http://www.bbc.co.uk/news/health-19561158

New blood 'booster' tested in UK-led clinical trials

A London hospital is leading a worldwide trial of a drug designed to aid the recovery of patients with heavy blood loss.

By Neil Bowdler Health reporter, BBC News

MP4OX is made from expired blood stocks and seeks to replicate the function of red blood cells in carrying oxygen around the body. It is being given to patients with heavy blood loss in 56 centres around the world.
The Royal London Hospital is leading the clinical trials.
MP4OX has been developed by US pharmaceutical company Sangart, which is funding the trial, and is a haemoglobin-based product processed from expired blood transfusion stocks.
Haemoglobin molecules are the proteins in red blood cells which carry oxygen to muscles and tissue around the body.
In trauma patients who have undergone heavy blood loss, these molecules are in short supply, and its makers claim MP4OX can deliver an oxygen boost to organs and tissue in the body, reducing the risk of organ failure.
They say it carries no infection risk and can be given safely to all patients.
Prof Karim Brohi, of the Barts and The Royal London Hospital, is leading the trials.
"We're giving it to people who been severely injured in car crashes, have fallen out of a window, been stabbed etc," he told BBC News. "Basically it's a drug which takes up oxygen and delivers it to cells which are starved of oxygen because there's not enough blood going around the body."
The drug has already been tested in a pilot trial of 50 patients, which appeared to show the drug was safe.
That pilot has now been extended to a worldwide trial encompassing some 360 patients, to further test its safety and efficacy. That trial is now approaching completion although the researchers have yet to process any of the results.
"In the initial trial, it seemed to show that people got out of hospital much quicker than patients who hadn't had the drug," he said.
"It was a small trial with lots of room for error, but there was a pretty strong signal that there were a lot more patients who were alive and out of hospital at 28 days compared to the ones who hadn't had the drug."
However, he stressed that it was only after results from the extended "Phase 2b" trial were in, that they would know how much promise the drug showed.
The trial is what is know as "randomised", with patients randomly prescribed the drug or a placebo according to instructions enclosed in a sealed paper envelope. The drug is also wrapped up in a black bag in the lab prior to delivery to the ward or theatre, so neither clinicians nor patient know what they are being given.
These measures are designed to improve the accuracy and impartiality of results.
The trial is one of many projects around the world in which researchers are trying to replicate some of the functions of blood.
A recent BBC Radio 4 documentary looked at some of the attempts, past and present, to create artificial blood products, including efforts to develop haemoglobin treatments from E.coli bacteria and from stem cells.
But Prof Brohi says MP4OX should not be regarded as "artificial blood".
"This isn't a substitute for blood because we give less than a Coke can's worth to each patient - while these patients may have lost up to five litres of blood - so in no way is it a substitute for giving red blood cells to patients," he said. "What it's doing is augmenting the ability of those red blood cells to do their job."

http://www.eurekalert.org/pub_releases/2012-10/acos-pnb092812.php

Preoperative needle breast biopsies can lead to improved treatment outcomes

Journal of American College of Surgeons study reports needle biopsy is a more efficient, less invasive way to get the same diagnosis as traditional open biopsy

Chicago: Women suspected of having breast cancer now have more reasons to be diagnosed with a needle biopsy instead of a traditional open surgical biopsy. Besides avoiding the risks and discomfort of an open surgical procedure, needle biopsies can also lead to improved treatment outcomes according to findings from a new study published in the October issue of the Journal of the American College of Surgeons.
Breast cancer is the number one form of cancer diagnosed in women in the United States, according to the U.S. Centers for Disease Control and Prevention. [1] In 2012, more than 226,000 women will be diagnosed, according to estimates from the National Cancer Institute. [2] Findings from an open biopsy or needle biopsy can confirm whether a suspicious breast lesion is actually malignant. During an open biopsy, an operation is performed to remove the concerning breast tissue and then it is examined in the laboratory to determine the

presence of any malignant cells. This open procedure typically involves a trip to the operating room, a full surgical incision, and some form of anesthesia. However, a percutaneous needle biopsy procedure, allows physicians to locate the breast lesion without actually opening the breast. Instead, they use imaging techniques and extract a sample of the concerning tissue through a needle. This minimally invasive approach can be performed using a topical anesthetic and takes place in the office setting or radiology suite. There is less discomfort and quicker recovery time compared with open surgical biopsies.

Despite the less invasive nature of needle biopsy, "some physicians are still doing open biopsy, perhaps because of limited resources or lack of awareness. Needle biopsies require special instruments, techniques, and skills that may not be available at all treatment sites," explained Ted A. James, MD, FACS, associate professor of surgery at the University of Vermont College of Medicine and lead author of the study. The advantage of the needle biopsy approach is that women may avoid an operation if the results are benign, and can get the benefit of appropriate preoperative planning if cancer is detected. "There are certainly some legitimate reasons to do an open biopsy, such as when the lesion is in a difficult position for the needle to reach. But the open approach should only be used for about 10 percent of cases, Dr. James estimates. "A needle biopsy is a more efficient, less invasive way to get the same diagnosis," he said.

Dr. James and colleagues investigated whether better patient outcomes could be added to the list of needle biopsy advantages. They analyzed data on 1,135 patients who had been diagnosed with breast cancer and treated at hospitals in Vermont between 1998 and 2006. Patient data came from the Vermont Breast Cancer Surveillance System (VBCSS), the Vermont Cancer Registry (VCR), and the Centers for Medicare and Medicaid Services (CMS) enrollment and claims data.

None of the patients had a previous history of breast cancer, and 62.8 percent were diagnosed after needle biopsies. Patient data included the tumor's size, stage, and estrogen receptor status. The surgeons also looked at education level and whether the patients were rural or urban residents, just in case there were correlations between socioeconomic status and biopsy procedure.

Data analysis revealed that needle biopsy became more common over time. Between 1998 and 2000 about 48.7 percent of patients underwent needle biopsies. That figure jumped to 73.6 percent between 2004 and 2006. Results showed that patients who had an open biopsy were more likely to have positive margins than those who had a needle biopsy. This finding indicates that after surgeons removed the breast lesion, cancerous cells were still present along the edges of the specimen—in 37.4 percent of open surgical patients—requiring another operation. This scenario was only true for 20.1 percent of patients diagnosed with needle biopsy.

Because the primary goal of open biopsy is to diagnose breast cancer rather than treat it, patients with open biopsy were less likely to have adequate amounts of the tumor excised. They were also less likely to have their lymph nodes assessed. Therefore, the open biopsy approach also led to more re-excisions—additional operations to remove more malignant tissue, as well as additional operations to assess lymph nodes when indicated. A single operation was needed 76.4 percent of the time for needle biopsy patients, but only 44 percent of the time for open biopsy patients.

Age and education status had no bearing on which type of biopsy was performed, but the researchers did discover residential differences. Urban patients were more likely to have a needle biopsy than rural patients—70.6 percent compared with 57.5 percent, respect-tively. "Again that finding could have a lot to do with resources at some smaller hospitals," Dr. James said. His team noticed that this gap was actually much narrower at the end of the study period. "That's a very encouraging sign that things are moving in the right direction; however, there is still much room for improvement."

Dr. James said the findings have implications for national health care policy, which has shifted toward declining reimbursement if patients are readmitted 30-days later for the same condition: "It's really about quality, and trying to find ways to deliver better outcomes to our patients. It's also only a matter of time before Medicare and Medicaid start looking at why patients at hospital A are going back for more reexcisions than patients at hospital B."

The study is also a call to action for women to be more proactive in weighing their health care options. "Patients have to be active partners in their care," he added. "I would recommend a woman with a suspicious breast lesions—who was told she needed to have an open biopsy—to ask, 'why not a needle biopsy?' If a needle biopsy is appropriate but just not available, it could simply mean being referred to a neighboring hospital or a colleague. But it starts with knowing there's a better option," he concluded.

[1] *http://apps.nccd.cdc.gov/uscs/toptencancers.aspx*

[2] *http//www.cancer.gov/cancertopics/types/breast*

http://www.eurekalert.org/pub_releases/2012-10/mu-nts100112.php

Nothing to sneeze at: Scientists find cheating ragweed behaves better with its kin

Cheating. Conflict. Competition. It may sound like a soap opera but this is the complex life of the despised ragweed plant.

And in the highly competitive fight for nutrients, researchers have found ragweed will behave altruistically with its siblings, investing precious resources for the benefit of the group.

A growing body of work suggests plants recognize and respond to the presence and identity of their neighbours and the findings, published online in the journal PLOS ONE, provide further evidence of the importance of family in preserving cooperation within and between species. Specifically, researchers examined the mutually beneficial relationship between common ragweed, or Ambrosia artemisiifolia L., and mycorrhizal fungi.

In this relationship, the plant provides carbohydrates to the fungi which allow it to grow and colonize the soil. In return, the plant receives water, much-needed nutrients and protection from dangerous pathogens.

"The stability of this relationship can be compromised by cheaters," says Amanda File, a graduate student in the Department of Biology at McMaster University and lead author of the study.

"That happens because a single fungal network may interact with many plants, which creates opportunities for individuals to reap the rewards and the nutrients, without actually donating carbohydrates," she says.

In this study, researchers conducted two separate experiments to determine how social environment affects the plants' investment in the network. That is, whether the presence of family or strangers affects their behaviour. When the ragweed was planted with its kin, the fungal network was larger—implying greater costs to the plants—but also creating greater benefits for them. Moreover, increased fungal colonization of the roots was associated with a reduced number of root lesions caused by pathogens.

"If plant kin recognition is a real thing, we predict that social environment will affect many kinds of plant interactions," says Susan Dudley, an associate professor in the Department of Biology. "We have seen kin recognition for traits involved in plant competition and here we see that cooperation between species is certainly enhanced by altruism towards relatives." The findings could have future implications for farming, she adds. "Mycorrhizal fungi are now available commercially as soil additives for garden plants. And while conventional agricultural practices generally disrupt mycorrhizal fungi, there is potential for it to play an important role in sustainable farming by promoting growth naturally."

A copy of the study can be found at: http://dx.plos.org/10.1371/journal. pone.0045648.

http://www.eurekalert.org/pub_releases/2012-10/uom-pam100112.php

Popular antidepressant might prevent heart failure

A medication usually used to help treat depression and anxiety disorders has the potential to help prevent heart failure, according to researchers at the University of Michigan.

ANN ARBOR—John Tesmer, research professor at the U-M Life Sciences Institute and professor in the Department of Pharmacology at the U-M Medical School, and his research team at the Tesmer lab found that paroxetine, a selective serotonin reuptake inhibitor (SSRI) sold under the name Paxil, inhibits G protein-coupled receptor kinase 2 (GRK2), a protein kinase that becomes over-expressed when people have heart failure. Although so-called "off target" effects are known for many commonly used drugs, this is the first report that identifies a direct link between a specific SSRI and a protein target in the signal system they study, said Kristoff Homan, a postdoctoral fellow in Tesmer's lab.

The paper, "Paroxetine is a Direct Inhibitor of G Protein-Coupled Receptor Kinase 2 and Increases Myocardial Contractility," was published electronically ahead of print on Aug. 21 in ACS Chemical Biology.

The discovery almost did not happen. "It was completely serendipitous," Homan said.

Before beginning a larger search for compounds that would inhibit GRK2, the researchers screened a small library of approximately 2,000 compounds that contains many FDA-approved drugs as a test of their screening procedure—and found that paroxetine binds to and inhibits the activity of GRK2.

GRK2 becomes increasingly expressed as the system that regulates normal heartbeat and the strength of the heart's contractions weakens. Paroxetine, the team found, improved the strength of the heart's contractions in an animal model without interfering with the heart rate.

Paroxetine is FDA-approved and has been clinically used as an SSRI for nearly 30 years, but at prescribed doses the compound probably does not inhibit GRK2 enough to be used for heart failure.

But if the researchers can identify modifications to the chemical structure of paroxetine that improve potency while decreasing SSRI activity, which Homan thinks they can do, the team hopes to start the process of optimization and to develop these compounds into therapeutic leads within the next several years, he said.

Study: http://pubs.acs.org/doi/abs/10.1021/cb3003013.

http://www.eurekalert.org/pub_releases/2012-10/esfm-sab092812.php

Should aspirin be used to prevent cancer?

Debate at ESMO 2012 Congress focuses on whether there is enough evidence to start using aspirin to reduce the risk of colorectal cancer

VIENNA, Austria - Aspirin, the everyday drug taken by countless people around the world to ward off pain and reduce their risk of developing heart disease, may have a new trick up its sleeve –-preventing cancer.

A growing body of evidence suggests that taking aspirin may reduce an individual's chances of developing colorectal cancer and perhaps other malignancies, but whether that evidence is strong enough to outweigh the risks of prescribing it to millions of healthy people is the subject of debate.

At the ESMO 2012 Congress in Vienna, both sides of that debate are being aired in front of an audience of experts in one of the meeting's popular Controversy sessions.

Arguing in favor of the question – "Is aspirin (NSAID) ready for chemoprevention of colorectal adenoma/cancer?" – is Prof Robert Benamouzig from the Department of Gastroenterology, Avicenne Hospital, Bobigny, France. "The efficacy of aspirin in preventing colorectal cancer has been made obvious by more than twenty years of research," said Prof Benamouzig.

"In 2010, researchers published the 20-year follow-up of five pooled randomized trials that assessed the effect of aspirin on colorectal cancer incidence and mortality. The study of more than 14,000 patients found that daily aspirin at any dose reduced risk of colorectal cancer by 24% and associated deaths by 35% after a delay of about 8 to 10 years." "In these trials, the reduction of colorectal cancer rates was in essence a side-effect of treatment. None of them had such a reduction as their primary outcome. Nevertheless, the evidence that aspirin is effective for preventing these colorectal cancers is very strong," Prof Benamouzig said.

Arguing that the answer to the question should be "No" is Prof Nadir Arber, Director of the Integrated Cancer Prevention at the Tel Aviv Sourasky Medical Center in Israel. "NSAIDs and in particular aspirin are very promising in secondary prevention of colorectal neoplasia, however their role in primary prevention is still not proven," Prof Arber said. "This means that the majority of the population does not need, and is not going to benefit from aspirin use. Having said that, specific high-risk populations definitely can benefit from aspirin intake, including people with hereditary non-polyposis colorectal cancer, familial adenomatous polyposis, existing colorectal cancer or adenoma. In the future based on genomic profile, we would be able to identify people who are at high risk of developing colorectal cancers and who might benefit from aspirin therapy."

During the discussion, Prof Arber will present preliminary data showing how the efficacy and toxicity of aspirin in preventing cancer can be predicted based on some single nucleotide polymorphisms.

Before aspirin can be used for preventing these cancers, we need to develop means of identifying people who are going to benefit from the drug without developing side-effects, Prof Arber said. Risks of taking aspirin include gastrointestinal bleeding and intracranial hemorrhage. "We need a study that will measure overall morbidity and mortality and not efficacy and toxicity in a single organ or disease such as cardio-vascular disease," he said.

The debate on aspirin is just one of 6 popular controversy sessions that will take place at the ESMO 2012 Congress on Monday, 1 October:

How soon will colorectal patient management be driven by molecular factors?
Deep DNA sequencing of tumor: ready for prime-time or not?
Are EGFR inhibitors the best choice for the first line treatment of EGFR mutated lung adenocarcinoma patients?
Can neo-adjuvant breast cancer data be used to accelerate drug approval?
Is thromboprophylaxis mandatory in the management of patients with advanced cancer?

http://www.eurekalert.org/pub_releases/2012-10/acos-afo092712.php

A form of small pox virus shows potential for treating triple-negative breast cancer

Combined oncolytic and antiangiogenic activity of new vacinnia virus kills TNBC tumors in mice

CHICAGO—Researchers from Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City have shown that a new vaccinia virus, acting as both an oncolytic and anti-angiogenic agent, can enter and kill triple-negative breast cancer (TNBC) cells. Study findings presented today at the 2012 Annual Clinical Congress of the American College of Surgeons could lead to a more targeted therapy against this deadly form of breast cancer.

