

U. of Colorado study shows acupressure effective in helping to treat traumatic brain injury

Treatment has implications for US veterans returning home from war

A new University of Colorado Boulder study indicates an ancient form of complementary medicine may be effective in helping to treat people with mild traumatic brain injury, a finding that may have implications for some U.S. war veterans returning home.

The study involved a treatment known as acupressure in which one's fingertips are used to stimulate particular points on a person's body -- points similar to those stimulated with needles in standard acupuncture treatments, said CU-Boulder Professor Theresa Hernandez, lead study author. The results indicate a link between the acupressure treatments and enhanced cognitive function in study subjects with mild traumatic brain injury, or TBI.

"We found that the study subjects with mild traumatic brain injury who were treated with acupressure showed improved cognitive function, scoring significantly better on tests of working memory when compared to the TBI subjects in the placebo control group," said Hernandez, a professor in CU-Boulder's psychology and neuroscience department. "This suggests to us that acupressure could be an effective adjunct therapy for those suffering from TBI."

The acupressure treatment type used in the study is called Jin Shin. For the study, Hernandez and her colleagues targeted the 26 points on the human body used in standard Jin Shin treatments ranging from the head to the feet. The study subjects all received treatments by trained Jin Shin practitioners.

According to practitioners, Jin Shin acupressure points are found along "meridians" running through the body that are associated with specific energy pathways. It is believed that each point is tied to the health of specific body organs, as well as the entire body and brain, Hernandez said.

"Think of the meridians as freeways and the pressure points as towns along the way," she said. "When there is a traffic jam in Denver that causes adverse effects as far away as Boulder, clearing the energy blocks, or in this case traffic jams, helps improve flow and overall health."

The study involved 38 study subjects, each of whom was randomly assigned to one of two groups - an experimental group that received active acupressure treatments from trained experts and a control group that received treatments from the same experts on places on the body that are not considered to be acupressure points, acting as a placebo. The study was "blinded," meaning the researchers collecting data and the study participants themselves did not know who was in the experimental group or the placebo group until the end of the study.

The team used a standard battery of neuropsychological tests to assess the results. In one test known as the Digit Span Test, subjects were asked to repeat strings of numbers after hearing them, in both forward and backward order, to see how many digits they could recall. Those subjects receiving active acupressure treatments showed increased memory function, said Hernandez.

A second standard psychology test used for the study, called the Stroop Task, measured working memory and attention. The test subjects were shown the names of colors like blue, green or red on a computer screen. When the names of the particular colors are viewed on the screen in a different color of ink -- like the word "green" spelled out in blue ink -- test subjects take longer to name the ink color and the results are more error-prone, according to Hernandez. The Stroop Test subjects in the CU-Boulder study wore special caps wired with electrodes to measure the brain activity tied to specific stimuli. The results showed those who received the active acupressure treatments responded to stimuli more rapidly than those who received the placebo treatments, Hernandez said.

"We were looking at synchronized neural activity in response to a stimulus, and our data suggest the brains of those in the active acupressure group responded differently when compared to those in the placebo acupressure group," she said.

A paper on the subject was published in the January issue of the Journal of Neurotrauma, a peer-reviewed publication on the latest advances in both clinical and laboratory investigations of traumatic brain and spinal cord injury. Co-authors on the study included CU-Boulder's Kristina McFadden, Kyle Healy, Miranda Dettman, Jesse Kaye and Associate Professor Tiffany Ito of psychology and neuroscience. Funded by the Colorado Traumatic Brain Injury Trust Fund, the study is believed to be one of the first placebo-controlled studies ever published in a peer-reviewed medical journal showing the benefit of acupressure to treat patients with TBI, Hernandez said.

"We would like to see if the Jin Shin treatment is useful to military veterans returning home with traumatic brain injury, a signature wound prevalent in the wars in Iraq and Afghanistan," said Hernandez. The Jin Shin

acupressure treatment can be taught to family and friends of those with TBI and can even be used as a self-treatment, which could allow for more independence, she said.

In a 2010 stroke study led by Hernandez, the researchers concluded that Jin Shin acupressure triggered a larger and faster relaxation response during active treatments and a decreased stress response following active treatments compared with what was seen in placebo treatments. Hernandez and her colleagues are embarking on a new study on the use of Jin Shin acupressure in athletes to see if the enhanced relaxation response and decreased stress seen in the stroke study can reduce the likelihood of athletic injury.

In 2002, Hernandez partnered with former Colorado Rep. Todd Saliman to initiate the Colorado Traumatic Brain Injury Trust Fund, a statute that has generated nearly \$2 million to the state annually since 2004 from surcharges to traffic offenses like driving while impaired and speeding. Roughly 65 percent of the money goes toward rehabilitation and care services for individuals with TBI, about 30 percent goes for TBI research and 5 percent for TBI education. Because of the statute, nearly 4,000 Colorado citizens with TBI have received care and rehabilitation services for brain injuries.

Hernandez will be honored on March 3 in Denver by the Colorado Traumatic Brain Injury Program with the establishment of the annual Theresa D. Hernandez TBI Trust Fund Community Award, becoming its first recipient. Saliman also will be honored at the ceremony.

http://www.eurekalert.org/pub_releases/2011-02/afot-aav022811.php

An Alzheimer's vaccine in a nasal spray

Tel Aviv University researchers develop a vaccine that staves off stroke as well

One in eight Americans will fall prey to Alzheimer's disease at some point in their life, current statistics say. Because Alzheimer's is associated with vascular damage in the brain, many of them will succumb through a painful and potentially fatal stroke.

But researchers led by Dr. Dan Frenkel of Tel Aviv University's Department of Neurobiology at the George S. Wise Faculty of Life Sciences are working on a nasally-delivered 2-in-1 vaccine that promises to protect against both Alzheimer's and stroke. The new vaccine repairs vascular damage in the brain by rounding up "troops" from the body's own immune system.

And in addition to its prophylactic effect, it can work even when Alzheimer's symptoms are already present. The research on this new technology was recently accepted for publication in the journal *Neurobiology of Aging*.

A natural way to fight Alzheimer's

"Using part of a drug that was previously tested as an influenza drug, we've managed to successfully induce an immune response against amyloid proteins in the blood vessels," says Dr. Frenkel, who collaborated on this project with Prof. Howard L. Weiner of Brigham and Women's Hospital, Harvard Medical School. "In early pre-clinical studies, we've found it can prevent both brain tissue damage and restore cognitive impairment," he adds.

