad Institute of Harvard and Massachusetts Institute of Technology. The study was funded by the American Kennel Club Canine Health Foundation and participating breed clubs.

Drug Making's Move Abroad Stirs Concerns

By GARDINER HARRIS

WASHINGTON — In 2004, when Bristol-Myers Squibb said it would close its factory in East Syracuse, N.Y. - the last plant in the United States to manufacture the key ingredients for crucial antibiotics like penicillin - few people worried about the consequences for national security. "The focus at the time was primarily on job losses in Syracuse," said Rebecca Goldsmith, a company spokeswoman.

But now experts and lawmakers are growing more and more concerned that the nation is far too reliant on medicine from abroad, and they are calling for a law that would require that certain drugs be made or stockpiled in the United States. "The lack of regulation around outsourcing is a blind spot that leaves room for supply disruptions, counterfeit medicines, even bioterrorism," said Senator Sherrod Brown, Democrat of Ohio, who has held hearings on the issue.

Decades ago, most pills consumed in the United States were made here. But like other manufacturing operations, drug plants have been moving to Asia because labor, construction, regulatory and environmental costs are lower there.

The critical ingredients for most antibiotics are now made almost exclusively in China and India. The same is true for dozens of other crucial medicines, including the popular allergy medicine prednisone; metformin, for diabetes; and amlodipine, for high blood pressure.

Of the 1,154 pharmaceutical plants mentioned in generic drug applications to the Food and Drug Administration in 2007, only 13 percent were in the United States. Forty-three percent were in China, and 39 percent were in India. Some of these medicines are lifesaving, and health care in the United States depends on them. Half of all Americans take a prescription medicine every day.

Penicillin, a crucial building block for two classes of antibiotics, tells the story of the shifting pharmaceutical marketplace. Industrial-scale production of penicillin was developed by an American military research group in World War II, and nearly every major drug manufacturer once made it in plants scattered throughout the country.

But beginning in the 1980s, the Chinese government invested huge sums in penicillin fermenters, "disrupting prices around the globe and forcing most Western producers from the market," said Enrico Polastro, a Belgian drug industry consultant who is an expert in antibiotics.

Part of the reason these plants went overseas is that the F.D.A. inspects domestic plants far more often than foreign ones, making production more expensive in the United States.

"U.S. companies are more regulated and are under more scrutiny than foreign producers, particularly those from emerging countries. And that's just totally backwards," said Joe Acker, president of the Synthetic Organic Chemical Manufacturers Association. "We need a level playing field."

The Bush administration spent more than $50 billion after the 2001 anthrax attacks to protect the country from bioterrorism attacks and flu pandemics; some of that money went to increase domestic manufacturing capacity for flu vaccines.

Even so, officials have said that during a pandemic the United States would not be able to rely on vaccines manufactured largely in Europe because of possible border closures and supply shortages. And the situation is similar with antibiotics like penicillin; researchers have found that during the 1918 flu pandemic, most victims died of bacterial infections, not viral ones.

The Centers for Disease Control and Prevention has a stockpile of medicines with enough antibiotics to treat 40 million people. If more are needed, however, the nation lacks the plants to produce them. A penicillin fermenter would take two years to build from scratch, Mr. Polastro said.

Dr. Yusuf K. Hamied, chairman of Cipla, one of the world's most important suppliers of pharmaceutical ingredients, says his company and others have grown increasingly dependent on Chinese suppliers. "If tomorrow China stopped supplying pharmaceutical ingredients, the worldwide pharmaceutical industry would collapse," he said.

Since drug makers often view their supply chains as trade secrets, the true source of a drug's ingredients can be difficult or impossible to discover. The F.D.A. has a public listing of drug suppliers, called drug master files. But the listing is neither up to date nor entirely reliable, because drug makers are not required to disclose supplier information. One federal database lists nearly 3,000 overseas drug plants that export to the United States; the other lists 6,800 plants. Nobody knows which is right.

Drug labels often claim that the pills are manufactured in the United States, but the listed plants are often the sites where foreign-made drug powders are pounded into pills and packaged. "Pharmaceutical companies do not like to reveal where their sources are," for fear that competitors will steal their suppliers, Mr. Polastro said.

China's position as the pre-eminent supplier of medicines is a result of government policy, said Guy Villax, the chief executive of Hovione, a maker of crucial drug ingredients with plants in Portugal and China.

The regional government in Shanghai has promised to pay local drug makers about $15,000 for any drug approval they garner from the F.D.A. and about $5,000 for any approval from European regulators, according to a document Mr. Villax provided. "This shows that there has been a government plan in China to become a pharmaceutical industry leader," Mr. Villax said.

The world's growing dependence on Chinese drug manufacturers became apparent in the heparin scare. A year ago, Baxter International and APP Pharmaceuticals split the domestic market for heparin, an anticlotting drug needed for surgery and dialysis. When federal drug regulators discovered that Baxter's product had been contaminated by Chinese suppliers, the F.D.A. banned Baxter's product and turned almost exclusively to the one from APP. But APP also got its product from China.

So for now, like it or not, China has the upper hand. As Mr. Polastro put it, "If China ever got very upset with President Obama, it could be a big problem."

Q & A

The Arctic Larder

By C. CLAIBORNE RAY

Q. We are always told a balanced diet with plenty of nutritious fresh produce is needed for good health. How did people avoid malnutrition in societies, like those in the Arctic, where historically there was little or no produce?

A. It is a misperception that traditional Eskimo and other Arctic diets included no fresh plant food, though it was limited. In fact, early explorers found that malnutrition and deficiency problems like scurvy could be avoided by adopting a "primitive" diet of fresh fish and meat, with occasional ground plants and berries.