According to the medical literature, TNBC is a form of breast cancer that is responsible for 10 to 20 percent of all breast cancer cases.* TNBC is most likely to occur in younger women (<35 years old), especially if they are African American or Hispanic. It is difficult to treat because women with TNBC lack three types of receptors - estrogen, progesterone, and HER2 - that would allow them to benefit from existing hormonal and immune

therapies. Although women diagnosed with TNBC, especially in later stages, do initially respond to chemotherapy, these tumors tend to be more aggressive and more likely to recur.
"We still don't have an understanding as to why this cancer is so aggressive and tends to recur after treatment," said Sepideh Gholami, MD, lead study author and surgical resident at Stanford University Medical Center, Palo Alto, CA. "One of the reasons I wanted to focus on TNBC is that there aren't many long-term treatment options for these patients." But oncolytic viruses, which can exploit the unique vulnerabilities of these specific cancer cells, are being intensely studied by the Yuman Fong, MD, research laboratory at MSKCC, and have shown promising results.
"The reason we used the vaccinia virus is that it is a member of the small pox family, and, as we know, small pox vaccine has been given to millions of people to eradicate small pox. So we thought it would be safer and more promising in terms of a clinical trial and actual application," Dr. Gholami said. "Our research is an extension of previous work performed in Dr. Fong's research lab, but it looks at a new oncolytic virus that targets TNBC with a dual effect," she added. The Clinical Congress is the first time research findings using this particular approach have been publicly presented, she said.
In this study, Dr. Gholami and her colleagues at MSKCC wanted to determine whether a new vaccinia virus, called GLV-1h164, carrying a protein that targets vascular endothelial growth factor (VEGF), could destroy TNBC tumors in a mouse animal model. TNBC has higher levels of VEGF, which can promote angiogenesis, the process by which tumors recruit blood vessels to support their growth.
First, researchers infected TNBC cells with the virus and achieved a more than 90 per-cent cell kill in the TNBC cells within four days of treatment with the virus. Next, researchers generated TNBC tumors in a mouse model. After treating the tumors with the virus, and measuring the change in tumor size over three weeks, they found extensive tumor destruction.
"Based upon pathology, we could see that at least 60 percent of the tumors were completely regressed and the other 40 percent had very little areas of tumor cells present with a lot of necrosis, which is a sign that the tumor was responding to therapy," Dr. Gholami said. This specific virus not only infects and breaks down cancer cells but also inhibits tumor blood vessel growth. "We performed ultrasound imaging of the tumors and we saw a significant reduction in blood flow supplied to treated tumors with our new virus. More specifically, when we looked at the stained vasculature of the tumors, the treated tumors showed at least one half of what control mice did," Dr. Gholami reported. These findings will allow the researchers to take the next step toward designing a clinical trial and evaluating the safety of this new virus in patients with TNBC, she concluded.
Other researchers involved in this study include Andrew A. Marano, BA; Nanhai G. Chen, PhD; Alexa Frentzen, PhD; Chun-Hao Chen, MD; Clarisse Eveno, MD; Emil Lou, MD, PhD; Laurence Belin, MD, MPH; Aladar A. Szalay, PhD; and Yuman Fong, MD, FACS.
This study was funded by Mr. William H. and Mrs. Alice Goodwin and the Commonwealth Foundation for Cancer Research and The Experimental Therapeutics Center of Memorial Sloan-Kettering Cancer Center.
** Source: Lehmann BD, Bauer JA, Chen X, et al. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest. 2011; 121(7):2750-2767.*

http://www.eurekalert.org/pub_releases/2012-10/uoih-pnc092812.php

Potential new class of drugs blocks nerve cell death

Potential new class of drugs protects nerve cells in models of Parkinson's disease and amyotrophic lateral sclerosis

Diseases that progressively destroy nerve cells in the brain or spinal cord, such as Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS), are devastating conditions with no cures.
Now, a team that includes a University of Iowa researcher has identified a new class of small molecules, called the P7C3 series, which block cell death in animal models of these forms of neurodegenerative disease. The P7C3 series could be a starting point for developing drugs that might help treat patients with these diseases. These findings are reported in two new studies published the week of Oct. 1 in PNAS Early Edition.
"We believe that our strategy for identifying and testing these molecules in animal models of disease gives us a rational way to develop a new class of neuroprotective drugs, for which there is a great, unmet need," says Andrew Pieper, M.D., Ph.D., associate professor of psychiatry at the UI Carver College of Medicine, and senior author of the two studies.
About six years ago, Pieper, then at the University of Texas Southwestern Medical Center, and his colleagues screened thousands of compounds in living mice in search of small, drug-like molecules that could boost production of neurons in a region of the brain called the hippocampus. They found one compound that appeared to be particularly successful and called it P7C3.

"We were interested in the hippocampus because new neurons are born there every day. But, this neurogenesis is dampened by certain diseases and also by normal aging," Pieper explains. "We were looking for small drug-like molecules that might enhance production of new neurons and help maintain proper functioning in the hippocampus."
However, when the researchers looked more closely at P7C3, they found that it worked by protecting the newborn neurons from cell death. That finding prompted them to ask whether P7C3 might also protect existing, mature neurons in other regions of the nervous system from dying as well, as occurs in neurodegenerative disease.
Using mouse and worm models of PD and a mouse model of ALS, the research team has now shown that P7C3 and a related, more active compound, P7C3A20, do in fact potently protect the neurons that normally are destroyed by these diseases. Their studies also showed that protection of the neurons correlates with improvement of some disease symptoms, including maintaining normal movement in PD worms, and coordination and strength in ALS mice.

Of mice and worms

In the ALS mouse model, a highly active variant of the original P7C3 molecule, known as P7C3A20, which the investigators synthesized, largely prevented death of the nerve cells within the spinal cord that are normally destroyed by this disease. The P7C3 molecule also worked, but was not as effective at protecting neurons in this model.
As cell survival increased in the ALS model, coordination and strength of the mice improved as well. Mice that were given P7C3A20 were able to stay on a rotating rod much longer than untreated animals or animals that received the less active compounds. Animals receiving P7C3A20 also performed better in analysis of their walking gait, which typically worsens in these animals as the disease progresses.
In PD, dopamine-producing neurons necessary for normal movement are gradually destroyed. In patients, loss of these brain cells leads to tremors, stiffness, and difficulty walking. The study again showed that P7C3 protects these neurons from cell death and the more active analogue, P7C3A20, provided even greater protection.
The two compounds also potently blocked cell death of dopaminergic neurons in a C. elegans worm model of PD. Moreover, reduced cell death in this model was associated with improved movement in the worms. Healthy C. elegans worms have a very characteristic swimming motion. This movement is disrupted in the PD worm. Hector De Jesus-Cortes, a graduate student of neuroscience at UT Southwestern Medical Center and lead author of the Parkinson's study, videotaped and analyzed the PD worms' mobility with and without treatment. Normal swimming was almost completely preserved with P7C3A20, and was also fairly well preserved with P7C3.

Tweaking the molecule

The research team compared the activity of several new P7C3-related compounds that they synthesized, in both the hippocampal neurogenesis screen and the mouse model of PD. "Every variation of our P7C3 molecule that works in the neurogenesis assay also works in the PD model," Pieper says. "As we continue to refine the molecule, our hope is that the results from the neurogenesis assay will accurately predict the neuroprotective potency of the compound, and thus aid in more rapidly optimizing a new neuroprotective agent."
The team plans to continue tweaking the structure of the P7C3 molecule to improve its neuroprotective ability while eliminating potential side effects. "Our hope is that this work will form the basis for designing a neuroprotective drug that could eventually help patients," Pieper says.
Pieper and De Jesus-Cortes conducted the study with colleagues at UT Southwestern Medical Center, including Steven McKnight, Ph.D., chairman of biochemistry, and Joseph Ready, Ph.D., professor of biochemistry. The work was funded in part by grants from the National Institute for Mental Health.

http://www.sciencedaily.com/releases/2012/10/121001083332.htm

Evidence-Based Guidelines to Help Physicians Manage Patients With Acute Low Back Pain

Radiologists have developed evidence-based guidelines to assist physicians with the process of managing patients with acute low back pain

ScienceDaily - According to an article in the October issue of the Journal of the American College of Radiology, radiologists at Emory University Hospital, in Atlanta, and Georgia Health Sciences University, in Augusta, Ga., have developed evidence-based guidelines to assist physicians with the process of managing patients with acute low back pain. Low back pain is one of the most common reasons for visits to physicians in the outpatient setting.

"The approach to the workup and management of low back pain by physicians and other practitioners is inconstant. In fact, there is significant variability in the diagnostic workup of back pain among physicians within and between specialties," said Scott E. Forseen, MD, co-author of the article.
The following process was developed to assist practitioners with the management of patients with low back pain:
At the initial visit, patients are categorized into 1 of 3 groups after a thorough history and physical examination: non-specific low back pain, low back pain potentially associated with radiculopathy or spinal stenosis, or low back pain potentially associated with a specific cause. Evidence-based order sets are provided for each category that are intended to guide practitioners through the process of evaluation, management and follow-up of patients.
Order set templates for use at the initial follow-up visit (4 weeks) provide evidence-based recommendations for appropriate imaging, laboratory workup, referral for invasive procedures or surgical consultation.
"We have presented a logical method of choosing, developing and implementing clinical decision support interventions that is based on the best available evidence. These templates may be reasonably expected to improve patient care, decrease inappropriate imaging utilization, reduce the inappropriate use of steroids and narcotics, and potentially decrease the number of inappropriate invasive procedures," said Forseen.
Scott E. Forseen, Amanda S. Corey. Clinical Decision Support and Acute Low Back Pain: Evidence-Based Order Sets. Journal of the American College of Radiology, 2012; 9 (10): 704 DOI: 10.1016/j.jacr.2012.02.014

http://phys.org/news/2012-10-solar-cells-black-silicon.html

Solar cells made from black silicon

Black silicon solar cells are specifically designed to absorb this part of the Sun's spectrum

Solar cells convert three-quarters of the energy contained in the Sun's spectrum into electricity – yet the infrared spectrum is entirely lost in standard solar cells. In contrast, black silicon solar cells are specifically designed to absorb this part of the Sun's spectrum – and researchers have recently succeeded in doubling their overall efficiency.
The Sun blazes down from a deep blue sky – and rooftop solar cells convert this solar energy into electricity. Not all of it, however: Around a quarter of the Sun's spectrum is made up of infrared radiation which cannot be converted by standard solar cells – so this heat radiation is lost.
One way to overcome this is to use black silicon, a material that absorbs nearly all of the sunlight that hits it, including infrared radiation, and converts it into electricity. But how is this material produced? "Black silicon is produced by irradiating standard silicon with femtosecond laser pulses under a sulfur containing atmosphere," explains Dr. Stefan Kontermann, who heads the Research group "Nanomaterials for Energy Conversion" within the Fraunhofer Project Group for Fiber Optical Sensor Systems at the Fraunhofer Institute for Telecommunications, Heinrich-Hertz-Institut, HHI. "This structures the surface and integrates sulfur atoms into the silicon lattice, making the treated material appear black." If manufacturers were to equip their solar cells with this black silicon, it would significantly boost the cells' efficiency by enabling them to utilize the full Sun spectrum.
Researchers at HHI have now managed to double the efficiency of black silicon solar cells – in other words, they have created cells that can produce more electricity from the infrared spectrum. "We achieved that by modifying the shape of the laser pulse we use to irradiate the silicon," says Kontermann.
This enabled the scientists to solve a key problem of black silicon: In normal silicon, infrared light does not have enough energy to excite the electrons into the conduction band and convert them into electricity, but the sulfur incorporated in black silicon forms a kind of intermediate level. You can compare this to climbing a wall: The first time you fail because the wall is too high, but the second time you succeed in two steps by using an intermediate level. However, in sulfur this intermediate level not only enables electrons to climb the 'wall', it also works in reverse, enabling electrons from the conduction band to jump back via this intermediate level, which causes electricity to be lost once again.
By modifying the laser pulse that drives the sulfur atoms into the atomic lattice, researchers can change the positions that these atoms adopt in the lattice and change the height of their 'levels', in other words their energy level. "We used the laser pulses to alter the embedded sulfur in order to maximize the number of electrons that can climb up while minimizing the number that can go back down," Kontermann sums up.
In the first stage of the project, the scientists modified the laser pulses and investigated how this changed the properties of black silicon and the efficiency of solar cells made from this material. Now they are working on using different shapes of laser pulses and analyzing how this changes the energy level of the sulfur. In the future, they hope that a system of algorithms will automatically identify how the laser pulse should be modified

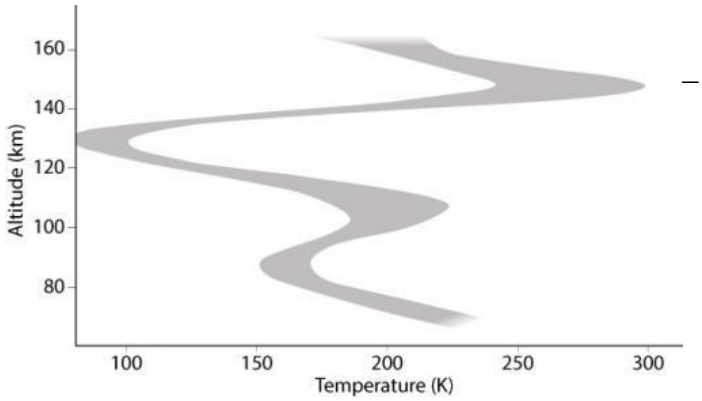
in order to achieve optimum efficiency. The 'Customized light pulses' project was one of this year's winners in the '365 Places in the Land of Ideas' competition; the awards ceremony is due to be held in Goslar on October 11, 2012.
The researchers have already successfully built prototypes of black silicon solar cells and their next step will be to try and merge these cells with commercial technology. "We hope to be able to increase the efficiency of commercial solar cells – which currently stands at approximately 17 percent – by one percent by combining them with black silicon," Kontermann says. Their starting point is a standard commercial solar cell: The experts simply remove the back cover and incorporate black silicon in part of the cell, thereby creating a tandem solar cell that contains both normal and black silicon. The researchers are also planning a spin-off: This will be used to market the laser system that manufacturers will be able to acquire to expand their existing solar cell production lines. Manufacturers would then be able to produce the black silicon.

http://phys.org/news/2012-10-curious-cold-layer-atmosphere-venus.html

A curious cold layer in the atmosphere of Venus

Venus Express has spied a surprisingly cold region high in the planet's atmosphere that may be frigid enough for carbon dioxide to freeze out as ice or snow.

Phys.org - The planet Venus is well known for its thick, carbon dioxide atmosphere and oven-hot surface, and as a result is often portrayed as Earth's inhospitable evil twin.
But in a new analysis based on five years of observations using ESA's Venus Express, scientists have uncovered a very chilly layer at temperatures of around 175ºC in the atmosphere 125 km above the planet's surface. The curious cold layer is far frostier than any part of Earth's atmosphere, for example, despite Venus being much closer to the Sun.
The discovery was made by watching as light from the Sun filtered through the atmosphere to reveal the concentration of carbon dioxide gas molecules at various altitudes along the terminator – the dividing line between the day and night sides of the planet.