Modifying a vaccine technology owned by Glaxo Smith Kline, a multinational drug company, Tel Aviv University's new therapeutic approach activates a natural mechanism in our bodies that fights against vascular damage in the brain.

The vaccine, Dr. Frenkel explains, activates macrophages - large proteins in the body that swallow foreign antigens. When the vaccine activates large numbers of these macrophages, they clear away the damaging build-up of waxy amyloid proteins in our brain's vascular system.

Animal models showed that once these proteins are cleared from the brain, further damage can be prevented, and existing damage due to a previous stroke can be repaired.

A new road to an Alzheimer's cure?

Could the breakthrough lead to both a vaccine and a long-sought cure for Alzheimer's disease? "It appears that this could be the case," says Dr. Frenkel, who worked on the study with his doctoral student Veronica Lifshitz and master degree students Ronen Weiss and Tali Benromano. "We've found a way to use the immune response stimulated by this drug to prevent hemorrhagic strokes which lead to permanent brain damage," he says.

In the animal models in mice, Dr. Frenkel's team worked with MRI specialist Prof. Yaniv Assaf and his Ph.D. student Tamar Blumenfeld-Katzir of Tel Aviv University's Department of Neurobiology and then with "object recognition" experiments, testing their cognitive functioning both before and after administration of the vaccine. MRI screenings confirmed that, after the vaccine was administered, further vascular damage was prevented, and the object recognition experiments indicated that those animals treated with the new vaccine returned to normal behavior.

Dr. Frenkel believes that this approach, when applied to a human test population, will be able to prevent the downward health spiral of Alzheimer's and dementia. The vaccine could be given to people who are at risk, those who show very early symptoms of these diseases, and those who have already suffered strokes to repair any vascular damage.

So far the vaccine has shown no signs of toxicity in animal models. Dr. Frenkel is hopeful that this new approach could lead to a cure, or at least an effective treatment, for the vascular dementia found in 80% of all people with Alzheimer's.

http://www.eurekalert.org/pub_releases/2011-02/f-mis022811.php

Minimally invasive surgeries: Laser suturing

More and more often, abdominal surgeries are being carried out in a minimally invasive manner.

A small incision in the abdominal wall is sufficient for the surgeon to be able to insert the instrument and make the organs visible with an endoscope. This technique is gentler and does not stress the body as much as traditional surgeries do. However, these minimally invasive surgeries pose a special challenge to the surgeons. In particular, the suturing – meaning joining the tissue with needle and suture material - demands great skill and dexterity. Very often, piercing the tissue and tying the knots is difficult – after all, the surgeons must perform surgeries in very tight quarters, while having very little room to move. Unlike when sewing textiles, a knot must be made after every stitch, which is a very exacting process that stresses the patient and can cause a number of complications. If the suture is too tight, there is the danger of a minor hemorrhage. In addition, the suture material can cut into the tissue and strangulate vessels. In worst cases the tissue may even die. However, if the suture is too loose, there may be bleeding at the edges of the wound.

Currently, setting the correct suture tension depends on the experience of the surgeon. He must subjectively estimate the optimum tension – and do this anew for every surgery. He does not have access to a reproducible, standardized setting. In the future, a minimally invasive suturing instrument shall make suturing easier. The researchers of the Fraunhofer Institute for Production Technology IPT in Aachen have developed this instrument within the scope of the InnoNet project "The Suture" (see below). In a new, semi-automatic process the suturing instrument enables the surgeon to connect the suture material with a previously set, predefined tension. Not only does it shorten the suturing process with respect to time, it also hastens the healing of the wound. The patient is able to recover more quickly. "With our new device, the edges of the wound can be joined quickly and safely, since it automatically ensures the optimum tension for the suture. The surgeon no longer has to deal with that. In the future, the difficult task of knotting the ends of the suture material will no longer be necessary, since they simply will be welded with the laser," explains Dipl.-Ing. Adrian Schütte, a scientist at the IPT.

The idea for this process is based on the laser welding process for plastics. During this process, two thermo-plastic pieces to be lasered together are welded together by means of laser energy. Adrian Schütte said: "In our case, the suture material is one of the two pieces to be lasered together, the other one is the sleeve. It is located in the tip of the new suturing device, which has a diameter of ten millimeters."

But, how does the new process work? First, the surgeons access the abdominal cavity through a small tube – the experts call it a trocar. After they pierce the tissue with a needle, they pull the end of the suture material out with the surgical forceps, through the trocar, and clip it into the sleeve. A defined tension can be set for the suture by pushing the sleeve through the trocar and simultaneously tensioning the suture. Once the desired tension has been achieved, the suture material is welded to the sleeve by laser. The laser is located at the end of the suturing instrument, the laser beam is sent via the light conducting fiber through the instrument. The superfluous suturing material is cut off behind the sleeve. And, as a last step, the surgeons pull the suturing instrument out through the trocar. After the lasering, the sleeve remains in the abdominal cavity. Schütte remarked: "Currently, the sleeve consists of polypropylene, in the future we would like to manufacture it from resorbing materials."

Together with the InnoNet Project Partners (see below), the scientist and his team were already able to successfully carry out the suturing process during tests in the laboratory. The expert remarked: "We were able to achieve the best results with a suture tension of zero to five Newton and a lasering time of 0.1 seconds." The preclinical studies are slated to start in the course of this year at the Aachen university hospital. To begin with, the suturing instrument will be utilized for minimally invasive surgeries in the abdominal area. The researcher is convinced that it can also be adapted to keyhole surgeries of the heart. The researchers from the IPT will display a prototype of the minimally invasive suturing instrument at the MEDTEC Europe Fair in Stuttgart (Hall 11, Booth 6211) from March 22 - 24, 2011.

http://www.eurekalert.org/pub_releases/2011-02/soa-dta022811.php

Development team achieves 1 terabit per second data rate on a single integrated photonic chip

Infinera Corp. to present research on high-speed photonic integrated circuits at OFC/NFOEC 2011

WASHINGTON - With worldwide Internet data traffic increasing by 50 percent each year, telecommunications companies that handle this digital torrent must be able to economically expand the capacities of their networks while also adapting to new, more-efficient data-handling technologies. Over the last decade, a development team at Infinera Corp. in Sunnyvale, Calif. has pioneered the design and manufacture of photonic integrated circuits (PICs) aimed at meeting that need. This technology has enabled the team to achieve a record one trillion bits per second (1 Terabit/s) speed on a single integrated indium phosphide chip. The findings will be presented at the Optical Fiber Communication Conference and Exposition/National Fiber Optic Engineers Conference (OFC/NFOEC) taking place March 6 – 10 at the Los Angeles Convention Center.