Victoria Roberts

A small 1979 study of Inuit living in a seal-hunting camp, published in the journal Arctic, found that they sometimes consumed plants like Yredysarum alpinurn, or licorice root, and Oxyria digyna, or mountain sorrel, which provided valuable supplements of vitamin C.

The researchers, from the University of Calgary, also found that the fresh animal foods these Inuit ate, including fish, birds and animals like seal, whale, polar bears, musk ox and caribou, provided them with surprisingly high levels of vitamin C, in some cases more than a Canadian national study found in the diets of Inuit living in places with more access to processed foods.

Raw, fresh seal and whale blubber were found to be especially rich in the vitamin; the Inuit diet also included the viscera of the animals they ate, yielding additional vitamin C.

Identifying the Bird After a Strike, When Not Much Bird Is Left

By MATTHEW L. WALD

WASHINGTON - Clues from the wreckage from US Airways Flight 1549, which crashed in the Hudson River, are going to the best investigators in the world: the black boxes to the National Transportation Safety Board, the engines to the manufacturer's experts and a bird feather to a Smithsonian museum.

The National Museum of Natural History in Washington may not leap to mind when both engines on a high-tech plane quit at 3,200 feet. But around the corner from the stuffed African elephant that greets the visiting

hordes of schoolchildren, down a back hall from the employee bike rack, a staff of four in the Feather Identification Lab took in samples from 4,600 bird-plane collisions, or bird strikes, last year. Arriving mostly in sealed plastic bags, these included birds' feet, whole feathers or tiny bits of down, and pulverized bird guts, known as snarge.

Correctly identifying the species involved in a bird strike can be important, said Carla J. Dove, the lab's director. "If people know the cause of a problem, they can do something about it," she said. "If you have cockroaches, you don't call an ant exterminator."

One key to reducing bird strikes is to move the species causing the problem, she said. That might mean mowing a certain area, or filling in a pond frequented by a species of duck.

The feathers or other bird parts submitted are compared against a library of 620,000 bird samples, some gathered by Darwin and Audubon. Another contributor was Theodore Roosevelt, who collected birds around the family home in Oyster Bay, on Long Island, before he switched to hunting big game. And if the feathers do not make the case, the snarge goes to the DNA section, which has a huge database. Between the two, the success rate of identifying the type of bird involved is 99 percent.

And for high-profile crashes, identification both by feather structure and by DNA will be performed. A bird strike over the Bronx reported by the pilot minutes after Flight 1549 took off from La Guardia Airport may have caused both engines to fail, forcing the emergency splash into the Hudson, which all 155 people on board survived. The feather was discovered attached to one of the plane's wings.

Researchers at the Smithsonian would not discuss their role in the US Airways investigation, but did talk about their work in other cases.

On a lab table under color-balanced lights, Dr. Dove opened a zip-top bag with some brown and white feathers from a recent bird strike involving an American military plane in Rota, Spain. In the field, investigators had identified the feathers as being from a long-eared owl, but putting one on the table, Dr. Dove saw that was not right. She reached for an eagle owl, a bigger bird of similar coloring. "See how nicely this matches," she said.

For forensic ornithologists, it just doesn't get any better than this.

Crash investigation is a relatively recent endeavor for the museum. "This collection started before there were even airplanes," said Marcy Heacker, one of the museum's investigators, referring to the vast repository of birds. But ever since an October 1960 crash at Logan Airport in Boston, in which an Eastern Airlines Electra hit a flock of starlings, safety investigators have called on the Smithsonian for help.

Most of the bird samples come from the Air Force and the Navy; the Pentagon wants every bird strike investigated. Military planes are more vulnerable to such strikes because they often fly at low altitudes and often in single-engine planes.

Often the military's bird strikes occur in far-removed places like Afghanistan and Iraq, but the lab, which stores about 85 percent of the world's bird species, is prepared.

Major airlines also send samples from around the country, from airports large and small, Dr. Dove said.

Crashes caused by bird strikes are intermittent in small planes and rare among airliners. Government records show five strikes with scheduled airliners in this decade, not counting Flight 1549, that have produced significant damage. Feathers that are intact can be matched against a sample. If fluff or down is all that survives, researchers using 100-power magnification will look at the pattern of nodes on the microscopic feather structures to identify them.

Turnaround time is usually very short, but sometimes the lab finds a problem. Faridah Dahlan, a geneticist, tested a sample a year ago that indicated it had come from a deer. Airplanes do sometimes hit deer, but a phone call to the pilot confirmed that this strike was at 1,500 feet, so more investigation was required.

Eventually, the lab used a tiny piece of feather to determine that the bird was a black vulture. The bird apparently had deer flesh in its belly. Ms. Dahlan said getting DNA samples from small bits of bird flesh was not a challenge. In a previous job, she said, "I used to do ants."

But the bird DNA database is not as good as the one for humans. In a crash like Flight 1549's, the lab will be able to determine whether there was more than one species involved but may not be able to say how many individual birds were involved.

Lately the lab has been branching out beyond bird-plane collisions — it recently analyzed the stomach contents of a Burmese python snake caught in the Everglades, to see what kinds of birds that invasive species was eating. The lab also identifies birds killed by windmills. If the remains came from a bat, the nearby mammalogy lab will help.

The lab is filled with aisles of floor-to-ceiling cabinets, with drawers brimming with samples of all kinds. There are eggs from ostriches the size of a big grapefruit, and from hummingbirds closer to the size of a breath mint.