The temperature profile along the terminator for altitudes of 70–160 km above the surface of Venus. The values were derived from the volume density of carbon dioxide molecules measured during solar occultation experiments by Venus Express' SOIR instrument. The graphic provides the average range of values calculated from 59 measurements taken along the terminator from 88ºN to 77ºS, during different orbits between 2006 and 2011. The new report finds a prominent cold layer at 125 km sandwiched between two comparatively warmer layers at around 100 km and 140 km. At some locations, the temperatures occasionally dip below the freezing temperature of carbon dioxide, which suggests that carbon dioxide ice or snow could exist at these altitudes. **ESA/AOES–A.V. Bernus**

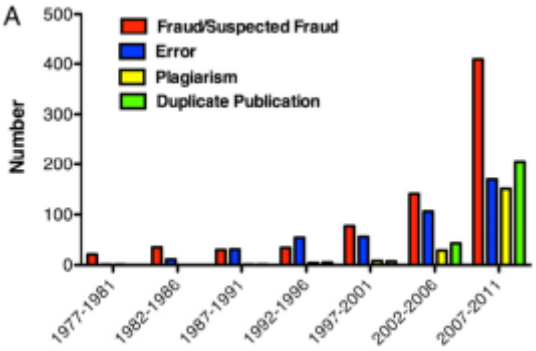
Armed with information about the concentration of carbon dioxide and combined with data on atmospheric pressure at each height, scientists could then calculate the corresponding temperatures.
"Since the temperature at some heights dips below the freezing temperature of carbon dioxide, we suspect that carbon dioxide ice might form there," says Arnaud Mahieux of the Belgian Institute for Space Aeronomy and lead author of the paper reporting the results in the Journal of Geophysical Research.
Clouds of small carbon dioxide ice or snow particles should be very reflective, perhaps leading to brighter than normal sunlight layers in the atmosphere. "However, although Venus Express indeed occasionally observes very bright regions in the Venusian atmosphere that could be explained by ice, they could also be caused by other atmospheric disturbances, so we need to be cautious," says Dr Mahieux.
The study also found that the cold layer at the terminator is sandwiched between two comparatively warmer layers. "The temperature profiles on the hot dayside and cool night side at altitudes above 120 km are extremely different, so at the terminator we are in a regime of transition with effects coming from both sides. "The night side may be playing a greater role at one given altitude and the dayside might be playing a larger role at other altitudes." Similar temperature profiles along the terminator have been derived from other Venus Express datasets, including measurements taken during the transit of Venus earlier this year.
Models are able to predict the observed profiles, but further confirmation will be provided by examining the role played by other atmospheric species, such as carbon monoxide, nitrogen and oxygen, which are more dominant than carbon dioxide at high altitudes. "The finding is very new and we still need to think about and understand what the implications will be," says Håkan Svedhem, ESA's Venus Express project scientist.

"But it is special, as we do not see a similar temperature profile along the terminator in the atmospheres of Earth or Mars, which have different chemical compositions and temperature conditions."

http://phys.org/news/2012-10-misconduct-error-accounts-scientific-paper.html

Misconduct, not error, accounts for most scientific paper retractions, new study finds

Misconduct is a major factor in retracted research



In sharp contrast to previous studies suggesting that errors account for the majority of retracted scientific papers, a new analysis—the most comprehensive of its kind—has found that misconduct is responsible for two-thirds of all retractions. In the paper, misconduct included fraud or suspected fraud, duplicate publication and plagiarism. The paper's findings show as a percentage of all scientific articles published, retractions for fraud or suspected fraud have increased 10-fold since 1975. The study, from a collaboration between three scientists including one at Albert Einstein College of Medicine of Yeshiva University, published online today in the Proceedings of the National Academy of Sciences (PNAS).

"Biomedical research has become a winner-take-all game—one with perverse incentives that entice scientists to cut corners and, in some instances, falsify data or commit other acts of misconduct," said senior author Arturo Casadevall, M.D., Ph.D. , the Leo and Julia Forchheimer Chair and professor of microbiology & immunology and professor of medicine at Einstein. Dr. Casadevall is also editor-in-chief of the journal mBio.

The study reviewed 2,047 papers retracted from the biomedical literature through May 2012. To determine the reasons for the retractions, the researchers consulted several secondary sources, such as the National Institutes of Health (NIH) Office of Research Integrity and Retractionwatch.com, which investigate scientific misconduct. The researchers found that about 21 percent of the retractions were attributable to error, while 67 percent were due to misconduct, including fraud or suspected fraud (43 percent), duplicate publication (14 percent), and plagiarism (10 percent). Miscellaneous or unknown reasons accounted for the remaining 12 percent.

"What's troubling is that the more skillful the fraud, the less likely that it will be discovered, so there likely are more fraudulent papers out there that haven't yet been detected and retracted," said Dr. Casadevall.

Earlier studies that underestimated the extent of scientific misconduct relied solely on the journals' retraction notices, which are written by the papers' authors, according to Dr. Casadevall. "Many of those notices are wrong," he said. "Authors commonly write, 'We regret we have to retract our paper because the work is not reproducible,' which is not exactly a lie. The work indeed was not reproducible—because it was fraudulent. Researchers try to protect their labs and their reputations, and these retractions are written in such a way that you often don't know what really happened."

The PNAS study also found that journals with higher impact factors (a measure of a publication's influence in scientific circles) had especially high rates of retractions. Dr. Casadevall attributes the growing number of retracted papers to the prevailing culture in science, which disproportionately rewards scientists for publishing large numbers of papers and getting them published in prestigious journals.

"Particularly if you get your papers accepted in certain journals, you're much more likely to get recognition, grants, prizes and better jobs or promotions," he said. "Scientists are human, and some of them will succumb to this pressure, especially when there's so much competition for funding. Perhaps our most telling finding is what happened after 2005, which is when the number of retractions began to skyrocket. That's exactly when NIH funding began to get very tight."

In a recent article in Infection and Immunity, Dr. Casadevall proposed various solutions to the problem of scientific misconduct, including:

- ***more emphasis on the quality of publications rather than quantity***
- ***less emphasis on impact measures when rating journals***
- ***fostering a cooperative and collaborative culture in the research community***
- ***developing more stable and sustainable sources of research funding.***
- ***creating more flexible career pathways to prevent the ongoing loss of capable scientists due to inadequate funding***

The retraction study's findings weren't all gloom and doom. "There is a very optimistic piece of data in the paper," noted Dr. Casadevall: 43 percent of all retractions came from just 38 of the thousands of labs worldwide. "So while we're not looking at a systemic disease, so to speak, in the scientific community, our findings do indicate a significant problem that needs to be addressed."

More information: The PNAS paper is titled, "Misconduct accounts for the majority of retracted scientific publications." Provided by Albert Einstein College of Medicine

http://www.eurekalert.org/pub_releases/2012-10/ki-nfo100212.php

New findings on the workings of the inner ear

The sensory cells of the inner ear have tiny hairs called stereocilia that play a critical part in hearing.

It has long been known that these stereocilia move sideways back and forth in a wave-like motion when stimulated by a sound wave. After having designed a microscope to observe these movements, a research team at Karolinska Institutet in Sweden has discovered that the hairs not only move sideways but also change in length. The discovery, which was made in collaboration with scientists at Baylor College of Medicine in Texas, USA provides new fundamental knowledge about the mechanisms of hearing. It is presented in the online scientific journal Nature Communications.

Before we can perceive speech, music and other sounds, the sound waves must be converted into electric impulses in the auditory nerve, a process mediated by the sensory cells of the inner ear. Previous studies revealed that sound causes a lateral movement of the tiny hairs that project from these cells that opens and closes mechanically sensitive ion channels to create the sensation of hearing.

It is impossible the study the movement of the human cilia because the sensory cells are deeply embedded in thick bone, but in guinea pigs and gerbils the inner ear is surrounded by thin bone. Using a special in-house designed microscope, the scientists have been able to observe the sound-induced ciliary motion.

"This revealed something surprising – that the hairs not only bend sideways but also change in length," says Dr Anders Fridberger, docent and physician at the Centre for Hearing and Communication Research at Karolinska Institutet's Department of Clinical Science, Intervention and Technology. "These longitudinal changes have an important effect on the process of converting sound waves into electrical signals, which is necessary for hearing."

The scientists show that the stereocilia's ability to change length was greater when the electric potential around the sensory cells was low, which is known to happen in connection with noise damage and age-related hearing loss. The voltage drop causes the hairs to become overly soft, thus impairing ear function.

"Our findings might possibly help us understand why the ear doesn't work as well in such cases," says Dr Fridberger. "And maybe one day they can be put to use in the development of a new treatment for impaired hearing. If we can use a drug to restore the cilia's normal stiffness we could make the ear work better, but this is something for the distant future, if it is even possible. What we must do now is to discover the exact mechanism that controls ciliary stiffness."

The study was financed with grants from the Swedish Research Council, the Swedish Council for Working Life and social research, the Wallenberg Foundations, the Tysta Skolan (Silent School) Foundation, the Swedish Association of Hard of Hearing People and the National Institutes of Health in the USA.

Publication: 'Sound-induced length changes in outer hair cell stereocilia', Pierre Hakizimana, William E. Brownell, Stefan Jacob och Anders Fridberger. Nature Communications, online 2 October 2012, doi: 10.1038/ncomms2100.

http://www.eurekalert.org/pub_releases/2012-10/acos-sre092712.php

Surgeons recreate eggs in vitro to treat infertility

Research may one day lead to method for helping infertile, premenopausal women produce enough eggs to become pregnant

CHICAGO - Regenerative-medicine researchers have moved a promising step closer to helping infertile, premenopausal women produce enough eggs to become pregnant. Today, surgeons at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine in Winston-Salem, NC, reported that they were able to stimulate ovarian cell production using an in vitro rat model, and observed as the cells matured into very early-stage eggs that could possibly be fertilized. Results from this novel study were presented at the 2012 American College of Surgeons Annual Clinical Congress.

"While conventional hormone replacement therapy is able to maintain female sexual characteristics, it's unable to restore ovarian tissue function, which includes the production of eggs," the study's authors reported. Ovarian tissue function is critical for premenopausal women who desire to conceive.

Several fertility disorders can leave premenopausal women without an adequate amount of eggs. These disorders can also prevent a woman's ovaries from secreting enough of the hormones that stimulate egg production. Events such as ovarian operations, an injury, or radiation therapy for cancer can interfere with ovarian function, according to Anthony Atala, MD, FACS, director of the Wake Forest Institute for Regenerative Medicine and chair of the department of urology at the Wake Forest Baptist Medical Center.

Although the causes may vary, about 10 percent of childbearing-age women struggle with infertility,* meaning that these women try for at least one year but are not able to conceive. The U.S. Centers for Disease Control and Prevention says that the most common cause of infertility in premenopausal women is polycystic ovarian syndrome*—an imbalance of sex hormones. This disorder causes irregular ovulation and higher levels of male hormones in affected women.

According to Dr. Atala, the goal of this study was to spur the ovaries to produce the female sex hormones estrogen and progesterone as well as stimulate egg production. The surgeons extracted ovarian cells from three-week old female rats, which would be equivalent to about 25 years old in humans. The cells were isolated in a culture of nutrient-dense growth factors for one week. Next, the cells were placed under a collagen gel that allows them to grow three dimensionally instead of in a single layer. The researchers then assessed cell growth, hormone production, and gene expression in the specimens.

In their early observations, the surgeons found immature oocytes protruding from clusters of ovarian cells. To help the oocytes mature, the surgeons developed a microwell system to keep oocytes inside clusters of ovarian cells. In humans, primordial germ cells or oogonium are the first stage of development into ovums, or mature eggs. The researchers also found that the cells expressed germ cell markers consistent with those of early stage eggs. They observed that the oocytes began to develop zona pellucida, a membrane that forms around an ovum as it develops, and showed a capacity to produce steroids similar to those produced by early stage eggs or follicles. "Now, the goal is creating more mature structures that could actually be used for fertilization," Dr. Atala explained.

Dr. Atala and his colleagues believe that the newly generated oocytes would be able to mature to a certain stage in humans. The oocytes would then be put back into the female patient to go through natural ovulation and conception, or the oocytes would be fertilized in vitro and then implanted in the uterus. Dr. Atala said because ovarian cell function is restored, a woman using this procedure may be able to produce the necessary hormones and would not need additional hormone replacement therapy.

Although the surgeons were able to generate early stage eggs in vitro, Dr. Atala cautions that the procedure has a while to go before it can be applied to humans: "This study represents the elementary, first stages of the research process," he said. "But we're showing the principle signs that this approach is a potential strategy for infertile women who want to have children," he concluded.

Other investigators in this study included Sunyoung Joo MD; Sittadjody Sivanandane, PhD; Emanuel C. Opara, PhD; John D. Jackson, PhD; and James J. Yoo, MD, PhD.

http://www.eurekalert.org/pub_releases/2012-10/lsoh-arn100212.php

Allergy rises not down to being too clean, just losing touch with 'old friends'

A new scientific report out today from the International Scientific Forum on Home Hygiene (IFH) dismantles the myth that the epidemic rise in allergies in recent years has happened because we're living in sterile homes and overdoing hygiene.

But far from saying microbial exposure is not important, the report concludes that losing touch with microbial 'old friends' may be a fundamental factor underlying rises in an even wider array of serious diseases. As well as allergies, there are numerous other 'chronic inflammatory diseases' (CIDs) such as Type 1 diabetes and multiple sclerosis which seem to stem from impaired regulation of our immune systems. Deficiencies in microbial exposure could be key to rises in both allergies and CIDs.

This detailed review of evidence, accumulated over more than 20 years of research since the 'hygiene hypothesis' was first proposed, now confirms that the original notion is not correct.

Presenting the report findings in Liverpool today at Infection Prevention 2012, the national conference of the UK and Ireland's Infection Prevention Society, co-author of the report and Honorary Professor at London School of Hygiene and Tropical Medicine, Professor Sally Bloomfield explains: "The underlying idea that microbial exposure is crucial to regulating the immune system is right. But the idea that children who have fewer infections, because of more hygienic homes, are then more likely to develop asthma and other allergies does not hold up."

Another author of the report, Dr Rosalind Stanwell-Smith, also from London School of Hygiene and Tropical Medicine said: "Allergies and chronic inflammatory diseases are serious health issues and it's time we recognised that simplistically talking about home and personal cleanliness as the cause of the problem is ill-advised, because it's diverting attention from finding workable solutions and the true, probably much more complex, causes." If worrying about 'being too clean' results in people needlessly exposing themselves and their children to pathogens that can make them ill, this would clearly be dangerous.

Professor Graham Rook, also co-author of the report, who developed the 'Old Friends' version of the hypothesis, said: "The rise in allergies and inflammatory diseases seems at least partly due to gradually losing contact with the range of microbes our immune systems evolved with, way back in the Stone Age. Only now are we seeing the consequences of this, doubtless also driven by genetic predisposition and a range of factors in our modern lifestyle - from different diets and pollution to stress and inactivity. It seems that some people now have inadequately regulated immune systems that are less able to cope with these other factors."
Dr Stanwell Smith explains the probable reasons why this has happened "since the 1800s, when allergies began to be more noticed, the mix of microbes we've lived with, and eaten, drunk and breathed in has been steadily changing. Some of this has come through measures to combat infectious diseases that used to take such a heavy toll in those days - in London, 1 in 3 deaths was a child under 5. These changes include clean drinking water, safe food, sanitation and sewers, and maybe overuse of antibiotics. Whilst vital for protecting us from infectious diseases, these will also have inadvertently altered exposure to the 'microbial friends' which inhabit the same environments".
But we've also lost touch with our "old friends" in other ways: our modern homes have a different and less diverse mix of microbes than rural homes of the past. This is nothing to do with cleaning habits: even the cleanest-looking homes still abound with bacteria, viruses, fungi, moulds and dust mites. It's mainly because microbes come in from outside and the microbes in towns and cities are very different from those on farms and in the countryside.
"The good news", says Professor Bloomfield "is that we aren't faced with a stark choice between running the risk of infectious disease, or suffering allergies and inflammatory diseases. The threat of infectious disease is now rising because of antibiotic resistance, global mobility and an ageing population, so good hygiene is even more vital to all of us." "How we can begin to reverse the trend in allergies and CID isn't yet clear", says Professor Rook. "There are lots of ideas being explored but relaxing hygiene won't reunite us with our Old Friends - just expose us to new enemies like E. coli O104."
"One important thing we can do", says Professor Bloomfield, "is to stop talking about 'being too clean' and get people thinking about how we can safely reconnect with the right kind of dirt".
A pdf file of the full report is available for downloading
IFH has also produced a short summary of the findings and conclusions from the report.

http://www.sciencedaily.com/releases/2012/10/121002092845.htm

Hospital Bedsores Linked to Patient Mortality

A new clinical study spearheaded by the dean of UCLA's School of Nursing has found a direct correlation between pressure ulcers - commonly known as bedsores - and patient mortality and increased hospitalization.