"Traditional transponder-based system architectures are inflexible and costly and time-consuming to upgrade," said Dr. Radhakrishnan Nagarajan, research fellow at Infinera and a senior member of Infinera's PIC development team. "Our PIC approach enables us to make optical networks more powerful, flexible and reliable than ever before using equipment that is significantly smaller, less expensive and uses much less energy."

Infinera's latest PIC is at the heart of a new 10-channel receiver, each channel operating at 100 Gbit/s data rates. This is the first in the industry to achieve a capacity of 1 Terabit/s on a single photonic integrated chip. It contains more than 150 optical components - such as frequency tunable local oscillator (LO) lasers, devices for mixing the LO and incoming signals, variable optical attenuators for LO power control, a spectral demultiplexer to separate the individual wavelength channels, and 40 balanced photodetector (receiver/transmitter) pairs - all integrated onto a chip smaller than a fingernail.

The key technical advance operating behind 100-Gbit/s-per-channel technology is the ability to detect incoming data encoded using the optical industry's most spectrally efficient modulation technique, called polarization multiplexed Quadrature Phase-Shift Keying, or PM-QPSK. To explain the acronym, first PM: it is similar to the wireless communications technique of alternating the polarization of adjacent channels. How does QPSK work? In virtually all types of data transmission, the information is encoded in ways that allow it to travel the farthest while occupying the least amount of signal spectrum. Just as radio's AM (amplitude modulation) and FM (frequency modulation) imprints information on, respectively, the amplitude and frequency of its broadcast waves, QPSK modifies the light's phase to represent the data. All in all, PM-QPSK permits four times more information to be conveyed each second than was possible with the previous method, which simply switched the laser light on and off.

The news here is not about the PM-QPSK modulation scheme per se, but rather that Infinera has, for the first time, integrated it all onto a single 10x100 Gbit/s photonic integrated circuit.

"But just as important as a transmitter's clever and efficient encoding method is a fast and reliable way for the receiver to convert the information back to its original form," said Dr. Nagarajan. "For PM-QPSK, we designed and integrated narrow-linewidth lasers that detect the phase encoded data very efficiently."

Infinera expects PICs with a capability of a terabit or more to be commercially available within a few years. The company has announced that a 500 Gbit/s PIC will be available in 2012. Infinera's 100 Gbit/s PICs are widely deployed in long-haul and metro networks worldwide.

Transmitter and receiver PICs are typically installed at critical nodes and at each end of "long haul" optical networks. Like non-stop flights between airline hubs, these intercity and intercontinental optical fiber links carry the bulk of Internet traffic. Worldwide, more than 20 exabytes - 20 trillion trillion bytes (or 160 exabits) - have been estimated to pass through the Internet every month.

PICs enable massive amounts of cost-effective bandwidth and facilitate the networks at the heart of the Internet to become more scalable and quicker to react to sudden changes in demand. "In many ways, PIC-based optical networks are starting to take on the intelligent features of routed (IP) networks, like the ability to reroute traffic in the event of a break in the fiber - but at a fraction of the cost and power consumption," Dr. Nagarajan added.

Dr. Nagarajan's presentation at OFC/NFOEC, titled "10-channel, 100Gbit/sec per channel dual polarization coherent QPSK, monolithic InP receiver photonic integrated circuit," will take place Monday, March 7 at 3:15 p.m. in the Los Angeles Convention Center.

http://www.eurekalert.org/pub_releases/2011-02/aaon-met022211.php

More evidence that Alzheimer's disease may be inherited from your mother

ST. PAUL, Minn. – Results from a new study contribute to growing evidence that if one of your parents has Alzheimer's disease, the chances of inheriting it from your mother are higher than from your father.

The study is published in the March 1, 2011, print issue of *Neurology*®, the medical journal of the American Academy of Neurology. "It is estimated that people who have first-degree relatives with Alzheimer's disease are four to 10 times more likely to develop the disease themselves compared to people with no family history," said study author Robyn Honea, DPhil, of the University of Kansas School of Medicine in Kansas City.

For the study, 53 dementia-free people age 60 and over were followed for two years. Eleven participants reported having a mother with Alzheimer's disease, 10 had a father with Alzheimer's disease and 32 had no history of the disease in their family. The groups were given brain scans and cognitive tests throughout the study.

The researchers found that people with a mother who had Alzheimer's disease had twice as much gray matter shrinkage as the groups who had a father or no parent with Alzheimer's disease. In addition, those who had a mother with Alzheimer's disease had about one and a half times more whole brain shrinkage per year compared to those who had a father with the disease. Shrinking of the brain, or brain atrophy, occurs in Alzheimer's disease.

"Using 3-D mapping methods, we were able to look at the different regions of the brain affected in people with maternal or paternal ties to Alzheimer's disease," said Honea. "In people with a maternal family history of the disease, we found differences in the break-down processes in specific areas of the brain that are also affected by Alzheimer's disease, leading to shrinkage. Understanding how the disease may be inherited could lead to better prevention and treatment strategies."

The study was supported by the National Institute on Aging and the National Institute of Neurological Disorders and Stroke.

<http://www.bbc.co.uk/news/uk-england-oxfordshire-12598054>

Oxford scientists say trumpets in daffodils are 'new organ'

A team of Oxford scientists claim to have defined exactly what the trumpet of a daffodil is.

Flowers are usually built from the same basic four parts: sepals, petals, stamens and carpels, but daffodils also have a fifth part, known as the trumpet, or corona.

Scientists have questioned since the 19th Century whether the trumpet is related to the stamens or the petals, and in the 1930s botanist Agnes Arber decided it was part of the latter. However, after dissecting hundreds of bulbs Professor Robert Scotland and his team at the University of Oxford have suggested that the trumpet is a new organ. "It's the way novelties evolve in nature," he told the BBC. "They don't use existing structures."



The daffodil has a large corona (trumpet) in addition to the other floral organs

Bleeding fingers

Professor Scotland was teaching a botany field course in the Algarve, Portugal, when upon examining a Hoop-Petticoat Daffodil a student asked him what the trumpet was. "It was one of those moments when a student asks one of the most basic questions and I looked at it and realised I had never thought about it before," Professor Scotland said. "It niggled away at me because I wasn't able to give a satisfactory answer to the student."