The specimens are skin and bones and feathers stuffed with cotton. Unlike the ones in museum display cases, these do not have glass eyeballs. They sit in what look like pizza boxes but are actually acid-free, museum-quality containers. One specimen, a Hudsonian godwit, is marked with a tag saying it was collected on East Falkland Island in 1833. The handwriting is probably Darwin's, Dr. Dove said. The collection also includes a bird that may be extinct, the ivory-billed woodpecker, and some others that certainly are, like the passenger pigeon.

And just as Darwin did not anticipate birds he collected being useful in plane crash investigations, the bird researchers today believe that future uses will be found for their library. It is already useful for gathering data that could indicate climate change, Dr. Dove said; birds are hitting planes in places and at times of year where they were probably not present years ago.

With years of experience, the investigators have a clear idea almost instantly what type of feather they are looking at. They spotted the one in this reporter's hat, and quickly decided it was part peacock and part chicken, dyed.

Details From Detached Engine

WASHINGTON — The engine of the Airbus A320 that was pulled from the Hudson River on Friday shows dents, dings and blades that are cracked or missing, the National Transportation Safety Board said Saturday night.

"A visual examination of the engine did not reveal evidence of organic material," the board said in a statement, but it added there was "evidence of soft body impact damage."

That engine and the one that remained on the right wing in the crash of US Airways Flight 1549 will be sent to the manufacturer, CFM International, for disassembly.

Pacific people spread from Taiwan

New research into language evolution suggests most Pacific populations originated in Taiwan around 5,200 years ago.

Scientists at The University of Auckland have used sospisticated computer analyses on vocabulary from 400 Austronesian languages to uncover how the Pacific was settled.

"The Austronesian language family is one of the largest in the world, with 1200 languages spread across the Pacific," says Professor Russell Gray of the Department of Psychology. "The settlement of the Pacific is one of the most remarkable prehistoric human population expansions. By studying the basic vocabulary from these languages, such as words for animals, simple verbs, colours and numbers, we can trace how these languages evolved. The relationships between these languages give us a detailed history of Pacific settlement."

"Our results use cutting-edge computational methods derived from evolutionary biology on a large database of language data," says Dr Alexei Drummond of the Department of Computer Science. "By combining biological methods and linguistic data we are able to investigate big-picture questions about human origins".

The results, published in the latest issue of the prestigious journal Science, show how the settlement of the Pacific proceeded in a series of expansion pulses and settlement pauses. The Austronesians arose in Taiwan around 5,200 years ago. Before entering the Philippines, they paused for around a thousand years, and then spread rapidly across the 7,000km from the Philippines to Polynesia in less than one thousand years. After settling Fiji, Samoa and Tonga, the Austronesians paused again for another thousand years, before finally spreading further into Polynesia eventually reaching as far as New Zealand, Hawaii and Easter Island.

"We can link these expansion pulses to the development of new technology, such as better canoes and social techniques to deal with the great distances between islands in Polynesia," says Research Fellow Simon Greenhill. "Using these new technologies the Austronesians and Polynesians were able to rapidly spread through the Pacific in one of the greatest human migrations ever. This suggests that technological advances have played a major role in the spread of people throughout the world."

The research was funded by the New Zealand Royal Society Marsden fund. The database of Austronesian basic vocabulary can be accessed at: http://language.psy.auckland.ac.nz/austronesian/

Altered brain activity in schizophrenia may cause exaggerated focus on self

MIT study links schizophrenia to key 'default mode' brain system

By Cathryn Delude

CAMBRIDGE, Mass. -- Schizophrenia may blur the boundary between internal and external realities by overactivating a brain system that is involved in self-reflection, and thus causing an exaggerated focus on self, a new MIT and Harvard brain imaging study has found.

The traditional view of schizophrenia is that the disturbed thoughts, perceptions and emotions that characterize the disease are caused by disconnections among the brain regions that control these different functions.

But this study, appearing Jan. 19 in the advance online issue of the Proceedings of the National Academy of Sciences, found that schizophrenia also involves an excess of connectivity between the so-called default brain regions, which are involved in self-reflection and become active when we are thinking about nothing in particular, or thinking about ourselves.

"People normally suppress this default system when they perform challenging tasks, but we found that patients with schizophrenia don't do this," said John D. Gabrieli, a professor in the McGovern Institute for Brain Research at MIT and one of the study's 13 authors. "We think this could help to explain the cognitive and psychological symptoms of schizophrenia."

Gabrieli added that he hopes the research might lead to ways of predicting or monitoring individual patients' response to treatments for this mental illness, which occurs in about 1 percent of the population.

Schizophrenia has a strong genetic component, and first-degree relatives of patients (who share half their genes) are 10 times more likely to develop the disease than the general population. The identities of these genes and how they affect the brain are largely unknown.

The researchers thus studied three carefully matched groups of 13 subjects each: schizophrenia patients, nonpsychotic first-degree relatives of patients and healthy controls. They selected patients who were recently diagnosed, so that differences in prior treatment or psychotic episodes would not bias the results.

The subjects were scanned by functional magnetic resonance imaging (fMRI) while resting and while performing easy or hard memory tasks. The behavioral and clinical testing were performed by Larry J. Seidman and colleagues at Harvard Medical School, and the imaging data were analyzed by first author Susan Whitfield-Gabrieli, a research scientist at the MIT Martinos Imaging Center at the McGovern Institute.

The researchers were especially interested in the default system, a network of brain regions whose activity is suppressed when people perform demanding mental tasks. This network includes the medial prefrontal cortex and the posterior cingulate cortex, regions that are associated with self-reflection and autobiographical memories and which become connected into a synchronously active network when the mind is allowed to wander.

Whitfield-Gabrieli found that in the schizophrenia patients, the default system was both hyperactive and hyperconnected during rest, and it remained so as they performed the memory tasks. In other words, the patients were less able than healthy control subjects to suppress the activity of this network during the task. Interestingly, the less the suppression and the greater the connectivity, the worse they performed on the hard memory task, and the more severe their clinical symptoms.