ScienceDaily - The research is believed to be the first of its kind to use data directly from medical records to assess the impact of hospital-acquired pressure ulcers on Medicare patients at national and state levels. According to the study, featured as the lead article in the current issue of the Journal of the American Geriatrics Society, seniors who developed pressure ulcers were more likely to die during their hospital stay, to have longer stays in the hospital, and to be readmitted to the hospital within 30 days of their discharge.
To arrive at their findings, the researchers tracked more than 51,000 randomly selected Medicare beneficiaries hospitalized across the United States in 2006 and 2007.
"Hospital-acquired pressure ulcers were shown to be an important risk factor associated with mortality," said Dr. Courtney Lyder, lead investigator on the study and dean of the UCLA School of Nursing. "It is incumbent upon hospitals to identify individuals at high risk for these ulcers and implement preventive interventions immediately upon admission." According to Lyder and his research team, individuals at the highest risk are those with existing chronic conditions, such as congestive heart failure, pulmonary disease, cardiovascular disease, diabetes and obesity, as well as those on steroids.
In conducting the study, the researchers were challenged by the fact that there is no large single database to help determine the incidence of pressure ulcers among hospitalized Medicare patients. They therefore culled their data from Medicare's claim history, a national surveillance system designed to identify adverse events -- or "unintended harm" -- within the hospitalized Medicare population. The researchers looked at this data to determine the cause and patterns of hospital-acquired pressure ulcers.
The study found that 4.5 percent of the patients tracked acquired a pressure ulcer during their stay in the hospital. The majority of these bedsores were found on the tailbone or sacrum, followed by the hip, buttocks and heels. The study also revealed that of the nearly 3,000 individuals who entered the hospital with a pressure

ulcer, 16.7 percent developed at least one new bedsore on a different part of their body during their hospitalization.
"This is a serious issue, and now we have data that can help the health care system address this ongoing problem," Lyder said. "When individuals enter the hospital with the risk conditions that we've identified, it should send up an immediate warning signal that appropriate steps should be taken to minimize the chance of pressure ulcers occurring."
In addition to Lyder, clinical researchers on this study included Yun Wang of Qualidigm, the Centers for Outcomes Research and Evaluation at Yale University, and Yale-New Haven Health; Mark Metersky of Qualidigm and the division of pulmonary and critical care medicine at the University of Connecticut School of Medicine; Maureen Curry of Qualidigm; Rebecca Kliman of the Office of Clinical Standards and Quality at the Centers for Medicare and Medicaid Services; Nancy Verzier of Qualidigm; and David Hunt of the Office of Health Information Technology Adoption in the Office of the National Coordinator for Health Information Technology.
Courtney H. Lyder, Yun Wang, Mark Metersky, Maureen Curry, Rebecca Kliman, Nancy R. Verzier, David R. Hunt. Hospital-Acquired Pressure Ulcers: Results from the National Medicare Patient Safety Monitoring System Study. Journal of the American Geriatrics Society, 2012; 60 (9): 1603 DOI: 10.1111/j.1532-5415.2012.04106.x

http://www.sciencedaily.com/releases/2012/10/121002161753.htm

Beta-Blocker Use May Not Prevent Heart Attack, Death and Stroke, New Study Reveals

Use of beta-blockers was not associated with a lower risk of a composite of cardiovascular events

ScienceDaily - Among patients with either coronary artery disease (CAD) risk factors only, known prior heart attack, or known CAD without heart attack, the use of beta-blockers was not associated with a lower risk of a composite of cardiovascular events that included cardiovascular death, nonfatal heart attack or nonfatal stroke, according to a study in the October 3 issue of JAMA.
"Treatment with beta-blockers remains the standard of care for patients with coronary artery disease, especially when they have had a myocardial infarction [MI; heart attack]. The evidence is derived from relatively old post-MI studies, most of which antedate modern reperfusion or medical therapy, and from heart failure trials, but has been widely extrapolated to patients with CAD and even to patients at high risk for but without established CAD. It is not known if these extrapolations are justified. Moreover, the long-term efficacy of these agents in patients treated with contemporary medical therapies is not known, even in patients with prior MI," according to background information in the article.
Sripal Bangalore, M.D., M.H.A., of the NYU School of Medicine, New York, and colleagues conducted a study to evaluate the association between beta-blocker use and long-term cardiovascular outcomes. The observational study included data from patients in the Reduction of Atherothrombosis for Continued Health (REACH) registry. From this registry, 44,708 patients met the study inclusion criteria of whom 14,043 patients (31 percent) had prior MI, 12,012 patients (27 percent) had documented CAD but without MI, and 18,653 patients (42 percent) had CAD risk factors only. The last follow-up data collection was April 2009. The primary outcome for this study was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. The secondary outcome was the primary outcome plus hospitalization for atherothrombotic events or a revascularization procedure. The overall median (midpoint) follow-up was 44 months. Among the 44,708 patients in the study, 21,860 were included in the propensity score-matched analysis.
The researchers found that in the prior MI group, the event rates were not significantly different among those with beta-blocker use (489 [16.93 percent]) vs. those without beta-blocker use (532 [18.60 percent]) for the primary outcome, or the secondary outcome (30.96 percent vs. 33.12 percent, respectively). In the CAD without MI cohort, the event rates were not different in those with beta-blocker use (391 [12.94 percent]) vs. those without p-blocker use (405 [13.55 percent]) for the primary outcome, for cardiovascular death, for stroke, and for MI. The event rates were higher in those with beta-blocker use (1,101 [30.59 percent] vs. those without beta-blocker use (1,002 [27.84 percent]) for the secondary outcome and for hospitalization in the propensity score-matched model.
In the risk factors alone group, the event rates were higher in those with beta-blocker use (467 [14.22 percent] vs. those without beta-blocker use (403 [12.11 percent]) for the primary outcome, for the secondary outcome (870 [22.01 percent] vs. 797 [20.17 percent], respectively) but not for MI or stroke. In the propensity score-matched model, there were similar event rates for cardiovascular death and for hospitalization.
The researchers also found that among patients with recent MI (one year or less), beta-blocker use was associated with a lower incidence of the secondary outcome.
"Among patients enrolled in the international REACH registry, beta-blocker use was not associated with a lower event rate of cardiovascular events at 44-month follow-up, even among patients with prior history of MI.

Further research is warranted to identify subgroups that benefit from beta-blocker therapy and the optimal duration of beta-blocker therapy," the authors conclude.

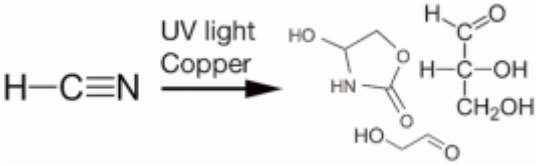
Sripal Bangalore et al. β-Blocker Use and Clinical Outcomes in Stable Outpatients With and Without Coronary Artery Diseaseβ-Blocker Use for Coronary Artery Disease. JAMA: The Journal of the American Medical Association, 2012; 308 (13): 1340 DOI: 10.1001/jama.2012.12559

http://arstechnica.com/science/2012/10/simple-reaction-makes-the-building-blocks-of-a-nucleic-acid/

Simple reaction makes the building blocks of a nucleic acid

"Cyanide to the RNA base cytosine" becomes a new clue for origin of life researchers.

by John Timmer - Oct 3 2012, 5:20am TST



Origin-of-life researchers face a deceptively straightforward question: how did simple chemicals produce complex biochemistry? The complexity of this starts to come in when you consider the many complex biomolecules that would have been useful or essential to the first biochemical reactions. And it gets worse when you consider that there are lots of simple organic chemicals that plausibly could have been present on the early Earth. Figuring out which reactions to even start looking at can be a real challenge.

The extent of that challenge was highlighted a few years back, when a Cambridge lab suggested most earlier researchers had gone down a dead end. Previously, researchers tried to build up a sugar and a nucleic acid base separately, and then link to them to form precursors of DNA and RNA. But the group from Cambridge showed it was possible to build relatively simple compounds into a three-ring chemical that could then be converted into cytosine, an RNA component. Now, they've revisited that work and shown that all of the precursors of that reaction can be made with little more than cyanide.

The reaction the group reported back in 2009 only required a set of two or three carbon precursors, but these molecules were already somewhat complex: cyanamide, cyanoacetylene, glycolaldehyde, and glyceraldehyde. We don't know that all of these chemicals would be common on a pre-biotic Earth, which leaves its relevance to the origin of life a somewhat open question.

In a new paper, the same lab tackles forming the simple, two- and three-atom sugars used in their earlier work (glycolaldehyde and glyceraldehyde). To get there, they started with nothing more complex than hydrogen cyanide, a simple molecule comprised of one atom each of hydrogen, carbon, and nitrogen. Hydrogen cyanide forms readily under a variety of conditions, and has been found on several bodies in our Solar System, as well as in the interstellar medium.

The authors were intrigued by reports in the literature of a cycle that involves a set of six cyanide molecules, coordinated by two copper atoms. In a water solution, this complex can cycle, driven by ultraviolet light, through a set of reactions that alternately spit out cyanide, protons, and electrons. These electrons get temporarily attached to water molecules, and typically end up being taken up by a scavenger molecule, usually nitrate. However, some reports in the literature noted that, when nitrate isn't added to the reaction, some undefined larger molecules formed.

The authors went back and checked these reaction products, and found that they included both glycolaldehyde and glyceraldehyde—the two chemicals that were key building blocks of the reaction that produced the RNA precursor. And all the reaction required was copper ions and some UV light.

If left to continue cycling, the products of the reaction also included some more complex, five-atom ringed structures that incorporate nitrogen and oxygen in the ring. But the authors suspect that with the right conditions—namely the ones identified in the earlier paper—the products of this new cycle could be sent directly on to form cytosine. They also suggest the addition of other metals could shift the products to additional chemicals that may have biological relevance.

Hopefully, it's safe to assume the lab already has these projects in the works.

Nature Chemistry, 2012. DOI: 10.1038/NCHEM.1467 (About DOIs).

http://www.eurekalert.org/pub_releases/2012-10/acs-neo100312.php

New evidence on easing inflammation of brain cells for Alzheimer's disease

Research proves the validity of an approach for combating Alzheimer's disease with medicines that treat some of the symptoms, and actually stop or prevent the disease

New research proves the validity of one of the most promising approaches for combating Alzheimer's disease (AD) with medicines that treat not just some of the symptoms, but actually stop or prevent the disease itself, scientists are reporting. The study, in the journal ACS Medicinal Chemistry Letters, also identifies a potential new oral drug that the scientists say could lead the way.

Wenhui Hu and colleagues point out that existing drugs for AD provide only "minimal" relief of memory loss and other symptoms, creating an urgent need for new medicines that actually combat the underlying destruction of brain cells. Research suggests that inflammation of nerve cells in the brain is a key part of that process. One medicine, Minozac, is in clinical trials. But Hu says Minozac still has more space to improve its efficacy. So the scientists sifted through compounds with a molecular architecture similar to Minozac in an effort to find more active substances.

The report describes success in doing so. They discovered one compound that appeared especially effective in relieving nerve inflammation and in improving learning and memory in lab mice widely used in AD research. "In general, this study not only proves that countering neuroinflammation is indeed a potential therapeutic strategy for Alzheimer's disease, but also provides a good lead compound with efficacy comparable to donepezil [an existing AD medicine] for further oral anti-AD drug discovery and development," the report states.

http://www.eurekalert.org/pub_releases/2012-10/afri-nsl100312.php

New study links caffeinated coffee to vision loss

A new study suggests caffeinated coffee drinkers should limit their intake to reduce their chances of developing vision loss or blindness.

Rockville, MD – According to a scientific paper in Investigative Ophthalmology & Visual Science, heavy caffeinated coffee consumption is associated with an increased risk of developing exfoliation glaucoma, the leading cause of secondary glaucoma worldwide. The study, The Relation between Caffeine and Coffee Consumption and Exfoliation Glaucoma or Glaucoma Suspect: A Prospective Study in Two Cohorts, is the first to examine the link between caffeinated coffee and exfoliation glaucoma in a U.S. –based population.

"Scandinavian populations have the highest frequencies of exfoliation syndrome and glaucoma," said author, Jae Hee Kang, ScD, of Channing Division of Network Medicine at Brigham and Women's Hospital in Boston, Mass. "Because Scandinavian populations also have the highest consumption of caffeinated coffee in the world, and our research group has previously found that greater caffeinated coffee intake was associated with increased risk of primary open-angle glaucoma, we conducted this study to evaluate whether the risk of exfoliation glaucoma or glaucoma suspect may be different by coffee consumption."

The study was composed of two cohorts: 78,977 women from the Nurses' Health Study (NHS) and 41,202 men from the Health Professionals Follow-up Study (HPFS) who were at least 40 years of age, did not have glaucoma and reported undergoing eye examinations from 1980 (for NHS participants) and 1986 (for HPFS participants) to 2008. The research team used questionnaires to obtain and validate the consumption of beverages containing caffeine and reviewed medical records to determine incident cases of exfoliation glaucoma, which contributes to elevated pressure sufficient enough to damage the optic nerve, or exfoliation glaucoma suspect that have milder or only suspect optic nerve damage.

A meta-analysis of the two cohorts showed that, compared to abstainers, participants who drank three cups or more of caffeinated coffee daily were at an increased risk of developing exfoliation glaucoma or glaucoma suspect. The researchers did not find associations with consumption of other caffeinated products, such as soda, tea, chocolate or decaffeinated coffee. The results also showed that women with a family history of glaucoma were at an increased risk.

Kang, along with his colleagues, report that this study represents a much needed effort to better understand the causes of exfoliation glaucoma, which are largely unknown. "Because this is the first study to evaluate the association between caffeinated coffee and exfoliation glaucoma in a U.S. population, confirmation of these results in other populations would be needed to lend more credence to the possibility that caffeinated coffee might be a modifiable risk factor for glaucoma," said Kang. "It may also lead to research into other dietary or lifestyle factors as risk factors.

http://www.eurekalert.org/pub_releases/2012-10/uoia-stm100312.php

Simple test may ease management of esophagitis

A simple new test, in which the patient swallows a string, can monitor treatment of eosinophilic esophagitis as effectively as an invasive, expensive and uncomfortable procedure that risks complications, particularly in children.