His team at the university decided to examine the flowers as they formed, dissecting so many of the bulbs that their fingers were bleeding from the effort. They discovered that the other organs were made before the corona began to form. "The four organs sit on a special little platform area and it's that platform where the corona is initiated, not as part of the petals or stamens, but actually as part of this region called the hypanthium.

"We've been able to look at very early flower development. What we've managed to document is that the whole flower is made - the sepals, petals, stamens and carpels - and at that stage there's no sign of the corona.

"All the floral groundplan is specified in floral development and then very late in the platform area there is a reawakening of some tissue that turns out to be the corona." The daffodil is one of the most recognisable flowers in the UK and will be widely worn on St David's Day as the national flower of Wales.

Professor Scotland said: "The fascination for me has been because there are only four organs to most flowers, and because there's so many different types of flowers and that basic system is highly conserved. "The evolution of novelty within such a highly conserved but diverse system is interesting.

"It's part of understanding the natural world. Whether that's new species, new genera or just what the trumpet of a daffodil is."

Spontaneous smoking cessation may be an early symptom of lung cancer, research suggests

48 percent of patients in study quit before diagnosis, most before onset of symptoms

Many longtime smokers quit spontaneously with little effort shortly before their lung cancer is diagnosed, leading some researchers to speculate that sudden cessation may be a symptom of lung cancer.

Most patients who quit did so before noticing any symptoms of cancer, according to the study, which was published in the March issue of the Journal of Thoracic Oncology (JTO), the official monthly journal of the International Association for the Study of Lung Cancer (IASLC).

"It is widely known that many lung cancer patients have stopped smoking before diagnosis," said Dr. Barbara Campling, professor in the Department of Medical Oncology at Thomas Jefferson University in Philadelphia. "This observation is often dismissed, by saying that these patients must have quit because of symptoms of their cancer. However, we found that the majority of lung cancer patients who stopped smoking before diagnosis quit before the onset of symptoms. Furthermore, they often quit with no difficulty, despite multiple previous unsuccessful quit attempts. This has led us to speculate that, in some cases, spontaneous smoking cessation may be an early symptom of lung cancer."

Researchers interviewed 115 lung cancer patients from the Philadelphia Veterans Affairs Medical Center, all of whom had been smokers. Fifty-five (48%) had quit smoking before diagnosis, and only six of those (11%) had experienced symptoms of lung cancer by the time they quit. Patients with lung cancer who quit were as dependent on nicotine, when their smoking was at its highest point, as those who continued to smoke. Yet 31% reported quitting with no difficulty.

For comparison, researchers also interviewed patients with prostate cancer and those who had suffered a heart attack. They found that the median interval between quitting smoking and lung cancer diagnosis was 2.7 years. This compared with 24.3 years for prostate cancer and 10 years for a heart attack.

Researchers speculated that spontaneous smoking cessation may be a presenting symptom of lung cancer, possibly caused by tumor secretion of a substance interfering with nicotine addiction.

The results should not encourage smokers to continue smoking, Campling said.

"There is a danger that this study could be misinterpreted as suggesting that heavy smokers should continue smoking," Campling said. "We emphasize that all smokers must be strongly encouraged to stop."

Watchful waiting no longer recommended for some high-risk Barrett's esophagus patients

New guidelines developed to address major clinical issues encountered in the treatment of Barrett's esophagus

Bethesda, MD - Endoscopic removal of pre-cancerous cells in patients with confirmed, high-risk Barrett's esophagus is recommended rather than surveillance, according to a new "Medical Position Statement on the Management of Barrett's Esophagus," published by the American Gastroenterological Association (AGA) Institute. The medical position statement was published in *Gastroenterology*, the official journal of the AGA Institute.

In patients with Barrett's esophagus, the normal cells lining the esophagus are replaced with tissue that is similar to the lining of the intestine. The goal of endoscopic eradication therapy is to permanently eliminate all intestinal-type cells in the esophagus. A small number of people with Barrett's esophagus develop a rare, but often deadly, type of cancer of the esophagus.

"The AGA's recommendations for the treatment of patients with Barrett's esophagus are based on the best data currently available within the medical literature," said John M. Inadomi, MD, AGAF, chair of the AGA Clinical Practice & Quality Management Committee. "When considering whether surveillance or endoscopic eradication therapy is the preferred management option for patients with Barrett's esophagus, the AGA strongly supports the concept of shared decision-making between the treating physician and patient."

The AGA recommends endoscopic eradication therapy with radiofrequency ablation (RFA), photodynamic therapy (PDT) or endoscopic mucosal resection (EMR), as follows for various patient groups:

* Patients with confirmed high-grade dysplasia (advanced pre-cancerous cells): endoscopic eradication therapy is recommended.

* Patients with confirmed low-grade dysplasia (beginning pre-cancerous cells): endoscopic eradication therapy is a treatment option and should be discussed with patients as such.

* Patients with Barrett's esophagus without abnormal cells: endoscopic eradication therapy is not recommended.

If eradication therapy is not indicated, is not available or is declined by a patient with Barrett's esophagus, surveillance by endoscopy should be performed every three months in patients with high-grade dysplasia, every six to 12 months in patients with low-grade dysplasia, and every three to five years in patients with no dysplasia.

"The recommendations in the medical position statement were made under the assumption that a patient's diagnosis and the presence or absence of low and high grade dysplasia would be accurate to the highest degree possible using the best current standards of practice," according to Stuart J. Spechler, MD, AGAF, a member of the AGA Institute Medical Position Panel. High grade dysplasia is an abnormal growth that has a high risk for cancer development.

Most patients (70 to 80 percent) with high-grade dysplasia can be successfully treated with endoscopic eradication therapy. Esophagectomy (surgical removal of all or part of the esophagus) in patients with high-grade dysplasia is an alternative; however, current evidence suggests that there is less morbidity with ablative therapy.

Other findings of the medical position statement on the management of Barrett's esophagus include:

* In patients with multiple risk factors associated with esophageal cancer (age ≥ 50 years, male gender, Caucasian, chronic gastroesophageal reflux disease [GERD], hiatal hernia, elevated body mass index and intra-abdominal distribution of body fat), AGA suggests screening for Barrett's esophagus. We recommend against screening the general population with GERD for Barrett's esophagus.

* The diagnosis of dysplasia in Barrett's esophagus should be confirmed by at least one additional pathologist, preferably one who is an expert in esophageal histopathology.