"We think this may reflect an inability of people with schizophrenia to direct mental resources away from internal thoughts and feelings and toward the external world in order to perform difficult tasks," Whitfield-Gabrieli explained.

The hyperactive default system could also help to explain hallucinations and paranoia by making neutral external stimuli seem inappropriately self-relevant. For instance, if brain regions whose activity normally signifies self-focus are active while listening to a voice on television, the person may perceive that the voice is speaking directly to them.

The default system is also overactive, though to a lesser extent, in first-degree relatives of schizophrenia patients who did not themselves have the disease. This suggests that overactivation of the default system may be linked to the genetic cause of the disease rather than its consequences.

The default system is a hot topic in brain imaging, according to John Gabrieli, partly because it is easy to measure and because it is affected in different ways by different disorders.

This study was supported by the Mental Illness and Neuroscience Discovery Institute, National Association of Research in Schizophrenia and Depression Stone Award, National Institute of Mental Health, Massachusetts Department of Mental Health's Commonwealth Research Center, the Poitras Center for Affective Disorders at the McGovern Institute/MIT and the National Center for Research Resources. Other contributors to the study were Heidi W. Thermenos, Snezana Milanovic, Robert W. McCarley, Martha E. Shenton and Joanne Wojcik (Harvard Medical School); Ming T. Tsuang (Harvard Institute of Psychiatric Epidemiology and Genetics); Stephen V. Faraone (State University of New York); Alan I. Green (Dartmouth Medical School), Alfonso Nieto-Castanon (MIT); and Peter LaViolette (Martinos Center for Biomedical Imaging).

Holographic discs set to smash storage records

* 17:06 22 January 2009 **by Colin Barras**

How quickly things change. Just as Blu-ray is starting to replace the DVDs in our homes, another technology is developed that could sound its death knell. A dual-layer Blu-ray disc can store an impressive 50 gigabytes, but discs which can hold 20 times as much data have just taken a step closer, thanks to new materials that make reading and writing 3D holograms more reliable.

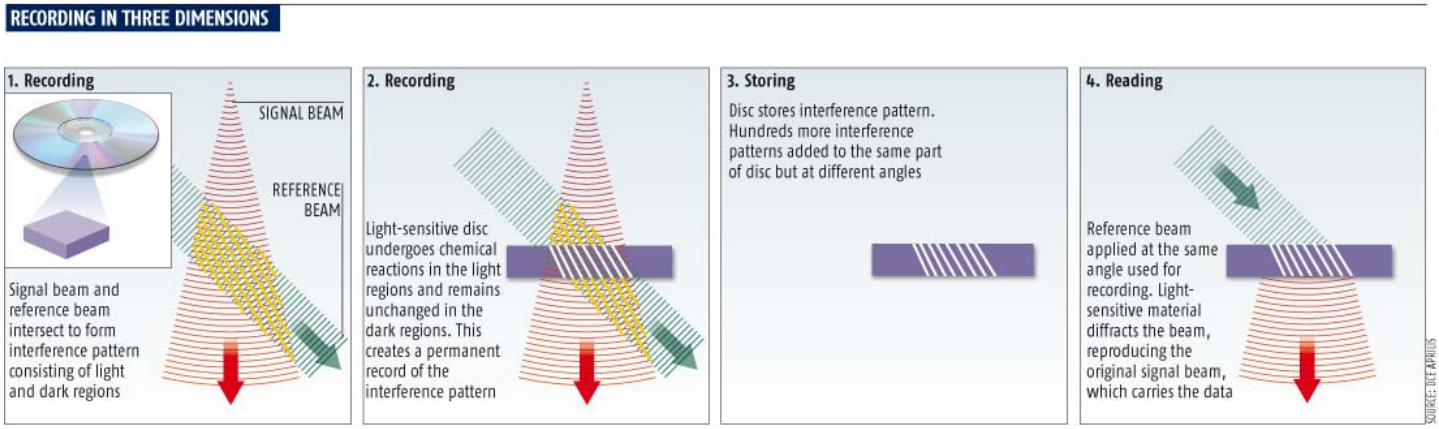
CDs and DVDs store data as pits on their surface that are read by a laser. A Blu-ray disc can hold over five times more data than a standard DVD because the pits are much smaller. Writing the data onto two layers

within the disc instantly doubles the volume of data that can be stored. But writing data to the whole thickness of the disc in the form of a hologram could dramatically increase storage capacity.

A pair of laser beams is used to write data into discs of light-sensitive plastic, with both aiming at the same spot. One beam shines continuously, while the other pulses on and off to encode patches that represent digital 0s and 1s.

At the points where the lasers meet, the intense light causes molecules in the disc's material to merge into chains, creating a physical pattern that locks the 0s and 1s into the disc. This pattern can be read back at a later date using another laser because the changed patches interact differently with light.

However, in the plastic normally used for holographic data storage, the structural changes caused by the laser also cause the material to shrink. Even though the volume change is tiny - around 0.23% - the distortion is enough to make reading the data from the disc tricky and means that the 1s and 0s can't be burned at the highest densities.



Two lasers are used to record data in the form of a 3D hologram

Denser data

Craig Hawker's team at the University of California in Santa Barbara has now solved that problem by replacing the polymer's small molecules with larger, branched ones. These need to make fewer bonds to create a patch of the alternate form of the material, cutting distortion to just 0.04%.

"For real-world applications, the shrinkage values should be below 0.1%," Hawker says. Pioneering companies developing holographic data-storage devices could benefit from the new technique by squeezing at least 1000 gigabytes of data onto a standard disc.