Researchers from the University of Illinois at Chicago College of Medicine, working in collaboration with clinician-investigators at the University of Colorado Denver/Children's Hospital Colorado and Lurie Children's Hospital in Chicago, reported their findings in a study published recently online in the journal Gut. Eosinophilic esophagitis, or EoE, is a food-allergy inflammatory disease of the esophagus in both children and adults. While

rare, it is steadily increasing in incidence. In EoE, inflammatory cells in the body called eosinophils attack the esophagus. The esophagus narrows until food cannot pass, causing painful impactions.
"Most cases are first encountered in the emergency room, where a child is brought in because something he ate is caught in his esophagus," says Steven Ackerman, UIC professor of biochemistry and molecular genetics and co-principal investigator on the study.
Eosinophils produce specific proteins. Because these inflammatory cells are not normally found in the esophagus, these proteins serve as biomarkers and can indicate the extent of inflammation in the esophagus. Currently, physicians diagnose EoE and monitor its treatment by endoscopy. A lighted, flexible instrument is inserted down the esophagus and used to obtain six to eight tissue samples for biopsy from sections along its length from throat to stomach.
A child may require 10, 15, or even 20 such procedures over three or four years, say two of the report's authors, co-principal investigator Dr. Glenn Furuta, professor of pediatrics at the University of Colorado at Denver, and Dr. Amir Kagalwalla, associate professor of pediatrics at Northwestern University.
The new method, the Esophageal String Test, or EST, uses a capsule containing a yard-long string. One end of the string is taped to the patient's cheek before the capsule is swallowed, and the string spools out of the dissolving capsule, stretching through the esophagus, the stomach and the small intestine. The string becomes coated with digestive tract secretions and can be removed for analysis.
Ackerman and Furuta tested samples from the string in the esophagus region looking for eosinophil proteins to show evidence of inflammation. Levels detected by the string test and by biopsy were both shown to indicate disease accurately.
The researchers recruited 41 patients ages 7-20, who were to undergo endoscopy and biopsy. Participants swallowed the capsule the night before endoscopy, and the string was removed just prior to that procedure. The researchers believe the string may not need to remain in place for so long, and the test could be performed in a single visit to the doctor's office. Although the string test may never completely replace endoscopy-with-biopsy, particularly for diagnosis, the authors conclude, "it certainly has the potential to significantly improve the evaluation and treatment of patients who require repeated assessments."
This study was supported by grants or gifts form NIH-R21AID79925, Thaser Research Fund, NIH/NICATS Colorado CCTS grant Ul1 TR000154, Shell, Mandell, Boyd and Savoie Families, American Gastroenterological Association, Campaign Urging Research for Eosinophilic Diseases, Buckeye Foundation, Pappas Foundation, American Partnership for Eosinophic Disorders, Sandhill Scientific, Mayo Foundation and NIH HL058732 and the SCRR K26 RR0109709 and NIH- 1UL1RR025741.

http://www.eurekalert.org/pub_releases/2012-10/ehs-nss100312.php

New study sheds light on cancer-protective properties of milk

Findings reported in the Journal of Dairy Science

Amsterdam, The Netherlands - Milk consumption has been linked to improved health, with decreased risks of diabetes, metabolic syndrome, and colon cancer. A group of scientists in Sweden found that lactoferricin4-14 (Lfcin4-14), a milk protein with known health effects, significantly reduces the growth rate of colon cancer cells over time by prolonging the period of the cell cycle before chromosomes are replicated. In a new study, investigators report that treatment with Lfcin4-14 reduced DNA damage in colon cancer cells exposed to ultraviolet (UV) light. Their results are published in the October issue of the Journal of Dairy Science®.
"We previously hypothesized that the prolongation of the cell cycle in colon cancer cells as a result of Lfcin4-14 treatment may give the cells extra time for DNA repair," says one of the lead investigators, Professor Stina Oredsson, of the Department of Biology at the University of Lund, Sweden. "Indeed, UV light-induced damage was decreased in colon cancer cells treated with Lfcin4-14 compared with controls. The differences were small but significant."
Investigators exposed colon cancer cells to UV light that caused DNA damage and then grew the cells in the absence or presence of Lfcin4-14. They evaluated DNA damage using a sensitive technique known as comet assay. After the cells are processed, the cells with DNA damage resemble a comet with a tail, and the intensity of the tail compared to the comet head indicates the number of DNA breaks. UV light exposure resulted in an increase in the number of comets while treatment with Lfcin4-14 reduced the number of comets in UV light-exposed cells.
To understand the mechanism by which Lfcin4-14 reduced DNA damage, investigators evaluated the levels of several proteins involved in cell cycle progression, DNA repair, and cell death. They found an increase in flap endonuclease-1, a protein associated with DNA synthesis; a decrease in b-cell lymphoma 2-associated X protein, which is involved with cell death; and a decrease in the level of □-H2AX, indicating more efficient

DNA repair. "These changes in expression support our hypothesis that Lfcin4-14 treatment resulted in increased DNA repair," says Dr. Oredsson.
Dr. Oredsson notes that cancer cells, in general, have defects in the DNA repair mechanisms. Thus, Lfcin4-14 may have a greater effect on normal cells than on cancer cells. "Our data suggest that the effects of Lfcin4-14 in prolonging the cell cycle may contribute to the cancer preventive effect of milk. This must be further investigated in different systems," she concludes.

http://www.eurekalert.org/pub_releases/2012-10/bmj-amt100212.php

Aspirin may temper brain power decline in elderly women at risk of heart disease

Inflammation has a role in heart disease and may also be implicated in aging brain

Daily low dose aspirin could slow the decline in brain power among elderly women at high risk of heart disease, indicates observational research published in the online journal BMJ Open.
The researchers base their findings on 681 women between the ages of 70 and 92, 601 of whom were at high risk of heart disease and stroke, defined as a 10% or greater risk on a validated risk scale (Framingham).
All the women were subjected to a battery of tests to measure their physical health and intellectual capacity, including verbal fluency and memory speed, and dementia (mini mental state exam, or MMSE for short) in 2000-1.
Their health was tracked over a period of five years, at the end of which the intellectual capacity of 489 women was assessed again. Some 129 women were taking low dose aspirin (75 to 160 mg) every day to ward off a heart attack or stroke when the monitoring period started. A further 94 were taking various other non-steroidal anti-inflammatory drugs (NSAIDs).
The MMSE score fell, on average, across the whole group at the end of the five years, but this decline was considerably less in the 66 women who had taken aspirin every day over the entire period.
This held true, even after taking account of age, genetic factors, the use of other NSAIDs, and the cardiovascular risk score.
The researchers then divided up the group into those who had taken aspirin for the entire five years (66); those who had stopped taking it by 2005-6 (18); those who were taking it by 2005-6 (67); and those who hadn't taken the drug at any point (338). Compared with women who had not taken aspirin at all, those who had done so for all five years, increased their MMSE score, while those who had taken aspirin at some point, registered only insignificant falls in MMSE score. The test results for verbal fluency and memory speed indicated similar patterns, although the findings weren't statistically significant.
There were no differences, however, in the rate at which the women developed dementia.
The researchers then looked only at the women with a Framingham risk score of more than 10%. Again, similar patterns were evident.
The fall in MMSE score was less among those taking aspirin than those who weren't, and there was no difference between those taking other NSAIDs and those who weren't. The same was true of the verbal and memory tests, although the differences were not statistically significant.
The authors caution that theirs was an observational study, and that the MMSE can't detect subtle changes in cognitive ability. But they suggest their findings indicate that aspirin may protect the brain—at least in women at high risk of a heart attack or stroke.

http://www.eurekalert.org/pub_releases/2012-10/giot-hat100312.php

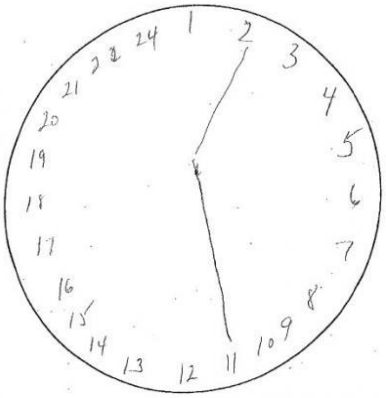
Home-based assessment tool for dementia screening

Georgia Tech researchers have created a tool that allows adults to screen themselves for early signs of dementia

With baby boomers approaching the age of 65 and new cases of Alzheimer's disease expected to increase by 50 percent by the year 2030, Georgia Tech researchers have created a tool that allows adults to screen themselves for early signs of dementia. The home-based computer software is patterned after the paper-and-pencil Clock Drawing Test, one of health care's most commonly used screening exams for cognitive impairment.
"Technology allows us to check our weight, blood-sugar levels and blood pressure, but not our own cognitive abilities," said project leader Ellen Yi-Luen Do. "Our ClockMe System helps older adults identify early signs of impairment, while allowing clinicians to quickly analyze the test results and gain valuable insight into the patient's thought processes."
Georgia Tech's ClockMe system eliminates the paper trail and computerizes the test into two main components: the ClockReader Application and the ClockAnalyzer Application. Click here to see a video demo.
ClockReader is the actual test and is taken with a stylus and computer or tablet. The participant is given a specific time and instructed to draw a clock with numbers and the correct minute and hour hands. Once

completed, the sketch is emailed to a clinician, who uses the ClockAnalyzer Application to score the test. The software checks for 13 traits. They include correct placement of numbers and hands without extra markings. People with cognitive impairment frequently draw clocks with missing or extra numbers. Digits are sometimes drawn outside of the clock. The time is often incorrect.

In addition to scoring automatically and consistently, ClockAnalyzer records the duration of the test and the time between each stroke. The software also replays the drawing in real-time, allowing a clinician to watch the drawing being created to observe any behavior abnormality.



"The traditional paper-and-pencil test is usually overseen by a technician and later scored by a clinician, who scores the test based only on the finished drawing," said Do, a professor in Georgia Tech's Colleges of Computing and Architecture. "By looking at the sketch, the scorer is not able to decipher whether the person struggled to remember certain numbers while drawing the clock. The ClockMe system's timing software highlights those delays."

And, because they're saved electronically, the drawings can be used to easily compare a person's cognitive ability progress or regression over time. Do's research found that traditional tests are often filed in a folder and are rarely used for future comparison.

People with cognitive impairment frequently draw clocks with missing or extra numbers. Digits are sometimes drawn outside of the clock. The time is often incorrect. **Credit: Georgia Institute of Technology**

The ClockMe system was initially tested at the Emory Alzheimer's Disease Research Center in Atlanta, where it's currently being used in addition to the traditional paper-and-pencil test. Despite a lack of computer literacy, all of the elderly patients who used the software during the study said they had no problems with the pen-based, computer technology.

"For this reason, as well as the ability to send the drawings directly to clinicians for convenient scoring, we envision ClockMe as a viable tool for home-based screening," said Do. "America's health care costs are expected to soar as baby boomers become senior citizens. If a screening tool can be used at home, unnecessary trips to clinics can be eliminated and medical expenses can be saved."

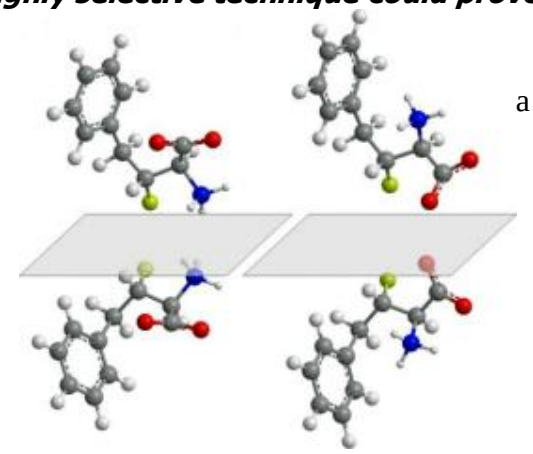
Do and her colleagues are hoping to commercialize the project in the future. Their research was published in September's Journal of Ambient Intelligence and Smart Environments.

This project is supported by the National Science Foundation (NSF) (Award Number SHB-1117665). The content is solely the responsibility of the principal investigators and does not necessarily represent the official views of the NSF.

http://phys.org/news/2012-10-introduction-fluorine-atoms-molecules-applications.html

Introduction of fluorine atoms into organic molecules could have applications for synthesis of pharmaceuticals

Introducing fluorine atoms into organic molecules using a highly selective technique could prove useful in the synthesis



Despite its small size, the fluorine atom has had a vast impact on the pharmaceutical industry. More often than not, introducing fluorine to drug molecule improves the drug's biological activity, earning it a reputation as a 'magic element'.

Amino acids—comprising an amino group and a carboxylic acid group—are also important to the medicinal chemist. Amino acids are not only the building blocks of proteins, they are commonly found in pharmaceutical drugs. Now, Mikiko Sodeoka and colleagues at the RIKEN Advanced Science Institute, Wako, have developed a synthesis technique that can selectively and efficiently combine fluorine and amino acids into the same organic molecule.

A schematic representation of the four different stereoisomers of the fluorinated amino acid derivatives that can be synthesized using the fluorination and hydroxy/amino derivative technique. **2012 Mikiko Sodeoka et al., RIKEN Advanced Science Institute**

The starting materials are alpha-keto esters that contain a carbonyl group and an ester group. The first reaction of the team's technique is the substitution of a hydrogen atom, on the carbon atom adjacent to the carbonyl group, for a fluorine atom. As there are two hydrogen atoms that could be replaced, two mirror images, or enantiomers could result. Sodeoka and colleagues use a palladium catalyst that preferentially forms one of these

enantiomers. This renders the reaction enantioselective; that is, one enantiomer is selectively formed over the other. The carbon atom to which the fluorine attaches becomes a stereogenic center as it has four different substituents. The interchange of any two substituents gives a pair of enantiomers. In the wider picture, these enantiomers are stereoisomers—molecules that differ only by their 3D orientation of the atoms.
Next, the carbonyl group of the fluorinated alpha-keto ester transforms to a hydroxyl group. Again, two possible stereoisomers of the molecule could form. By exploiting the existing stereogenic center and using different reagents, the researchers could synthesize one stereoisomer in preference to the other. Hence, the technique not only introduces fluorine, but two stereogenic centers to the molecule. The formation of two stereogenic centers creates the possibility of four different stereoisomers (Fig. 1). By tuning the reagents, the team isolated all four stereoisomers in separate reaction sequences.
Overcoming the chemical instability of the intermediate, however, is challenging. "The fluorinated alpha-keto esters easily convert to their hydrated form, so care is required to exclude water from the reaction mixture," Sodeoka explains. "However, the hydroxy and amino acid derivatives are stable and easy to handle."
In the future, Sodeoka and colleagues hope to widen the scope of the fluorination reaction to other starting materials. This would create the possibility of making numerous biologically active compounds.
More information: Suzuki, S., Kitamura, Y., Lectard, S., Hamashima, Y. & Sodeoka, M. Catalytic asymmetric mono-fluorination of α-keto esters: Synthesis of optically active β-fluoro-α-hydroxy and β-fluoro-α-amino acid derivatives. Angewandte Chemie International Edition 51, 4581–4585 (2012). dx.doi.org/10.1002/anie.201201303

http://www.wired.com/wiredscience/2012/10/cute-image-concentration/

Looking at Cute Images May Improve Concentration

An investigation into the kawaii phenomenon

By Ian Steadman, Wired UK

Before reading any further it is imperative that you flick through the gallery of kittens and puppies that accompanies this story. Now. Go on. Seriously, we'll wait.
Back? Good. You should be ready to concentrate fully on the task at hand - examining a study which claims to have found that exposure to cute animals increases the brain's concentration levels for a short time afterward.
"The Power of Kawaii", published in the open access journal Plos One, details an investigation into the kawaii phenomenon - that essential quality of cuteness which permeates so much of Japanese culture.
The team from Hiroshima University reference the results of a 2009 study which found that being exposed to cute pictures made a sample group better at playing a surgery board game similar to Operation. Even more intriguing, the cuter the image the better the improvement in dexterity. So the Hiroshima team devised three new experiments to test what kinds of concentration are improved by exposure to cute images, and to hopefully shed some light on why that might be the case.
First, they had to define cuteness. In this instance, the researchers said that "cute objects are assumed to be characterised by baby schema" - that means big eyes and round faces. This fed into their hypothesis that concentration might be improved around cute things as a kind of instinctual behavioural reflex that occurs when humans are around babies that can't care for themselves.
In the first experiment, 48 participants were split into two groups. They all played a similar game as in the 2009 study, and then each group was shown either a collection of baby animal pictures or adult animal pictures. Then they played the game again - and the group who had been exposed to the photos of baby animals both scored higher and finished faster than the other group, who saw no change. That replicated the results of the 2009 study.
The second experiment saw a different group of 48 participants split into two like before, with each group asked to count how many times a certain number appeared among a random string of numbers, as well as what letter was appearing within a shape next to the number string. After the same baby/adult animal picture exposure, the group with the baby animal pictures experience a dramatic increase in accuracy and speed (just like in the first experiment) compared to no change in the other group.
The third experiment, however, didn't find any improvement in reaction times among a group of 36 participants who had to identify a letter flashed quickly on a screen in front of them. That implies that cuteness works as an aid to concentration, not some kind of general aid to mental ability.
So why the improved concentration when looking at baby animals? The researchers note that "the psychophysiological state underlying the feeling of cuteness has to be explored" before any firm conclusions as to why cuteness improves concentration can be reliably concluded. There are also cultural responses to cuteness which need to be explored - while the Japanese participants come from a culture where the different reactions to kawaii aren't that big, gender might play a bigger role in a European society, for example.