* For patients with Barrett's esophagus, GERD therapy with medication effective to treat GERD symptoms and to heal reflux is clearly indicated, as it is for patients without Barrett's esophagus. However, evidence to support the use of acid-reducing agents, specifically proton pump inhibitors, in patients with Barrett's esophagus solely to reduce the risk of progression to dysplasia or cancer is indirect and has not been proven in a long-term controlled trial.

* Given that cardiovascular deaths are more common than deaths from esophageal cancer among patients with Barrett's esophagus, screening for cardiovascular risk factors and interventions is warranted.

It is expected that, each year, every one in 200 patients diagnosed with Barrett's esophagus will develop esophageal cancer, which is a devastating disease. For advanced esophageal cancers, the current treatment options are limited and odds of survival remain low; it is nearly universally terminal. However, while patients diagnosed with Barrett's esophagus, especially those with pre-cancerous cells, feel an increased level of anxiety and emotional burden, the actual risk of death from esophageal cancer remains low. Patients with Barrett's esophagus appear to have an increased risk of death from cardiovascular disease, perhaps due to an association with obesity.

The conclusions of the medical position statement are based on the best available evidence (as the technical review discusses), or in the absence of quality evidence, the expert opinions of the medical position panel convened to critique the technical review and structure the medical position statement.

To develop the guidelines, a set of 10 broad questions were identified by experts in the field to encapsulate the most common management questions faced by clinicians. To review recommendations and grades, view the American Gastroenterological Association Medical Position Statement on the Management of Barrett's Esophagus.

<http://www.ars.usda.gov/is/AR/2011/mar11/tea0311.htm>

Reading Herbal Tea Leaves: Benefits and Lore

These days, there is a lot of talk about health benefits from drinking teas.

Green, black, and oolong are considered the three major classes, and each comes from the age-old *Camellia sinensis* tea bush. But there is an even wider variety of herbal teas - infusions derived from anything other than *C. sinensis*.

According to folklore, some herbal teas also provide benefits. But there is little clinical evidence on the effects of drinking these teas. Now, Diane McKay and Jeffrey Blumberg have looked into science-based evidence of health benefits from drinking three of the most popular herbals in America. McKay and Blumberg are with the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston, Massachusetts. Both work at the center's Antioxidants Research Laboratory, which Blumberg directs.

One popular herbal, chamomile tea, has long been considered a soothing brew. In the early 20th century, it was mentioned in a classic children's book about a little rabbit named Peter. At the end of a rough day, Peter's mom served him some chamomile tea. Interestingly, when Blumberg and McKay reviewed scientific literature on the bioactivity of chamomile, they found no human clinical trials that examined this calming effect.

They did, however, publish a review article on findings far beyond sedation - describing test-tube evidence that chamomile tea has moderate antioxidant and antimicrobial activities and significant antiplatelet-clumping activity. Also, animal feeding studies have shown potent anti-inflammatory action and some cholesterol-lowering activity.

The researchers also published a review article describing evidence of bioactivity of peppermint tea. In test tubes, peppermint has been found to have significant antimicrobial and antiviral activities, strong antioxidant and antitumor actions, and some antiallergenic potential. When animals were fed either moderate amounts of ground leaves or leaf extracts, researchers also noted a relaxation effect on gastrointestinal tissue and an analgesic and anesthetic effect in the nervous system.

The researchers found several human studies involving peppermint oil, but they found no data from human clinical trials involving peppermint tea. McKay and Blumberg have concluded that the available research on herbal teas is compelling enough to suggest clinical studies.

McKay has led a human clinical trial to test whether drinking hibiscus tea affects blood pressure. She tested 65 volunteers, aged 30 to 70 years, who were pre- or mildly hypertensive. Blood pressure readings of 120/80 or greater are considered a risk factor for heart disease, stroke, and kidney disease.

For 6 weeks, about half the group was randomly selected to drink 3 cups of hibiscus tea daily. The others drank a placebo beverage containing artificial hibiscus flavoring and color. All participants were advised to follow their usual diet and maintain their normal level of activity. Before the start of the study, blood pressure was measured twice - 1 week apart - and at weekly intervals thereafter.

The findings show that the volunteers who drank hibiscus tea had a 7.2-point drop in their systolic blood pressure (the top number), and those who drank the placebo beverage had a 1.3-point drop.

In a subgroup analysis of the 30 volunteers who had the highest systolic blood pressure readings (129 or above) overall at the start of the study, those assigned to drink hibiscus tea showed the greatest response to hibiscus tea drinking. Their systolic blood pressure went down by 13.2 points, diastolic blood pressure went down by 6.4 points, and mean arterial pressure went down by 8.7 points.

"This data supports the idea that drinking hibiscus tea in an amount readily incorporated into the diet may play a role in controlling blood pressure, although more research is required," says McKay. - By Rosalie Marion Bliss, Agricultural Research Service Information Staff. The 2010 study was published in the Journal of Nutrition.

This research is part of Human Nutrition, an ARS national program (#107) described at www.nps.ars.usda.gov. Diane L. McKay is with the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington St., Boston, MA 02111-1524; (781) 608-7183.

"Reading Herbal Tea Leaves: Benefits and Lore" was published in the [March 2011 issue of Agricultural Research magazine. \(html\)](#) or [\(pdf\)](#)

http://www.eurekalert.org/pub_releases/2011-03/yu-sts030111.php

Stronger than steel, novel metals are moldable as plastic

New Haven, Conn. - *Imagine a material that's stronger than steel, but just as versatile as plastic, able to take on a seemingly endless variety of forms.*

For decades, materials scientists have been trying to come up with just such an ideal substance, one that could be molded into complex shapes with the same ease and low expense as plastic but without sacrificing the strength and durability of metal.

Now a team led by Jan Schroers, a materials scientist at Yale University, has shown that some recently developed bulk metallic glasses (BMGs) - metal alloys that have randomly arranged atoms as opposed to the orderly, crystalline structure found in ordinary metals - can be blow molded like plastics into complex shapes that can't be achieved using regular metal, yet without sacrificing the strength or durability that metal affords. Their findings are described online in the current issue of the journal *Materials Today*.

"These alloys look like ordinary metal but can be blow molded just as cheaply and as easily as plastic," Schroers said. So far the team has created a number of complex shapes - including seamless metallic bottles, watch cases, miniature resonators and biomedical implants - that can be molded in less than a minute and are twice as strong as typical steel.