One such company is Colorado-based InPhase Technologies, that sells bespoke products to the 20 or so companies around the world that are developing holograph-based data drives.

The company's vice president of sales, Art Rancis, thinks Hawker's work is promising. "We look forward to future results as [Hawker's team] evaluates the performance of the material in an actual high-density digital recording system," he told New Scientist. *Journal reference: Chemical Communications (DOI: 10.1039/b816298k)*

WineCrisp -- new apple was more than 20 years in the making

A new, late-ripening apple named WineCrisp™ which carries the Vf gene for scab resistance was developed over the past 20 plus years through classical breeding techniques, not genetic engineering. License to propagate trees will be made available to nurseries through the University of Illinois.

Being resistant to apple scab is a big plus for growers, said University of Illinois plant geneticist Schuyler Korban, as it significantly reduces the number of chemical fungicide sprays. "Apple scab is the number one disease that growers have to spray for – 15 to 20 times per season – so not having to spray for apple scab lowers the cost for the grower and is better for the environment."

Why does it take over 20 years to make an apple? "It takes a long time to develop an apple because you want to test it in different locations, you want to observe it over a number of years, and it takes awhile for an apple to get noticed," said geneticist Schuyler Korban. "I liked it the first time I saw it and I liked the flavor. It has an excellent mix of sugar and acid and a very pleasant flavor, but I was hesitant because of the finish - it's not glossy."

Korban thought the finish might pose a problem because consumers are accustomed to seeing waxed fruit in stores and may not like the matte finish that Korban calls "scarfy" or dull. "Red Delicious is a very good looking apple, but has no flavor, very bland. It's still ranked as the number one apple in the industry; however, there are more new apple varieties available now."

After some time, Korban decided that the crispness and the flavor would be more important factors to consumers than the finish and continued to develop the new apple.

His research, in collaboration with breeders at Rutgers and Purdue Universities, will be published in a 2009 issue of the journal of HortScience, and a U.S. patent is currently pending. The apple is available now to nurseries who want to apply for a license to propagate trees and make them available to apple growers nationwide. "There is a nursery in the southeastern part of the United States that really liked the apple and feel that there is a market for it in the south so they're getting a license to grow it."

It also takes time for a new orchard or even for an existing orchard to plant new apple varieties. But when WineCrisp™ cuttings are grafted into a fast-growing root stock, Korban says there could be fruit on the tree in as little as three years.

Korban said that the tree is extremely productive and the fruit is firm, but it's not a bright red color. "It's more of a dark red and looks like a deep red wine so we wanted to include 'wine' in the name. It also resembles an older variety that consumers are familiar with called Winesap. "When you pick it up and squeeze it, it's very firm," he said. "We used to call it 'the Rock.' We wanted that characteristic to be in the name so we added 'crisp' and named it WineCrisp™.

"There's a market for apples with different flavors, different textures, different ripening and maturity dates – you don't know what the likes and dislikes of the consumer will be," said Korban. "Some of our recent releases are varieties that focus on late ripening which would prolong the apple-growing season and WineCrisp™ matures two weeks after Red Delicious. They can be harvested all the way through to the end of October. And in good cold storage, they'll keep for eight to nine months. That's another important trait of this variety – it keeps very well in cold storage."

The original cross in the breeding process was done at Rutgers in 1989. The seeds were grown into seedlings and inoculated with apple scab at Purdue. Those seedlings that demonstrated resistance to apple scab were split between the three universities as a part of the Purdue-Rutgers-Illinois (PRI) Cooperative Breeding Program, which has been very successful in naming and releasing over 25 disease-resistant apple varieties, some with other collaborating partners around the world. Because the University of Illinois made the selection, U of I will be the primary licensing institution. *Funding for the research was provided by the University of Illinois and PRI.*

New study provides further evidence that apple juice can delay onset of Alzheimer's disease

Amsterdam, The Netherlands – A growing body of evidence demonstrates that we can take steps to delay age-related cognitive decline, including in some cases that which accompanies Alzheimer's disease, according to a study published in the January 2009 issue of the Journal of Alzheimer's Disease.

Thomas B. Shea, PhD, of the Center for Cellular Neurobiology; Neurodegeneration Research University of Massachusetts, Lowell and his research team have carried out a number of laboratory studies demonstrating that drinking apple juice helped mice perform better than normal in maze trials, and prevented the decline in performance that was otherwise observed as these mice aged.

In the most recent study Shea and his team demonstrated that mice receiving the human equivalent of 2 glasses of apple juice per day for 1 month produced less of a small protein fragment, called "beta-amyloid" that is responsible for forming the "senile plaques" that are commonly found in brains of individuals suffering from Alzheimer's disease.

Dr. Shea commented that "These findings provide further evidence linking nutritional and genetic risk factors for age-related neurodegeneration and suggest that regular consumption of apple juice can not only help to keep one's mind functioning at its best, but may also be able to delay key aspects of Alzheimer's disease and augment therapeutic approaches."

The article is "Dietary Supplementation with Apple Juice Decreases Endogenous Amyloid-β Levels in Murine Brain" by Amy Chan and Thomas B. Shea. It is published in the Journal of Alzheimer's Disease 16:1 (January 2009).

The continents as a heat blanket

Drifting of the large tectonic plates and the superimposed continents is not only powered by the heat-driven convection processes in the Earth's mantle, but rather retroacts on this internal driving processes. In doing so, the continents function as a thermal blanket, which leads to an accumulation of heat underneath, and which in turn can cause the break-up of the super-continents. These results of numerical modelling have been published by scientists from the GFZ German Research Centre for Geosciences in the latest volume of the journal Physics Of The Earth And Planetary Interiors (Vol. 171, S. 313-322).