Regardless, if you're studying for an exam you might want to start filling your breaks with lolcats. How else are you going to get that A?

http://www.sciencedaily.com/releases/2012/10/121003111153.htm

Common Medicine Helps Repair Brain After Stroke, Study in Rats Suggests

Study on rats suggests that effectiveness of neurorehabilitation after a stroke can be improved by anti-inflammatory drugs.

ScienceDaily - Strokes often cause loss or impairment of vital brain functions -- such as speech, movement, vision or attention. Restoration of these functions is often possible, but difficult. One of the factors impeding brain plasticity is inflammation. A study on rats, carried out at the Nencki Institute in Warsaw, suggests that effectiveness of neurorehabilitation after a stroke can be improved by anti-inflammatory drugs.

Post-stroke inflammation slows down recovery and impairs brain plasticity, reveal the results from the lab of Professor Małgorzata Kossut at the Nencki Institute in Warsaw. The popular anti-inflammatory drug ibuprofen restores the ability of brain cortex to reorganize -- a process necessary for recovery of stroke-damaged functions.

"Our research was conducted on rats, but we have good reasons to suppose that in future our results will help improve effectiveness of rehabilitation of stroke patients," says Prof. Kossut.

The Nencki Institute team stresses that so far there are no proofs that the treatment will be effective in humans and that they did not investigate if the ibuprofen therapy prevents strokes, but concentrated on post-stroke recovery.

The most frequent cause of stroke is blocking of brain arteries. Without supply of oxygen, neurons die quickly. In the region of stroke-induced damage pathological changes cause decrease of brain tissue metabolism, impairment of neurotransmission and edema.

Brain control over physiological and voluntary functions may be lost, depending on the localization of the infarct. Impairments of movement, vision, speech and attention are frequent. In most cases these functions return either partially or completely. Sometimes they return spontaneously, more often after neurorehabilitation.

"In both instances recovery is based on neuroplasticity, the ability of the brain to reorganize, that is to change the properties of neurons and to alter the connections between them," says Dr. Monika Liguz-Lęcznar (Nencki Institute).

After a stroke, neuroplasticity is impaired. Scientists from the Nencki Institute suppose that this may be due to inflammation developing at the site of the stroke. The proof that decreasing inflammation helps neurorehabilitation came from experiments done on rats with experimentally induced stroke. The stroke was localized in a special region of the brain cortex, receiving information from whiskers.

The whiskers are important sensory organs of rodents, allowing the animals to orient themselves in their environment in darkness. Every whisker activates a small, precisely delineated chunk of brain cortex.

In healthy rats neuroplastic changes can be induced by cutting off some of the whiskers, that is by eliminating part of the sensory input to the brain. The brain reacts to that by letting the remaining whiskers take over more cortical space, expand their cortical representation, at the expense of the cut off ones.

"This plastic change does not occur when the site of stroke-induced damage is near the region of cortex 'belonging' to the whiskers. We showed that application of ibuprofen decreases inflammation and restores neuroplasticity -- the brain cortex reorganizes like in healthy animals," says Prof. Kossut.

The result obtained on rats indicates that ibuprofen (and probably other anti-inflammatory medicines) may be beneficial in treating stroke patients. Ibuprofen therapy should support brain plasticity by reducing post-stroke inflammation and so speed up recovery of functions lost due to the stroke. If the results on rats are verified in a proper clinical trial, they may be influential in shaping the treatment of stroke patients.

The research of Prof. Kossut's team on the effects of anti-inflammatory drugs on neuroplasticity was funded by the Polish-German Cooperation Program in Neuroscience and grants from the Ministry of Science and Education.

http://www.sciencedaily.com/releases/2012/10/121003150902.htm

New Evidence On Easing Inflammation of Brain Cells for Alzheimer's Disease

Research proves a promising approach for combating Alzheimer's disease (AD) treats not just some of the symptoms, can actually stop or prevent the disease itself

ScienceDaily - New research proves the validity of one of the most promising approaches for combating Alzheimer's disease (AD) with medicines that treat not just some of the symptoms, but actually stop or prevent the disease itself, scientists are reporting. The study, in the journal ACS Medicinal Chemistry Letters, also identifies a potential new oral drug that the scientists say could lead the way.

Wenhui Hu and colleagues point out that existing drugs for AD provide only "minimal" relief of memory loss and other symptoms, creating an urgent need for new medicines that actually combat the underlying destruction of brain cells. Research suggests that inflammation of nerve cells in the brain is a key part of that process. One medicine, Minozac, is in clinical trials. But Hu says Minozac still has more space to improve its efficacy. So the scientists sifted through compounds with a molecular architecture similar to Minozac in an effort to find more active substances.

The report describes success in doing so. They discovered one compound that appeared especially effective in relieving nerve inflammation and in improving learning and memory in lab mice widely used in AD research. "In general, this study not only proves that countering neuroinflammation is indeed a potential therapeutic strategy for Alzheimer's disease, but also provides a good lead compound with efficacy comparable to donepezil [an existing AD medicine] for further oral anti-AD drug discovery and development," the report states.

Wei Zhou, Guifa Zhong, Xiurong Rao, Hui Xie, Shaogao Zeng, Tianyan Chi, Libo Zou, Donghai Wu, Wenhui Hu. Identification of Aminopyridazine-Derived Antineuroinflammatory Agents Effective in an Alzheimer's Mouse Model. ACS Medicinal Chemistry Letters, 2012; : 120913133048003 DOI: 10.1021/ml3001769

http://www.sciencedaily.com/releases/2012/10/121003132012.htm

Caffeinated Coffee Linked to Vision Loss

A study suggests caffeinated coffee drinkers should limit their intake to reduce their chances of developing vision loss or blindness.

ScienceDaily - A new study suggests caffeinated coffee drinkers should limit their intake to reduce their chances of developing vision loss or blindness. According to a scientific paper in Investigative Ophthalmology & Visual Science, heavy caffeinated coffee consumption is associated with an increased risk of developing exfoliation glaucoma, the leading cause of secondary glaucoma worldwide.

The study, The Relation between Caffeine and Coffee Consumption and Exfoliation Glaucoma or Glaucoma Suspect: A Prospective Study in Two Cohorts, is the first to examine the link between caffeinated coffee and exfoliation glaucoma in a U.S. -based population.

"Scandinavian populations have the highest frequencies of exfoliation syndrome and glaucoma," said author, Jae Hee Kang, ScD, of Channing Division of Network Medicine at Brigham and Women's Hospital in Boston, Mass. "Because Scandinavian populations also have the highest consumption of caffeinated coffee in the world, and our research group has previously found that greater caffeinated coffee intake was associated with increased risk of primary open-angle glaucoma, we conducted this study to evaluate whether the risk of exfoliation glaucoma or glaucoma suspect may be different by coffee consumption."

The study was composed of two cohorts: 78,977 women from the Nurses' Health Study (NHS) and 41,202 men from the Health Professionals Follow-up Study (HPFS) who were at least 40 years of age, did not have glaucoma and reported undergoing eye examinations from 1980 (for NHS participants) and 1986 (for HPFS participants) to 2008. The research team used questionnaires to obtain and validate the consumption of beverages containing caffeine and reviewed medical records to determine incident cases of exfoliation glaucoma, which contributes to elevated pressure sufficient enough to damage the optic nerve, or exfoliation glaucoma suspect that have milder or only suspect optic nerve damage.

A meta-analysis of the two cohorts showed that, compared to abstainers, participants who drank three cups or more of caffeinated coffee daily were at an increased risk of developing exfoliation glaucoma or glaucoma suspect. The researchers did not find associations with consumption of other caffeinated products, such as soda, tea, chocolate or decaffeinated coffee. The results also showed that women with a family history of glaucoma were at an increased risk.

Kang, along with his colleagues, report that this study represents a much needed effort to better understand the causes of exfoliation glaucoma, which are largely unknown.

"Because this is the first study to evaluate the association between caffeinated coffee and exfoliation glaucoma in a U.S. population, confirmation of these results in other populations would be needed to lend more credence to the possibility that caffeinated coffee might be a modifiable risk factor for glaucoma," said Kang. "It may also lead to research into other dietary or lifestyle factors as risk factors.

The above story is reprinted from materials provided by Association for Research in Vision and Ophthalmology (ARVO).

Note: Materials may be edited for content and length. For further information, please contact the source cited above.

L. R. Pasquale, J. L. Wiggs, W. C. Willett, J. H. Kang. The Relationship between Caffeine and Coffee Consumption and Exfoliation Glaucoma or Glaucoma Suspect: A Prospective Study in Two Cohorts. Investigative Ophthalmology & Visual Science, 2012; 53 (10): 6427 DOI: 10.1167/iovs.12-10085

http://www.eurekalert.org/pub_releases/2012-10/yu-hkd100212.php

How ketamine defeats chronic depression

Raises hopes for new class of antidepressant

Many chronically depressed and treatment-resistant patients experience immediate relief from symptoms after taking small amounts of the drug ketamine. For a decade, scientists have been trying to explain the observation first made at Yale University.

Today, current evidence suggests that the pediatric anesthetic helps regenerate synaptic connections between brain cells damaged by stress and depression, according to a review of scientific research written by Yale School of Medicine researchers and published in the Oct. 5 issue of the journal Science.

Ketamine works on an entirely different type of neurotransmitter system than current antidepressants, which can take months to improve symptoms of depression and do not work at all for one out of every three patients. Understanding how ketamine works in the brain could lead to the development of an entirely new class of antidepressants, offering relief for tens of millions of people suffering from chronic depression.

"The rapid therapeutic response of ketamine in treatment-resistant patients is the biggest breakthrough in depression research in a half century," said Ronald Duman, Elizabeth Mears and House Jameson Professor of Psychiatry and Professor of Neurobiology.

Duman and George K. Aghajanian, also professor of psychiatry at Yale, are co-authors of the review.

Understanding how ketamine works is crucial because of the drug's limitations. The improvement in symptoms, which are evident just hours after ketamine is administered, lasts only a week to 10 days. In large doses, ketamine can cause short-term symptoms of psychosis and is abused as the party drug "Special K."

In their research, Duman and others show that in a series of steps ketamine triggers release of neurotransmitter glutamate, which in turn stimulates growth of synapses. Research at Yale has shown that damage of these synaptic connections caused by chronic stress is rapidly reversed by a single dose of ketamine.

The original link between ketamine and relief of depression was made at the Connecticut Mental Health Center in New Haven by John Krystal, chair of the department of psychiatry at Yale, and Dennis Charney, now dean of Mt. Sinai School of Medicine, who helped launch clinical trials of ketamine while at the National Institute of Mental Health.

Efforts to develop drugs that replicate the effects of ketamine have produced some promising results, but they do not act as quickly as ketamine. Researchers are investigating alternatives they hope can duplicate the efficacy and rapid response of ketamine.

http://www.eurekalert.org/pub_releases/2012-10/plos-deb100112.php

Dating encounters between modern humans and Neandertals

To discover why Neandertals are most closely related to people outside Africa scientists have estimated the date when Neandertals and modern Europeans last shared ancestors

To discover why Neandertals are most closely related to people outside Africa, Harvard and Max Planck Institute scientists have estimated the date when Neandertals and modern Europeans last shared ancestors. The research, published in the journal PLOS Genetics, provides a historical context for the interbreeding. It suggests that it occurred when modern humans carrying Upper Paleolithic technologies encountered Neandertals as they expanded out of Africa.

When the Neandertal genome was sequenced in 2010 it revealed that people outside Africa share slightly more genetic variants with Neandertals than Africans do. One scenario that could explain this observation is that modern humans mixed with Neandertals when they came out of Africa. An alternative, but more complex, scenario is that African populations ancestral to both Neandertals and modern humans remained subdivided over a few hundred thousand years and that those more related to Neandertals subsequently left Africa.

Dr. Sriram Sankararaman and colleagues measured the length of DNA pieces in the genomes of Europeans that are similar to Neandertals. Since recombination between chromosomes when egg and sperm cells are formed reduces the size of such pieces in each generation, the Neandertal-related pieces will be smaller the longer they have spent in the genomes of present-day people.

The team estimate that Neandertals and modern humans last exchanged genes between 37,000 and 86,000 years ago, well after modern humans appeared outside Africa but potentially before they started spreading across Eurasia. This suggests that Neandertals (or their close relatives) had children with the direct ancestors of present-day people outside Africa.

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http://phys.org/news/2012-10-onset-flu-season-human-to-pet-transmission.html

Onset of flu season raises concerns about human-to-pet transmission

Researchers are concerned that cats, dogs and other pets may face risks in getting the flu from their owners.

Phys.org - As flu season approaches, people who get sick may not realize they can pass the flu not only to other humans, but possibly to other animals, including pets such as cats, dogs and ferrets.

This concept, called "reverse zoonosis," is still poorly understood but has raised concern among some scientists and veterinarians, who want to raise awareness and prevent further flu transmission to pets. About 80-100 million households in the United States have a cat or dog.

It's well known that new strains of influenza can evolve from animal populations such as pigs and birds and ultimately move into human populations, including the most recent influenza pandemic strain, H1N1. It's less appreciated, experts say, that humans appear to have passed the H1N1 flu to cats and other animals, some of which have died of respiratory illness. There are only a handful of known cases of this phenomenon and the public health implications of reverse zoonosis of flu remain to be determined. But as a concern for veterinarians, it has raised troubling questions and so far, few answers.

Veterinary researchers at Oregon State University and Iowa State University are working to find more cases of this type of disease transmission and better understand any risks they pose to people and pets. "We worry a lot about zoonoses, the transmission of diseases from animals to people," said Christiane Loehr, an associate professor in the OSU College of Veterinary Medicine. "But most people don't realize that humans can also pass diseases to animals, and this raises questions and concerns about mutations, new viral forms and evolving diseases that may potentially be zoonotic. And, of course, there is concern about the health of the animals."

The researchers are surveying flu transmission to household cat and dog populations, and suggest that people with influenza-like illness distance themselves from their pets. If a pet experiences respiratory disease or other illness following household exposure to someone with the influenza-like illness, the scientists encourage them to take the pet to a veterinarian for testing and treatment.

The first recorded, probable case of fatal human-to-cat transmission of the pandemic H1N1 flu virus occurred in Oregon in 2009, Loehr said. Details were published in Veterinary Pathology, a professional journal. In that instance, a pet owner became severely ill with the flu and had to be hospitalized. While she was still in the hospital, her cat – an indoor cat with no exposure to other sick people, homes or wildlife – also died of pneumonia caused by an H1N1 infection.

Since then, researchers have identified a total of 13 cats and one dog with pandemic H1N1 infection in 2011 and 2012 that appeared to have come from humans. Pet ferrets have also been shown to be infected, and some died. All of the animals' symptoms were similar to that of humans - they rapidly develop severe respiratory disease, stop eating and some die. Serological studies suggest there is far more exposure to flu virus in cats and dogs than previously known.

"It's reasonable to assume there are many more cases of this than we know about, and we want to learn more," Loehr said. "Any time you have infection of a virus into a new species, it's a concern, a black box of uncertainty. We don't know for sure what the implications might be, but we do think this deserves more attention."

Natural and experimental transmission of the H3N2 influenza virus from dogs to cats in South Korea showed the potential for flu viruses to be transmitted among various animal species, Loehr said. It's unknown if an infected cat or other pet could pass influenza back to humans.

The primary concern in "reverse zoonosis," as in evolving flu viruses in more traditional hosts such as birds and swine, is that in any new movement of a virus from one species to another, the virus might mutate into a more virulent, harmful or easily transmissible form.

"All viruses can mutate, but the influenza virus raises special concern because it can change whole segments of its viral sequence fairly easily," Loehr said. "In terms of hosts and mutations, who's to say that the cat couldn't be the new pig? We'd just like to know more about this."