The materials cost about the same as high-end steel, Schroers said, but can be processed as cheaply as plastic. The alloys are made up of different metals, including zirconium, nickel, titanium and copper.

The team blow molded the alloys at low temperatures and low pressures, where the bulk metallic glass softens dramatically and flows as easily as plastic but without crystallizing like regular metal. It's the low temperatures and low pressures that allowed the team to shape the BMGs with unprecedented ease, versatility and precision,

Schroers said. In order to carefully control and maintain the ideal temperature for blow molding, the team shaped the BMGs in a vacuum or in fluid.

"The trick is to avoid friction typically present in other forming techniques," Schroers said. "Blow molding completely eliminates friction, allowing us to create any number of complicated shapes, down to the nanoscale."

Schroers and his team are already using their new processing technique to fabricate miniature resonators for microelectromechanical systems (MEMS) - tiny mechanical devices powered by electricity - as well as gyroscopes and other resonator applications.

In addition, by blow molding the BMGs, the team was able to combine three separate steps in traditional metal processing (shaping, joining and finishing) into one, allowing them to carry out previously cumbersome, time- and energy-intensive processing in less than a minute.

"This could enable a whole new paradigm for shaping metals," Schroers said. "The superior properties of BMGs relative to plastics and typical metals, combined with the ease, economy and precision of blow molding, have the potential to impact society just as much as the development of synthetic plastics and their associated processing methods have in the last century."

Other authors of the paper include Thomas M. Hodges and Golden Kumar (Yale University); Hari Raman and A.J. Barnes (SuperformUSA); and Quoc Pham and Theodore A. Waniuk (Liquidmetal Technologies).

<http://www.nytimes.com/2011/03/01/science/01dinosaur.html>

Dinosaur-Hunting Hobbyist Makes Fresh Tracks for Paleontology

By SINDYA N. BHANOO

Last week, Mike Taylor identified a new dinosaur called *Brontomerus mcintoshi*, a sauropod with uncommonly large, powerful thighs.

It is the second dinosaur he's named in five years and his 13th paleontology publication.

That would be impressive though not unusual for a hard-working full-time paleontologist. But Mike Taylor is a 42-year-old British computer programmer who writes code for a living in a quaint English village called Ruardean.

Hunting for dinosaurs is just a hobby, albeit one he pursues seriously.

One day 10 years ago, while reading a paleontology paper on a long plane trip, he had an epiphany.

"I thought, well, blimey, I could do better than that," he said. "And then I decided, why shouldn't I? What's stopping me?"

His childhood interest in dinosaurs was rekindled in 2000 and he got hold of classic books like "The Dinosaur Heresies," "The Complete Dinosaur" and the "Dinosaur Encyclopedia." He amassed a collection of paleontology journals and studied them with the intensity of a graduate student.

Dr. Taylor, whose numerous papers earned him a formal Ph.D. in paleontology in 2009 from the University of Portsmouth, is not alone in his love for dinosaurs. The public has long had a fascination for the magnificent creatures that lived millions of years ago, some dwarfing elephants in size.

"There are many dino fan boys out there," Dr. Taylor said. "And I was just another one of them."

His latest discovery, *Brontomerus mcintoshi*, is named after John McIntosh, one other such "fan boy."

Dr. McIntosh spent his career as a physics professor at Wesleyan. But he spent his spare hours poring over bones in museums around the world. And when he retired 20 years ago, he devoted himself to the study of sauropods, the order of large, plant-eating dinosaurs that Dr. Taylor also favors.

Over the course of more than 30 years, Dr. McIntosh made major contributions to the field, writing many papers and several books. In 1979, he helped prove that paleontologists had mounted the wrong head on a sauropod named *Apatosaurus*. "Even a minor paleontologist can make a major contribution," Dr. Taylor said.

Other scientific disciplines, like physics and genetics, require fancy equipment, large labs and major funding. Although paleontology has come to depend more and more on CT scans and even molecular analyses, it still has plenty of room for the time-honored pursuit of puzzling through bones and piecing them together.

"You just need a decent camera, a little time and money to travel to museums, some experience, a good eye," said Nicholas Longrich, a paleontologist at Yale. "It's still hard - not just anybody can do it - but the barrier to entry is a lot lower than for other fields."

Dr. Taylor has never participated in an excavation, instead choosing to study the scores of unnamed fossils that are collecting dust in the basements of museums. He takes pictures from many angles and makes detailed measurements that he studies.

"Given the limited time I have available for paleo, conferences and museum visits are more important," he said.

His first discovery, a bone belonging to an elephant-size herbivorous dinosaur called Xenoposeidon, was excavated in the early 1890s. It was acquired by the Natural History Museum in London, and remained unidentified until Dr. Taylor began studying it. And the dinosaur he recently named was found at a site in Utah in 1995 and housed in the Sam Noble Oklahoma Museum of Natural History, unidentified.

“Our museums are chock-full of things that have never been studied, or explained at all,” said Mathew Wedel, a paleontologist and anatomist at Western University of Health Sciences and Dr. Taylor’s co-author on the Brontomerus paper.

He and Dr. Taylor became pen pals 10 years ago, when Dr. Taylor sent him an e-mail about one of his publications. Then they began brainstorming and sharing ideas. The two are now best friends, and usually meet about once a year at paleontology conferences and museums to collaborate.

Although Dr. Wedel is employed in paleontology full time, he sees great benefits to working with Dr. Taylor, who provides a fresh perspective.

“There was no such thing as the professional scientist at one time,” he said. “Along the way we lost something, and it’s this idea that anybody can contribute to human knowledge.”

<http://news.discovery.com/tech/portable-scanner-analyzes-cancer-cells-in-an-hour-110301.html>

Portable Scanner Analyzes Cancer Cells in an Hour

By Amy Dusto | Tue Mar 1, 2011 09:41 AM ET

Waiting for pathology results on suspicious cells can take days, and long, anxious ones at that.

But tech-savvy doctors could soon use a device built at the Massachusetts General Hospital to get biopsy results in less than an hour, from right in the office.

The machine is a portable nuclear magnetic resonance (NMR) scanner which can identify molecules by measuring how a magnetic field affects their nuclei. First the physician collects patient cell samples, which are miniscule enough to be aspirated with a fine needle from multiple sites of a suspect tumor, increasing the accuracy of the results. Then the physician puts the cells into the scanner and connects it to a smartphone, of all things. The device looks for signs of nine proteins specific to cancer cells in order make its diagnosis. With a custom app, the doctor can read the results from the machine within the hour.