Alfred Wegener's theory of continental drift was turned up when the driving forces for continental drift were discovered during the 50s and 60s: The enormous heat in the Earth's core and Earth's mantle generates the flow of rocks within the Earth's mantle, a process similar to the movement of warm water in a cooking pot. This

heat-driven mass transport is called convection. On the Earth's surface, this process leads not only to plate movement but also to drifting of the continents floating on the plates.

To date however, there has been no realistic mathematical–physical theory describing the interaction between the convective movement in the Earths mantle and the continental drift. V. Trubitsin, M. Kaban und M. Rothacher from the GFZ have now developed a numerical model, based on the current position of the continents, the structures of the Earth's mantle obtained through geophysical measurements, and the current displacement rates on the surface. Hence they were able to calculate the future position of the continents in hundreds of millions of years.

It could be shown that the enormous heat in the Earth's interior does not generally lead to a chaotic mass transport within the Earth's mantle. On the contrary, the continents influence the heat distribution within the Earth's mantle and the associated convective mass flow. In other words the continents act as a thermal blanket causing heat to accumulate beneath. A self-regulating system develops, beginning and ending with a super-continent. This super-continent breaks apart due to heat accumulation which in turn leads to a reorganization of mantle convection with the pieces ultimately joining again to form a large super-continent.

V. Trubitsin, M. Kaban and M. Rothacher: "Mechanical and thermal effects of floating continents on the global mantle convection", Physics Of The Earth And Planetary Interiors (Vol. 171, S. 313-322).

New treatment reduces severity of asthma attacks in preschoolers

Study led by Sainte-Justine Hospital Research Center and University of Montreal published in New England Journal of Medicine

This release is available in French.

Montreal– The largest study of its kind on preschoolers has demonstrated that preventive treatment with high doses of inhaled corticosteroids is effective in reducing the severity and duration of asthma attacks triggered by colds. Dr. Francine Ducharme, assistant director of clinical research at the Sainte-Justine Hospital Research Center and a pediatrics professor at the Université de Montréal, led the study published in the New England Journal of Medicine.

The research team found that high doses of corticosteroids (fluticasone), when inhaled at the onset of a cold and taken for up to 10 days, reduces the number of moderate or severe asthma attacks that require emergency oral steroids. This is the first study whose findings clearly demonstrate the treatment's efficacy in young children requiring oral corticosteroids or hospital admission because of the severity of this type of asthma attack.

The breakthrough is all the more important, since this age group represents more than half (60 percent) of children that go to emergency departments or are admitted to hospital for asthma attacks. Although viral-induced asthma is frequent in preschool-aged children, optimal management of this disease remains elusive. That's why Dr. Ducharme has focused her research on improving treatment for asthmatic children, particularly those of preschool age.

The basic treatment for asthma, which consists of administering weak doses of inhaled steroids such as fluticasone on a daily basis, has not proven to be effective in children with viral-induced asthma. For the purposes of the study, 2243 children were screened. Some 17 percent met the criteria for having asthma that was triggered solely by colds, no signs of allergy and had not experienced moderate to severe asthma attacks or symptoms between colds.

The new therapeutic approach was tested in 129 children aged 12 months to six years. By increasing the usual pediatric dose six-fold over a maximum of 10 days and beginning administration as soon as colds started, the team noted a 50 percent decrease in asthma attacks that required oral steroids in children.

A 20 percent reduction in the duration of the illness was also noted. The research team also noted that children who had received fluticasone had milder symptoms of shorter duration compared with the placebo group, thereby reducing the impact of the disease on the parents' quality of life.

The scientists were interested in evaluating both the efficacy of the treatment and its side-effects. Over the 40-week monitoring period, Dr. Ducharme observed a slightly slower growth rate (4 percent) in this group of children than in the placebo group.

In fact, the findings indicate that the average growth rate of the untreated children was about 6.5 cm as opposed to 6.0 cm in the children treated with fluticasone. This corresponds to what is seen when patients take the usual daily dose of fluticasone over 12 months.

A slower average weight gain was also noted in the children taking the placebo (approximately 2 kg) than in the children treated with corticosteroids (1.5 kg). Since this type of asthma is temporary and usually disappears before the age of 6, the treatment probably has a transient effect on growth. For the research team, it remains to be confirmed whether the children will be able to make up for this slight growth retardation.

About the study:

This research, funded by GlaxoSmithKline, the Fonds de la Recherche en Santé du Québec and the Canadian Institutes of Health Research, was conducted at the Sainte-Justine Hospital Research Center, the McGill University Health Centre, the CHU Sherbrooke, Maisonneuve-Rosemont Hospital and La courte Échelle Pediatric Clinic.

Historic trial to treat spinal injury with stem cells

* 14:09 23 January 2009 **by Andy Coghlan**

Patients with spinal cord injuries will be first humans to receive repair cells derived from embryonic stem cells.

The first ever clinical trial using stem cells derived from embryonic stem cells (ESCs) received the go-ahead today from the US Food and Drug Administration.

Geron Corporation, a company based in Menlo Park, California, hopes to mend the spines of patients paralysed from the chest down by injecting injury sites with stem cells that restore connections and repair damage. "This marks the beginning of what is potentially a new chapter in medical therapeutics, one that reaches beyond pills to a new level of healing: the restoration of organ and tissue function achieved by the injection of healthy replacement cells," said the company's president, Tom Okarma.

"My hat is off to Geron – this is what we've all been waiting for," says Robert Lanza, chief scientist at Advanced Cell Technology, a stem cell company in Worcester, Massachusetts. "It's been over a decade since embryonic stem cells were discovered, and this sends a message that we're ready at last to start helping people."