Veterinarians who encounter possible cases of this phenomenon can obtain more information from Loehr or Jessie Trujillo at Iowa State University. They are doing ongoing research to predict, prevent or curtail emergent events.

http://www.eurekalert.org/pub_releases/2012-10/luhs-bae100112.php

Botox as effective as medication for urinary urgency incontinence

Loyola research sheds light on treatments for common condition in women

MAYWOOD – Botox® (onabotulinum toxin-A) injections to the bladder are as effective as medication for treating urinary urgency incontinence in women, but the injection is twice as likely to completely resolve symptoms. These findings were published in the latest issue of The New England Journal of Medicine by a National Institutes of Health clinical trials network including Loyola University Chicago Stritch School of Medicine (SSOM).

Urgency incontinence is urinary incontinence with a strong or sudden need to urinate. Traditionally, this condition has been treated with drugs known as anticholinergics, which reduce bladder contractions by targeting the bladder muscle through the nervous system. However, many women who take anticholinergic medications experience side effects, including constipation, dry mouth and dry eyes.

"Prior to this study, we reserved onabotulinum toxin-A for women who did not respond to traditional oral medication," said Linda Brubaker, MD, MS, co-author and dean, SSOM. "However, this research supports the use of either of these approaches as appropriate first-line treatment in women."

An estimated 15.7 percent of U.S. women experience urinary incontinence. Women are twice as likely to experience urinary incontinence as men.

This study evaluated 241 women with urinary urgency incontinence. One group of participants received six-months of daily oral medication plus a saline injection. The other group received one injection of onabotulinum toxin-A (Botox) plus a daily oral placebo capsule. At the beginning of the study, patients had an average of five urgency incontinence episodes a day. The average reduction in episodes over six months was 3.4 with oral medication and 3.3 with onabotulinum toxin-A. The proportion of women with complete resolution of urgency incontinence was 13 percent with anticholinergics and 27 percent with onabotulinum toxin-A. Quality of life improved in both groups without significant differences. More participants in the anticholinergic group reported dry mouth (46 percent versus 31 percent) while the onabotulinum toxin-A group had more urinary tract infections (28 percent versus 15 percent) and more incomplete bladder emptying, requiring temporary bladder catheterization (5 percent versus 0 percent).

"These results will help doctors weigh treatment options for women and make recommendations based on individual patient needs," said Dr. Brubaker, who is in the Division of Female Pelvic & Reconstructive Surgery, Loyola University Health System.

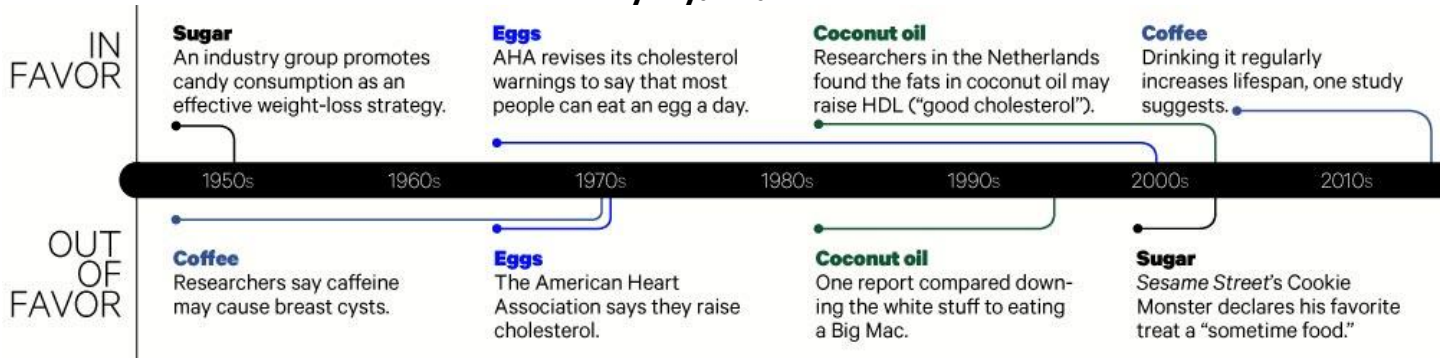
LUHS' Division of Female Pelvic Medicine and Reconstructive Surgery was the first of its kind in greater Chicago. It is still one of the few centers in the country that offers a single location for the multi-disciplinary diagnosis and treatment of women with pelvic floor disorders. LUHS' urogynecological surgeons, doctors with the combined expertise of gynecology and urology, provide the most advanced medical and surgical care available for women with problems related to the lower urinary tract and the pelvic floor.

http://www.wired.com/wiredscience/2012/10/mf-beware-of-food-trends/

Beware of Food Trends

When it comes to food, good-for-you often turns into bad-for-you—and vice versa. Here are a few consumables that have fallen in and out of favor.

By Bryan Lufkin



http://www.sciencedaily.com/releases/2012/10/121005134326.htm

A New Chapter for Chinese Medicine

When comes to minor complaints, chronic conditions and even fatal illnesses, people sometimes turn to ginseng and other herbal remedies.

ScienceDaily - A team of scientists from The Hong Kong Polytechnic University (PolyU) has been working on a new approach to drug development involving chemistry, biotechnology, mathematics, computer power and 5000-year ancient practices in Chinese medicine. The groundbreaking regime for herbal study and testing called quantitative-pattern-activity-relationship ("QPAR" in short) verifies the quality and health benefits of traditional herbs. While Western pharmacology focuses on purified chemical compounds such as Vitamin C, Prof. Chau Foo Tim from the Department of Applied Biology and Chemical Technology and Dr Daniel Sze from the Department of Health Technology and Informatics studied the impact from a mix of compounds, a unique property in herbs. "Information-rich pattern called chromatographic fingerprint were used to prove the authenticity of a medicinal plant. Our research team has further utilized the 'big data' three dimensional (3D) fingerprints to give a good presentation of active ingredients and bioactivities that allow scientists to excavate any healing power from a mix of compounds," said Prof. Chau.

To further bridge the gap between Chinese and Western medicines, Prof. Chau and Dr Sze have been working on a completely new drug classification and rating standard to establish a scientific link between traditional herbs and various diseases. The new QPAR standard for the first time links medicinal properties to cells, genes and proteins that trigger or contribute to a disease. For example, the magic fungus Ganoderma (靈芝) could be investigated for its ability to improve immunity by stimulating Dendritic Cells and therefore cell-mediated immune responses in our body.

"This is an innovative framework that quantifies the effect of traditional herbs would have on human health and common diseases on a sound scientific basis. QPAR can be used to verify how well Ganoderma can boost immunity and give a rating," said Dr Sze. The research is still at an early stage but if successful, scientists will only have to do laboratory tests and crunch on computers to build databases, and get an accurate projection of active ingredients, efficacy and toxicity for preliminary herbal study in the future.

Another breakthrough is that QPAR uses mathematical methods to make predictions and the sophisticated algorithms tapped into 5000-year ancient system of Chinese medicine which was based on the flow and balance of positive (yang) and negative (yin) energies in the body. "We believed that blending the Chinese understanding of diseases into the western medicines would yield an approach more successful in unlocking the full potential of Chinese herbs," Dr Sze continued.

Dr Albert B. Wong, the founding president of the Modernised Chinese Medicine Association who was also a member of Hong Kong SAR Government's Panel on Promoting Testing and Certification Services in Chinese Medicine Trade, shared his views on this novel technique. "Health benefits of herbal remedies are widely known but not yet proven. People don't want to waste money or gamble on unproven treatments and then miss the chance of beating the diseases. New innovations are needed to bring transparency and credibility into herbal medicine."

Dr Wong also believed that this innovation would drive the evolution of herbal trade. "Herbs can be grown, hand-picked or collected. The quality of active ingredients and medicinal effects also varies with region, altitude, growing techniques and processing methods. QPAR provides a scientific way to quickly verify the authenticity and active ingredients by different sources, making herbal trade fairer and more transparent. Drug companies would better control the prices and quality of raw herbs and also enforce standardisation and consistence across products. From the consumers' point of view, it is worth to spend the money on products that can give exactly what they want for their health benefits."

http://www.eurekalert.org/pub_releases/2012-10/uoc--urd100412.php

UCLA researchers discover that the sleeping brain behaves as if it's remembering something

UCLA researchers have for the first time measured the activity of a brain region known to be involved in learning, memory and Alzheimer's disease during sleep.

They discovered that this part of the brain behaves as if it's remembering something, even under anesthesia, a finding that counters conventional theories about memory consolidation during sleep.

The research team simultaneously measured the activity of single neurons from multiple parts of the brain involved in memory formation. The technique allowed them to determine which brain region was activating other areas of the brain and how that activation was spreading, said study senior author Mayank R. Mehta, a professor of neurophysics in UCLA's departments of neurology, neurobiology, physics and astronomy.

In particular, Mehta and his team looked at three connected brain regions in mice - the new brain or the neocortex, the old brain or the hippocampus, and the entorhinal cortex, an intermediate brain that connects the new and the old brains. While previous studies have suggested that the dialogue between the old and the new brain during sleep was critical for memory formation, researchers had not investigated the contribution of the entorhinal cortex to this conversation, which turned out to be a game changer, Mehta said. His team found that the entorhinal cortex showed what is called persistent activity, which is thought to mediate working memory during waking life, for example when people pay close attention to remember things temporarily, such as recalling a phone number or following directions.

"The big surprise here is that this kind of persistent activity is happening during sleep, pretty much all the time." Mehta said. "These results are entirely novel and surprising. In fact, this working memory-like persistent activity occurred in the entorhinal cortex even under anesthesia."

The study appears Oct. 7, 2012 in the early online edition of the journal Nature Neuroscience.

The findings are important, Mehta said, because humans spend one-third of their lives sleeping and a lack of sleep results in adverse effects on health, including learning and memory problems.

It had been shown previously that the neocortex and the hippocampus "talk" to each other during sleep, and it is believed that this conversation plays a critical role in establishing memories, or memory consolidation. However, no one was able to interpret the conversation.

"When you go to sleep, you can make the room dark and quiet and although there is no sensory input, the brain is still very active," Mehta said. "We wanted to know why this was happening and what different parts of the brain were saying to each other."

Mehta and his team developed an extremely sensitive monitoring system that allowed them to follow the activities of neurons from each of three targeted portions of the brain simultaneously, including the activity of a single neuron. This allowed them to decipher the precise communications, even when the neurons were seemingly quiet. They then developed a sophisticated mathematical analysis to decipher the complex conversation.

During sleep, the neocortex goes into a slow wave pattern for about 90 percent of that time. During this period, its activity slowly fluctuates between active and inactive states about once every second. Mehta and his team focused on the entorhinal cortex, which has many parts.

The outer part of the entorhinal cortex mirrored the neocortical activity. However, the inner part behaved differently. When the neocortex became inactive, the neurons in the inner entorhinal cortex persisted in the active state, as if they were remembering something the neocortex had recently "said," a phenomenon called spontaneous persistent activity. Further, they found that when the inner part of the entorhinal cortex became spontaneously persistent, it prompted the hippocampus neurons to become very active. On the other hand, when the neocortex was active, the hippocampus became quieter. This data provided a clear interpretation of the conversation.

"During sleep the three parts of the brain are talking to each other in a very complex way," he said. "The entorhinal neurons showed persistent activity, behaving as if they were remembering something even under anesthesia when the mice could not feel or smell or hear anything. Remarkably, this persistent activity sometimes lasted for more than a minute, a huge timescale in brain activity, which generally changes on a scale of one thousandth of a second."

The findings challenge theories of brain communication during sleep, in which the hippocampus is expected to talk to, or drive, the neocortex. Mehta's findings instead indicate that there is a third key actor in this complex dialogue, the entorhinal cortex, and that the neocortex is driving the entorhinal cortex, which in turn behaves as if it is remembering something. That, in turn, drives the hippocampus, while other activity patterns shut it down.

"This is a whole new way of thinking about memory consolidation theory. We found there is a new player involved in this process and it's having an enormous impact," Mehta said. "And what that third player is doing is being driven by the neocortex, not the hippocampus. This suggests that whatever is happening during sleep is not happening the way we thought it was. There are more players involved so the dialogue is far more complex, and the direction of the communication is the opposite of what was thought."

Mehta theorizes that this process occurs during sleep as a way to unclutter memories and delete information that was processed during the day but is irrelevant. This results in the important memories becoming more salient and readily accessible. Notably, Alzheimer's disease starts in the entorhinal cortex and patients have impaired sleep, so Mehta's findings may have implications in that arena.

For this study, Mehta teamed with Thomas Hahn and Sven Berberich of Heidelberg University in Germany and the Max Planck Institute for Medical Research and James McFarland of Brown University and the UCLA

Department of Physics. Going forward, the team will further study this brain activity to uncover the mechanisms behind it and determine if it influences subsequent behavioral performance. These results and related findings can be found at http://www.physics.ucla.edu/~mayank .
"These results provide the first direct evidence for persistent activity in medial entorhinal cortex layer neurons in vivo, and reveal its contribution to cortico-hippocampal interactions, which could be involved in working memory and learning of long behavioral sequences during behavior, and memory consolidation during sleep," the study states.
The study was funded by the Whitehall Foundation, the National Institutes of Health, the National Science Foundation, the W. M. Keck Foundation, the German Ministry of Education and Research and the Max Planck Society.

http://www.scientificamerican.com/podcast/episode.cfm?id=the-2012-nobel-prize-in-physiology-12-10-08

The 2012 Nobel Prize in Physiology or Medicine

The 2012 Nobel Prize in Physiology or Medicine was awarded jointly to John B. Gurdon and Shinya Yamanaka for the discovery that mature cells can be reprogrammed to become pluripotent

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The Press Release from the Nobel Assembly at Karolinska Institute
The Nobel Prize in Physiology or Medicine 2012 goes jointly to John B. Gurdon and Shinya Yamanaka for the discovery that mature cells can be reprogrammed to become pluripotent

Summary

The Nobel Prize recognizes two scientists who discovered that mature, specialised cells can be reprogrammed to become immature cells capable of developing into all tissues of the body. Their findings have revolutionised our understanding of how cells and organisms develop.
John B. Gurdon discovered in 1962 that the specialisation of cells is reversible. In a classic experiment, he replaced the immature cell nucleus in an egg cell of a frog with the nucleus from a mature intestinal cell. This modified egg cell developed into a normal tadpole. The DNA of the mature cell still had all the information needed to develop all cells in the frog.
Shinya Yamanaka discovered more than 40 years later, in 2006, how intact mature cells in mice could be reprogrammed to become immature stem cells. Surprisingly, by introducing only a few genes, he could reprogram mature cells to become pluripotent stem cells, i.e. immature cells that are able to develop into all types of cells in the body.
These groundbreaking discoveries have completely changed our view of the development and cellular specialisation. We now understand that the mature cell does not have to be confined forever to its specialised state. Textbooks have been rewritten and new research fields have been established. By reprogramming human cells, scientists have created new opportunities to study diseases and develop methods for diagnosis and therapy.

Life – a journey towards increasing specialisation

All of us developed from fertilized egg cells. During the first days after conception, the embryo consists of immature cells, each of which is capable of developing into all the cell types that form the adult organism. Such cells are called pluripotent stem cells. With further development of the embryo, these cells give rise to nerve cells, muscle cells, liver cells and all other cell types - each of them specialised to carry out a specific task in the adult body. This journey from immature to specialised cell was previously considered to be unidirectional. It was thought that the cell changes in such a way during maturation that it would no longer be possible for it to return to an immature, pluripotent stage.