Normally, this process involves a doctor sending a sample out to a pathology lab, waiting for them to analyze it, and relaying the result back to a patient. The mini-NMR setup deletes the middle man and eases the process for doctor and patient.

Better still, in tests so far, the device has been more accurate than some standard results. In fact, one test on 20 patients was 100 percent correct. Another was correct for 48 out of 50 people. The [results of the study](#) were published on February 23rd in the journal Science Translational Medicine.

And while waiting for results ... Angry Birds, anyone?

http://www.sciencenews.org/view/generic/id/70311/title/Lab-engineered_organism_fights_malaria

Lab-engineered organism fights malaria

Fungus attacks not just mosquitoes, but parasites inside them

By Daniel Strain

Malaria’s new worst enemy may be a fungus.

A fungus? Try stealth assassin. Strains of a common fungus engineered by a U.S.-British team can eliminate more than 90 percent of malaria parasites deep within the insects that carry them, the team reports February 25 in Science.

Malaria is caused by several species of single-celled organisms known as protozoans. But the disease is really an insect’s game. Mosquitoes are malaria’s taxi service, shuttling pathogens from person to person and town to town. Good malaria control, then, is about good insect control, says Andrew Read, an evolutionary biologist at Penn State University in University Park, Pa.

'SHROOMED*In a new approach to malaria control, killer lab-built fungi poison infect mosquitos and poison the malaria parasites living inside the insects. The mosquitos die a few days later. Weiguo Fang*

The flow of pesticides to malaria-prone regions like Africa and Asia, however, has put mosquitoes under big pressure to evolve resistance to insect-killing chemicals. “These things work until the mosquito becomes resistant, and then you’re in trouble,” says Read, who was not involved in this study.

The tiny fungus *Metarhizium anisopliae* could present a solution. This fungus naturally infects mosquitoes but, unlike pesticides, takes days to kill them. That doesn’t sound like a good thing - more time means the mosquitoes have longer to mate, which means more mosquitoes. But the more bugs mate, the less reason they have to evolve resistance, since they are already able to pass along their genes. The fungus seems to walk a fine



line between promoting resistance by killing insects too early, and allowing too many chances to spread the disease by killing them too late.

Yet Raymond St. Leger and his colleagues didn't want to just kill insects. The team added a few new genes to the fungal DNA, turning *M. anisopliae* into a drug-producing factory. First, the modified fungus bores a hole into the mosquito. Inside, the added genes turn on and, depending on the fungal strain used, generate a host of malaria-killing chemicals, from scorpion toxins to proteins from the human immune system. The chemicals are bad for parasites but don't do any extra harm to mosquitoes, says St. Leger, an entomologist at the University of Maryland in College Park, Md.

"They're catching the malaria as it swims from the insect gut to the insect salivary gland," he says. One fungal strain cured malarial infections in about 75 percent of dosed insects, and killed more than 90 percent of the pathogens in the rest.

No one's sure how many malaria parasites it takes to actually launch the disease, says Adriana Costero-Saint Denis, a scientist with the National Institute of Allergy and Infectious Diseases, which funded the study. Rigorous testing will show whether St. Leger's super-fungi work under real-world conditions. "Even though this discovery is extremely exciting, it's still a long way from being a tool in the field," she says.

Genetic engineering involves a suite of regulatory issues and inevitably public critics, says Tom Miller, an entomologist currently on a fellowship in Washington, D.C., with the U.S. State Department. The modified fungi are safe but not miracle cures, adds Miller, who is working with St. Leger on a separate study. He'd like to see such tools used alongside new and better medicines.

St. Leger sees a lot of potential for lab-engineered assassin fungi - which scientists can mix into house paint or weave into mosquito nets. His newest efforts focus on killing Lyme disease inside tick innards. "We're not limited to what we already have," he says, "or what even nature has."

<http://www.nytimes.com/2011/03/01/science/01eyeball.html>

In a Marine Worm's Eyes, the Theory of Evolution

By CARL ZIMMER

Charles Darwin considered the evolution of the human eye one of the toughest problems his theory had to explain.

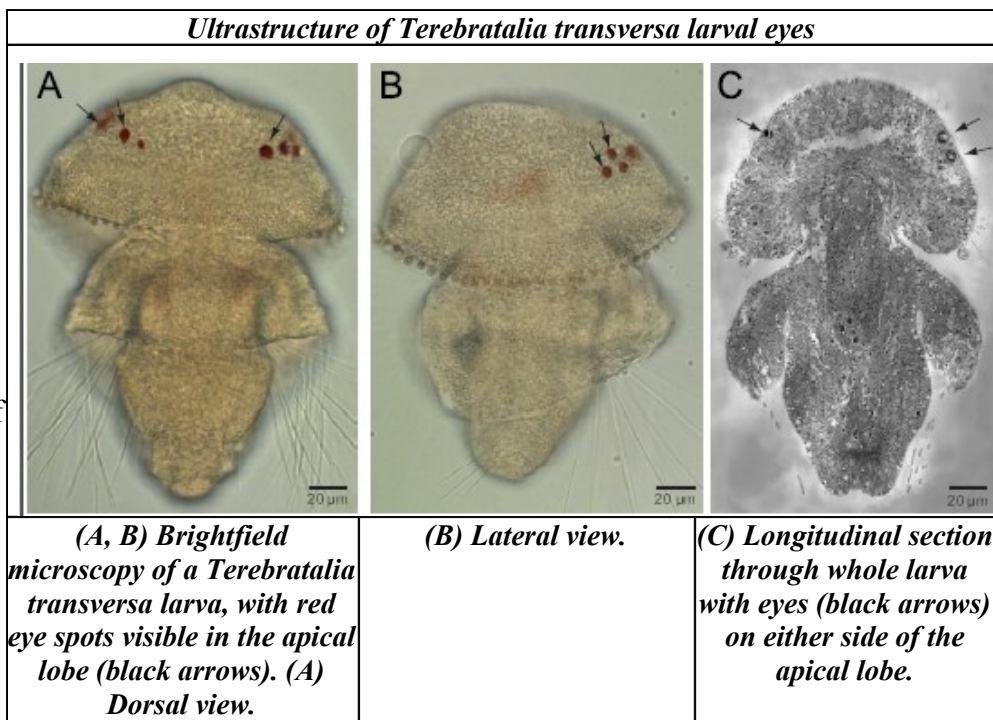
In "On the Origin of Species," he wrote that the idea that natural selection could produce such an intricate organ "seems, I freely confess, absurd in the highest possible degree."