The trial had been "on clinical hold" for years over concerns that the cells could form tumours, but the FDA is now satisfied that this risk is low enough to allow the trial to proceed.

New political climate

Ethical concerns have also dogged the trial, because obtaining the cell lines involved destruction of embryos. The previous US president, George Bush, had obstructed research using such cells for eight years to appease his conservative supporters. However, the new president, Barack Obama, promised in his inaugural address to "restore science to its rightful place", so approval of the trial could be an early sign that he will lift all the Bush restrictions on stem-cell research, first imposed in 2001.

Hundreds of trials are already under way around the world with stem cells derived from adult or fetal tissue, but these cells are limited in the types of tissue they can turn into and repair. The spine repair trial could open up a new era in medicine because embryonic stem cells are the only type that generate all 200 or so tissues of the body.

Revolutionary treatments

ESCs can't be used directly, because they can form cancers called teratomas. But they can be used in the lab to generate potentially inexhaustible supplies of all other types of cell that might be needed for repair.

The type to be used in the trial are neural stem cells called oligodendrocyte progenitor cells. These support other neurons in the brain and nerves by supplying growth factors and by producing the myelin sheaths that protect neurons from damage.

In previous research with these cells, Geron showed that they could improve the mobility of rats whose hind legs had been made immobile by spinal injuries. The treated rats could walk better and post-mortems showed that the injected cells had multiplied in the injury site and restored lost connections. The hope now is that the same will happen in people.

Geron says that the main objective is to prove the cells are safe, especially given the FDA's earlier misgivings over the cancer risk. But for one year after treatment, the company will also look closely for any recovery of function and movement in the lower body lost through the injury. In all, the patients will be monitored for 15 years. If the cells appear safe, it could open the floodgates for a host of other trials using cells originally derived from ESCs. Geron itself has developed such cells for treating heart attacks, diabetes, bone damage, arthritis, liver failure and cancer.

Obama influence?

The trial is the second revolutionary stem cell therapy to receive approval within a week. On Monday, a UK company, ReNeuron, received clearance to inject stem cells into the brain, with the aim of repairing tissue damaged by strokes.

But John Sinden, chief scientist at ReNeuron, doubts whether the UK approval spurred the FDA to approve the Geron trial. "It's great news all round," he says. "It's like London buses, with two arriving together."

Sinden doubts that Obama's arrival as president had any direct bearing on the outcome of the Geron trial, but it will undoubtedly have a benign influence on the FDA in the coming months. "You don't expect the FDA to move as quickly as that," said Sinden. "They probably had it in mind to approve the trial for a while."

As to pressure on the FDA behind the scenes from the new administration, he said he could only guess. "The FDA will change, and the new management will be very much aligned with Obama's views on stem cells," he said.

Sinden is now hopeful that the Geron approval could signal potential willingness by the FDA to approve ReNeuron's application to conduct a planned stroke trial in the US, which has been on hold for two years.

Likewise, Lanza's company hopes to apply to the FDA this summer to begin a trial using retinal stem cells derived from ESCs to prevent a form of blindness.

Implants mimic infection to rally immune system against tumors

Subcutaneous antigen-laden disks successfully marshal T cells against deadly melanoma

CAMBRIDGE, Mass Bioengineers at Harvard University have shown that small plastic disks impregnated with tumor-specific antigens and implanted under the skin can reprogram the mammalian immune system to attack tumors.

The research - which ridded 90 percent of mice of an aggressive form of melanoma that would usually kill the rodents within 25 days - represents the most effective demonstration to date of a cancer vaccine. Harvard's David J. Mooney and colleagues describe the research in the current issue of the journal Nature Materials.

"Our immune systems work by recognizing and attacking foreign invaders, allowing most cancer cells -which originate inside the body - to escape detection," says Mooney, Gordon McKay Professor of Bioengineering in Harvard's School of Engineering and Applied Sciences. "This technique, which redirects the immune system from inside the body, appears to be easier and more effective than other approaches to cancer vaccination."

Most previous work on cancer vaccines has focused on removing immune cells from the body and reprogramming them to attack malignant tissues. The altered cells are then reinjected back into the body. While Mooney says ample theoretical work suggests this approach should work, in experiments more than 90 percent of the reinjected cells have died before having any effect.

The implants developed by Mooney and colleagues are slender disks measuring 8.5 millimeters across. Made of an FDA-approved biodegradable polymer, they can be inserted subcutaneously, much like the implantable contraceptives that can be placed in a woman's arm.

The disks are 90 percent air, making them highly permeable to immune cells. They release cytokines, powerful attractants of immune-system messengers called dendritic cells.

These cells enter an implant's pores, where they are exposed to antigens specific to the type of tumor being targeted. The dendritic cells then report to nearby lymph nodes, where they activate the immune system's T cells to hunt down and kill tumor cells throughout the body.

"Much as an immune response to a bacterium or virus generates long-term resistance to that particular strain, we anticipate our materials will generate permanent and body-wide resistance against cancerous cells, providing durable protection against relapse," says Mooney, a core member of the recently established Wyss Institute for Biologically Inspired Engineering at Harvard.

The implants could also be loaded with bacterial or viral antigens to safeguard against an array of infectious diseases. They could even redirect the immune system to combat autoimmune diseases such as type 1 diabetes, which occurs when immune cells attack insulin-producing pancreatic cells.

"This study demonstrated a powerful new application for polymeric biomaterials that may potentially be used to treat a variety of diseases by programming or reprogramming host cells," Mooney and his co-authors write in Nature Materials. "The system may be applicable to other situations in which it is desirable to promote a destructive immune response (for example, eradicate infectious diseases) or to promote tolerance (for example, subvert autoimmune disease)."