Frogs jump backwards in development

John B. Gurdon challenged the dogma that the specialised cell is irreversibly committed to its fate. He hypothesised that its genome might still contain all the information needed to drive its development into all the different cell types of an organism. In 1962, he tested this hypothesis by replacing the cell nucleus of a frog's egg cell with a nucleus from a mature, specialised cell derived from the intestine of a tadpole. The egg developed into a fully functional, cloned tadpole and subsequent repeats of the experiment yielded adult frogs. The nucleus of the mature cell had not lost its capacity to drive development to a fully functional organism. Gurdon's landmark discovery was initially met with scepticism but became accepted when it had been confirmed by other scientists. It initiated intense research and the technique was further developed, leading eventually to the cloning of mammals. Gurdon's research taught us that the nucleus of a mature, specialized cell can be returned to an immature, pluripotent state. But his experiment involved the removal of cell nuclei with pipettes followed by their introduction into other cells. Would it ever be possible to turn an intact cell back into a pluripotent stem cell?

A roundtrip journey – mature cells return to a stem cell state

Shinya Yamanaka was able to answer this question in a scientific breakthrough more than 40 years after Gurdon´s discovery. His research concerned embryonal stem cells, i.e. pluripotent stem cells that are isolated from the embryo and cultured in the laboratory. Such stem cells were initially isolated from mice by Martin Evans (Nobel Prize 2007) and Yamanaka tried to find the genes that kept them immature. When several of these genes had been identified, he tested whether any of them could reprogram mature cells to become pluripotent stem cells.

Yamanaka and his co-workers introduced these genes, in different combinations, into mature cells from connective tissue, fibroblasts, and examined the results under the microscope. They finally found a combination that worked, and the recipe was surprisingly simple. By introducing four genes together, they could reprogram their fibroblasts into immature stem cells!

The resulting induced pluripotent stem cells (iPS cells) could develop into mature cell types such as fibroblasts, nerve cells and gut cells. The discovery that intact, mature cells could be reprogrammed into pluripotent stem cells was published in 2006 and was immediately considered a major breakthrough.

From surprising discovery to medical use

The discoveries of Gurdon and Yamanaka have shown that specialised cells can turn back the developmental clock under certain circumstances. Although their genome undergoes modifications during development, these modifications are not irreversible. We have obtained a new view of the development of cells and organisms. Research during recent years has shown that iPS cells can give rise to all the different cell types of the body. These discoveries have also provided new tools for scientists around the world and led to remarkable progress in many areas of medicine. iPS cells can also be prepared from human cells.

For instance, skin cells can be obtained from patients with various diseases, reprogrammed, and examined in the laboratory to determine how they differ from cells of healthy individuals. Such cells constitute invaluable tools for understanding disease mechanisms and so provide new opportunities to develop medical therapies.

Sir John B. Gurdon was born in 1933 in Dippenhall, UK. He received his Doctorate from the University of Oxford in 1960 and was a postdoctoral fellow at California Institute of Technology. He joined Cambridge University, UK, in 1972 and has served as Professor of Cell Biology and Master of Magdalene College. Gurdon is currently at the Gurdon Institute in Cambridge.

Shinya Yamanaka was born in Osaka, Japan in 1962. He obtained his MD in 1987 at Kobe University and trained as an orthopaedic surgeon before switching to basic research. Yamanaka received his PhD at Osaka University in 1993, after which he worked at the Gladstone Institute in San Francisco and Nara Institute of Science and Technology in Japan. Yamanaka is currently Professor at Kyoto University and also affiliated with the Gladstone Institute.

Key publications:

Gurdon, J. B. (1962). The developmental capacity of nuclei taken from intestinal epithelium cells of feeding tadpoles. Journal of Embryology and Experimental Morphology 10:622-640.

Takahashi, K., Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126:663-676.

http://www.eurekalert.org/pub_releases/2012-10/ohri-fbn100412.php

Fresh blood not better, clinical trial shows

Acutely ill premature babies who received fresher blood did not fare better than those who received the current standard of care

Ottawa - In a finding that runs counter to commonly held beliefs about fresh being better, a clinical trial published today by the Journal of the American Medical Association shows that acutely ill premature babies who received fresher blood did not fare better than those who received the current standard of care. There was no difference between the two approaches with respect to major organ injury, mortality and infection.

"Before now, most of the literature on the subject suggested that fresh red blood cells are better," says lead author Dr. Dean Fergusson, who heads up the Clinical Epidemiology Program at the Ottawa Hospital Research Institute and is an associate professor at the University of Ottawa.

"However, the effect of fresher blood on clinical outcomes had never been examined using a randomized clinical trial in human patients, which is considered the gold standard in medical science. Now it has, and we found the standards currently in place are no different for this highly vulnerable population of pre-term infants than a policy and system that would favour fresh blood."

Previous observational studies of patient outcomes used already existing clinical data, which is problematic for a number of key reasons. Determining the average age of blood and its impact for those transfused more than

once is very difficult because the age of red blood cells used in each transfusion could range dramatically within the acceptable shelf life of 42 days.
Called the ARIPI Randomized Trial, which stands for Age of Red Blood Cells in Premature Infants, this study involved 377 babies weighing less than 1,250 grams and requiring red blood cell transfusions. Randomly, they either received blood that had been stored a week or less, or received the current standard of practice used by blood banks. It turned out that there was no difference in outcome between the two groups.
"Over the years, the number of retrospective studies showing possible harm from older blood has created pressure to change the management of the blood supply to provide fresher transfusion products," says Dr. Dana Devine, Vice President, Medical, Scientific & Research Affairs of Canadian Blood Services. "This is a huge undertaking that would require many more donations than we currently have and greatly increase the cost of operating the blood system.
"To have this particular human clinical trial saying otherwise is important because it is the first such study using the highest level of evidence, the randomized controlled trial, and it was done in a very vulnerable patient population."
The findings of this trial, which took place between May 2006 and June 2011, could not have happened without the hundreds of parents who consented to enroll their children in the study.
"For the families, it's a difficult decision at a difficult time to allow their tiny and fragile child to be a part of a clinical trial. On behalf of the entire team involved in this trial, I salute and thank the families for allowing us to make this important finding," says Dr. Nicole Rouvinez-Bouali, an academic neonatologist at the Children's Hospital of Eastern Ontario.
The ARIPI trial included six Canadian hospitals: The Ottawa Hospital, Children's Hospital of Eastern Ontario (Ottawa), Jewish General Hospital (Montreal), Royal University Hospital (Saskatoon), Children's and Women's Health Centre of British Columbia (Vancouver), and CHU Sainte-Justine (Montreal).
The article is titled "Effects of Fresh Red Blood Cell Transfusions on Clinical Outcomes in Premature, Very Low-Birth-Weight Infants" and was published online by the Journal of the American Medical Association on Oct. 8, 2012.
Funding for the ARIPI Randomized Trial was provided by the Canadian Institutes of Health Research.

http://www.sciencedaily.com/releases/2012/10/121008082949.htm

Novel One-Step System for Restoring Voice in Throat Cancer Patients

Patients who have lost their voice box through disease such as throat cancer may be able to speak immediately after a procedure to create a small opening at the throat.

ScienceDaily - A novel system developed through an Engineering-in-Medicine project led by Dr Chui Chee Kiong, NUS Department of Mechanical Engineering, and Dr David Lau, Consultant Ear, Nose & Throat (ENT) Surgeon at Raffles Hospital, cuts down a two-week duration before patients can speak, to about 10 minutes after the initial procedure.
People who undergo laryngectomy and lose their voice box can recover approximately 80 per cent of normal speech by having a voice prosthesis fitted into an opening or fistula between the trachea (windpipe) and esophagus (food pipe). To speak, the patient covers the stoma (breathing opening in the neck) with his or her thumb and forces air through the prosthesis into the esophagus and out through the mouth. Before the prosthesis can be inserted, the doctor needs to make a small puncture (tracheo-esophageal puncture or TEP) in the wall between the trachea and esophagus. During the puncture, a guide-wire is inserted into the fistula to prevent the creation of false passages. Two "dilators" are inserted to widen the fistula, with the second one a little wider in circumference. Previously, a temporary rubber tube is placed into the fistula and the voice prosthesis is not inserted until about two weeks later, when the fistula is "mature." However, the new device changes this.
Explaining their invention, Dr Chui said, "We have merged all the steps into a single procedure. Most significantly, although doctors still need the nasal endoscope to guide and monitor progress during the procedure, our system ensures an immediate snug fit of the prosthesis in the passageway created between the trachea and the esophagus. Until now, this can take some trial and error to achieve good sizing of the prosthesis."
Voice prostheses vary in length for different individuals, depending on the thickness between the food pipe and the windpipe. The length of the TEP needs to be accurate. Usually, the length ranges between 6mm to 26mm. It is important that the prosthesis fits well otherwise it may be ineffective, or leak and cause discomfort.
Said Mr Chng Chin Boon, Research Engineer from NUS Department of Mechanical Engineering and member of the research team, "We added markings onto the cannula used for inserting the prosthesis. From the endoscopy, we would know the distance between the anterior esophageal wall (front wall of the food pipe) and the posterior tracheal wall (back wall of the windpipe), allowing us to size the prosthesis appropriately."

This takes away a lot of discomfort such as coughing and gagging, should the prosthesis need to be removed and fitted again if the measurement is not right.
"Most prostheses need to be changed due to wear and tear, depending on each individual. And each time, the size of the prosthesis to be inserted may differ due to tissue changes in the patient. Our invention will offer patients a more fuss-free system, cutting down time and discomfort. It will also cut down the cost for the patient as the number of procedures is reduced," added Mr Chng.
The system has been successfully tested on animals, and is now ready for clinical human trial.
Said Dr David Lau, "Patients requiring voice restoration after surgery for laryngeal cancer have to make multiple visits to the clinic, and I had often thought how a simple, one step solution would save them time, discomfort and money. So we decided to go out and design that solution."
Dr Lau added, "The system we designed has several advantages over existing methods as it not only reduces the number of steps and complexity, but also increases accuracy of placement and safety, and allows for immediate voicing. However patients will still need to put in some effort, and work with the speech therapist to get the best voicing results."

http://www.sciencedaily.com/releases/2012/10/121008091554.htm

Liquorice Offers Clue to Cleaner Medical Implants

A new coating utilizing nanotechnology will allow surgeons to sterilize medical devices that contain biological components.

ScienceDaily - A nanotech material containing an extract from liquorice can be used to sterilize and protect medical devices and implants which include biological components, and protects these functional bio-components during the sterilization process.
Publishing their findings in the latest issue of Materials Today, a team of researchers from Germany and Austria explain how conventional sterilization techniques based on a blast of radiation, or exposure to toxic gas can damage the functional biological components of the device. The coating, containing a component found in liquorice and developed by German biotech company LEUKOCARE AG, protects these sensitive components.
Joachim Koch of the Georg-Speyer Haus, Institute for Biomedical Research in Frankfurt am Main in Germany and colleagues explain how medical devices and implants are increasingly functionalized using pharmacologically active proteins, antibodies and other biomolecules. Harsh sterilization procedures, including beta and gamma irradiation or exposure to toxic ethylene oxide can damage these sensitive molecules and render the device useless. However, without sterilization the patient is at risk of infection when the device is used or implanted.
The team has now successfully evaluated the nano-coating; a technology which employs a composition of stabilizing nano-molecules. One important ingredient is a compound known as glycyrrhizic acid, a natural, sweet-tasting chemical found in liquorice. Unlike other stabilizing approaches used in biopharmaceutical formulations, the nano-coating contains no sugars, sugar-alcohol compounds or proteins that might otherwise interfere with the biological activity of the device.
The team has tested the nano-coating by coupling and stabilizing an anti-inflammatory antibody to a porous polyurethane surface. This carrier acts as a surrogate for a medical device. Such a system might be used as a therapeutic implant to reduce inflammation caused by an overactive immune system in severely ill patients. The researchers found that even if the test device is blasted with radiation to sterilize it entirely, neither the nano-coating nor the proteins are damaged by the radiation and the activity of the device is maintained.
"This nano-coating formulation can now be applied for the production of improved biofunctionalized medical devices such as bone implants, vascular stents, and wound dressings and will ease the application of biomedical combination products," Koch explains.
Rupert Tscheliessnig, Martin Zörnig, Eva M. Herzig, Katharina Lückerath, Jens Altrichter, Kristina Kemter, Adnana Paunel-Görgülü, Tim Lögters, Joachim Windolf, Silvia Pabisch, Jindrich Cinatl, Holger F. Rabenau, Alois Jungbauer, Peter Müller-Buschbaum, Martin Scholz, Joachim Koch. Nano-coating protects biofunctional materials. Materials Today, 2012; 15 (9): 394 DOI: 10.1016/S1369-7021(12)70166-9

http://www.sciencedaily.com/releases/2012/10/121008091454.htm

First Successful Clinical Trial to Protect the Brain from Damage Caused by Stroke

A neuroprotectant drug protects the human brain against the damaging effects of stroke

ScienceDaily - A team of Canadian scientists and clinicians, led by Dr. Michael Hill of the Calgary Stroke Program at Foothills Medical Centre and University of Calgary's Hotchkiss Brain Institute (HBI), have demonstrated that a neuroprotectant drug, developed by Dr. Michael Tymianski at the Krembil Neuroscience

Centre, located at the Toronto Western Hospital, protects the human brain against the damaging effects of stroke.

The study, "Safety and efficacy of NA-1 for neuroprotection in iatrogenic stroke after endovascular aneurysm repair: a randomized controlled trial," published online October 8 in The Lancet Neurology, was conducted concurrently with a laboratory study published in Science Translational Medicine, that predicted the benefits of the stroke drug.

This landmark clinical trial was a randomized, double blinded, multi-centre trial that was conducted in Canada and the USA. The study evaluated the effectiveness of NA-1[Tat-NR2B9c] when it was administered after the onset of small strokes that are incurred by patients who undergo neurointerventional procedures to repair brain aneurysms. This type of small ischemic stroke occurs in over 90% of aneurysm patients after such a procedure, but usually does not cause overt neurological disability.

In the clinical trial, patients were randomized to receive either Tat-NR2B9c or placebo. Those treated with Tat-NR2B9c showed a reduction in the amount of brain damage sustained as a result of the aneurysm repair procedure. Also, in patients who had ruptured brain aneurysm, which comprise a population of patients at very high risk of neurological damage, those treated with Tat-NR2B9c all had good neurological outcomes, whereas only 68% of those treated with placebo had good outcomes.

"The results of this clinical trial represent a major leap forward for stroke research," said Dr. Hill. "There have been over 1,000 attempts to develop such drugs, which have failed to make the leap between success in the lab and in humans."

"This clinical trial is, to our knowledge, the first time that a drug aimed at increasing the resistance of the brain to stroke, has been shown to reduce stroke damage in humans. No efforts should be spared to develop it further," said Dr. Michael Tymianski, who oversaw the development of Tat-NR2B9c from its invention in his lab, through to clinical trials.

Currently, t-PA is the only widely approved acute stroke therapy. It works by unblocking the arteries to the brain, however, this treatment is only beneficial for a portion of stroke victims. It also has serious potential for side-effects, including bleeding in the brain.

"Through our lab research and clinical trial, we now have a better method of predicting whether a stroke drug may be effective in humans and we now have the evidence that there is a neuroprotectant that can prevent damage in the brain caused by reduced blood flow," said Dr. Tymianski, inventor of NA-1 and one of the study's authors. "The benefits of this can be explored not only for stroke, but for other conditions such as vascular dementia."

Michael D Hill, Renee H Martin, David Mikulis, John H Wong, Frank L Silver, Karel G terBrugge, Geneviève Milot, Wayne M Clark, R Loch MacDonald, Michael E Kelly, Melford Boulton, Ian Fleetwood, Cameron McDougall, Thorsteinn Gunnarsson, Michael Chow, Cheemun Lum, Robert Dodd, Julien Poublanc, Timo Krings, Andrew M Demchuk, Mayank Goyal, Roberta Anderson, Julie Bishop, David Garman, Michael Tymianski. Safety and efficacy of NA-1 in patients with iatrogenic stroke after endovascular aneurysm repair (ENACT): a phase 2, randomised, double-blind, placebo-controlled trial. The Lancet Neurology, 2012; DOI: 10.1016/S1474-4422(12)70225-9