Mooney's co-authors are Omar A. Ali, Nathaniel Huebsch, and Lan Cao of Harvard's School of Engineering and Applied Sciences and Glenn Dranoff of the Dana-Farber Cancer Institute, Brigham and Women's Hospital, and Harvard Medical School. The research was funded by the National Institutes of Health and Harvard University.

Eating less may not extend life

Caloric restriction only benefits obese mice: The Journal of Nutrition

If you are a mouse on the chubby side, then eating less may help you live longer.

For lean mice – and possibly for lean humans, the authors of a new study predict – the anti-aging strategy known as caloric restriction may be a pointless, frustrating and even dangerous exercise.

"Today there are a lot of very healthy people who look like skeletons because they bought into this," said Raj Sohal, professor at the University of Southern California's School of Pharmacy.

He and Michael Forster, of the University of North Texas Health Science Center, compared the life span and caloric intake of two genetically engineered strains of mice.

The "fat" strain, known as C57BL/6, roughly doubles in weight over its adult life. That strain benefited from caloric restriction, Sohal said. The "lean" strain, DBA/2, does not become obese. Caloric restriction did not extend the life of these mice, confirming previous work by Forster and Sohal.

The results appeared online Jan. 13 in advance of print publication in the Journal of Nutrition.

"Our study questions the paradigm that caloric restriction is universally beneficial," Sohal said. "Contrary to what is widely believed, caloric restriction does not extend (the) life span of all strains of mice."

By measuring the animals' metabolic rate, Sohal and his colleagues came to a deceptively simple conclusion: Caloric restriction is only useful when, as in the case of the obese mice, an animal eats more than it can burn off.

"Your energy expenditure and your energy intake should be in balance," Sohal said. "It's as simple as that. And how do you know that? By gain or loss of weight. "The whole thing is very commonsensical."

For humans of normal weight, Sohal strongly cautions against caloric restriction. In a 2003 study, he and Forster found that caloric restriction begun in older mice – both in DBA and leaner C57 individuals – actually shortened life span.

However, Sohal said that obese individuals are probably better off cutting calories than increasing their exercise to make up for overeating. Overly vigorous exercise can lead to injuries and long-term wear and tear. In other words, it is better to skip the double cheeseburger than to turn up the treadmill after binging at Carl's Jr. Sohal's study is not the first to question the allegedly universal benefits of caloric restriction. A study by Ross et al. published in Nature in 1976 ("Dietary practices and growth responses as predictors of longevity") found that caloric restriction works best in mice that gain weight rapidly in early adulthood, Sohal said. Studies of caloric restriction in wild types of mouse strains have shown minimal life span extension, he added. ext, the researchers want to understand why the obese mice have a lower metabolic rate that promotes weight gain.

The other members of the research team were Melissa Ferguson and Barbara Sohal of the USC School of Pharmacy.
Funding for the study came from the National Institute on Aging, part of the National Institutes of Health.
Read the study at http://jn.nutrition.org/cgi/content/abstract/jn.108.100313v1

Dramatic expansion of dead zones in the oceans

Unchecked global warming would leave ocean dwellers gasping for breath. Dead zones are low-oxygen areas in the ocean where higher life forms such as fish, crabs and clams are not able to live. In shallow coastal regions, these zones can be caused by runoff of excess fertilizers from farming. A team of Danish researchers have now shown that unchecked global warming would lead to a dramatic expansion of low-oxygen areas zones in the global ocean by a factor of 10 or more.

Whereas some coastal dead zones could be recovered by control of fertilizer usage, expanded low-oxygen areas caused by global warming will remain for thousands of years to come, adversely affecting fisheries and ocean ecosystems far into the future. The findings are reported in a paper 'Long-term ocean oxygen depletion in response to carbon dioxide emissions from fossil fuels' published on-line in the scientific journal Nature Geoscience.

Professor Gary Shaffer of the Niels Bohr Institute, University of Copenhagen, who is the leader of the research team at the Danish Center for Earth System Science (DCESS), explains that "such expansion would lead to increased frequency and severity of fish and shellfish mortality events, for example off the west coasts of the continents like off Oregon and Chile".

Large extinction events

Together with senior scientists Steffen Olsen oceanographer at Danish Meteorological Institute and Jens Olaf Pepke Pedersen, physicist at National Space Institute, Technical University of Denmark, Professor Shaffer has performed projections with the newly-developed DCESS Earth System Model, projections that extend 100,000 years into the future.

He adds that "if, as in many climate model simulations, the overturning circulation of the ocean would greatly weaken in response to global warming, these oxygen minimum zones would expand much more still and invade the deep ocean." Extreme events of ocean oxygen depletion leading to anoxia are thought to be prime candidates for explaining some of the large extinction events in Earth history including the largest such event at the end of the Permian 250 million years ago.

Series of changes

Furthermore, as suboxic zones expand, essential nutrients are stripped from the ocean by the process of denitrification. This in turn would shift biological production in the lighted surface layers of the ocean toward plankton species that are able to fix free dissolved nitrogen. This would then lead to large, unpredictable changes in ocean ecosystem structure and productivity, on top of other large unpredictable changes to be expected from ocean acidification, the other great oceanic consequence of high atmospheric carbon dioxide concentrations from fossil fuel burning.

Professor Shaffer warns that as a result, "the future of the ocean as a large food reserve would be more uncertain. Reduced fossil fuel emissions are needed over the next few generations to limit ongoing ocean oxygen depletion and acidification and their long-term adverse effects".

Nature Geoscience Advanced Online Publication: http://www.nature.com/ngeo/journal/vaop/ncurrent/index.html