But Darwin dispelled that seeming absurdity by laying out a series of steps by which the evolution could take place. Making this sequence all the more plausible was the fact that some of the transitional forms Darwin described actually existed in living invertebrates.

Now, a team of American and European researchers report that they have discovered an eye that could represent the first step in this evolution. They have found, in effect, a swimming eyeball.

"This is in no way the ancestor of the human eye, but it's the first time we have had a model of it," said Yale Passamanek, a postdoctoral researcher at the University of Hawaii. He and his colleagues [report the discovery](#) in the online journal *EvoDevo*.

The researchers made the discovery while studying a species of brachiopods, or lamp shells, which live in shells but are marine worms unrelated to mollusks like clams and oysters. Lamp shells have existed for over half a billion years, but their biology has long remained a mystery - including the simple question of whether they can see.



Four-day-old lamp shell larvae, for example, have puzzling dark spots on either side of the front end of their bodies. Recently, Carsten Lüter, a biologist at the Berlin Museum of Natural History, and his colleagues dissected the eyespots of some lamp shell larvae. They discovered that each spot was actually a pair of neurons, one for capturing light and one containing pigment. The neurons connected to a brainlike clump of neurons inside the larva.

Their anatomy suggested the spots were simple eyes. So Dr. Lüter and his colleagues contacted Dr. Passamanek and his colleagues at the University of Hawaii, who are experts on the genes for animal photoreceptors. The Hawaii researchers discovered that, indeed, photoreceptor genes were active in the dark spots. But to be thorough, Dr. Passamanek checked to see if the photoreceptor genes were active at other stages. "I thought, 'I'm just going to eliminate that possibility,'" he said.

Just the opposite happened. Dr. Passamanek discovered that the genes were active much earlier, just 36 hours after fertilization, when the lamp shell embryo was merely a cup-shaped mass of a few hundred cells.

Dr. Passamanek was baffled. "There are no neurons at that stage," he said. Nevertheless, it was clear that the outer surface of the cup was covered with photoreceptors.

To see if the embryos were doing something with the light, Dr. Passamanek and his colleagues put a light on one side of a dish of embryos. The lamp shell embryo is covered with tiny beating hairs, which it uses to swim in a spiral pattern. Dr. Passamanek found that after 20 minutes, twice as many embryos would end up on the illuminated side of the dish as on the dark side.

Dr. Passamanek and his colleagues hypothesize that the cells can detect the direction of light because it is blocked in some directions by the embryo's yolk. It can then use this information to change the rhythm of its hair.

It is possible, Dr. Passamanek said, that in the course of evolution, our own eyes started out as swimming eyeballs. Only later did the job of catching light get relegated to only some cells, which could send signals to their neighbors. And only much later did these specialist cells relay signals to brains.

Todd Oakley of the University of California, Santa Barbara, an expert on the evolution of vision, called the results "tantalizing." But he cautioned that just because the photoreceptor gene was active in the early embryo, that did not necessarily mean that the lamp shells were able to see. "Other possible photoreceptive mechanisms should also be ruled out," Dr. Oakley said. "Correlation does not mean causation."

Dr. Passamanek is making plans for these sorts of studies. For now, though, he remains a bit stunned at what he has stumbled across. "It's like Yogi Berra said," he said. "You can observe a lot by watching."

<http://www.bbc.co.uk/news/health-12610972>

Prostate cancer test is 'twice as good', say researchers

By Adam Brimelow Health Correspondent, BBC News

Scientists say they have developed an improved test for prostate cancer.

Researchers at the University of Surrey say their check is more accurate and less invasive than the current tests.

The new method could be widely available within 18 months, they say. Cancer Research UK has welcomed the findings, but says more work is needed. More than 36,000 men are diagnosed with prostate cancer in the UK every year. But the initial blood-test used by doctors - the PSA test - is unreliable.

Scientists at the University of Surrey have discovered that prostate cancers secrete a chemical called EN2 that can be found in a urine test.

More accurate

Their findings from a study of 288 patients, published in the journal *Clinical Cancer Research*, suggest this is better than the PSA check at detecting cancers, with far fewer false positives.

One of the researchers, Professor Hardev Pandha, said the new EN2 test was more reliable and accurate.

"In this study we showed that the new test was twice as good at finding prostate cancer as the standard PSA test," he said. "Only rarely did we find EN2 in the urine of men who were cancer free so, if we find EN2, we can be reasonably sure that a man has prostate cancer."

Larger-scale trials are now being planned in the UK and the United States. The researchers envisage the EN2 urine check would be used alongside the PSA blood test.

Stick test

Professor Pandha says it would be easy to develop a simple EN2 stick test - like a pregnancy test - that would allow men to get a result within five minutes.

PSA test

***Prostate-specific antigen (PSA) is a protein produced by the prostate gland
The test measures the level of PSA in the blood
The PSA level alone does not give doctors enough information about a possible cancer so it is used alongside other checks such as a rectal examination
Source: National Cancer Institute***

"The prospect of an immediate result that doesn't involve a blood test or an embarrassing examination may be helpful in getting more men with urinary symptoms to seek medical help."

The researchers are also examining whether the amount of EN2 in the urine could indicate the severity of the cancer, and whether immediate treatment is needed.

Professor Malcolm Mason, Cancer Research UK's prostate cancer expert, welcomed the findings. "The test seems to be simple, requiring only a urine sample, and may help in the early detection of prostate cancer. "However, more work needs to be done to find out whether or not EN2 is capable of distinguishing between aggressive prostate cancers that need treatment, and non-aggressive ones that don't."

The scientist and TV presenter Professor Robert Winston said this was an "exciting discovery which advances the early detection of this study".

But the Chief Executive of the Prostate Cancer Charity, John Neate, cautioned that the new test was not perfect.

"Given the known limitations of the PSA blood test, we welcome this research into a new potential test for prostate cancer; however, this is a relatively small study that first needs to be validated on a much larger scale."

http://www.eurekalert.org/pub_releases/2011-03/uorm-rfo030211.php

Researchers focus on human cells for spinal cord injury repair

Derived from stem cells -- restore movement in animal models

For the first time, scientists discovered that a specific type of human cell, generated from stem cells and transplanted into spinal cord injured rats, provide tremendous benefit, not only repairing damage to the nervous system but helping the animals regain locomotor function as well.

The study, published today in the journal PLoS ONE, focuses on human astrocytes – the major support cells in the central nervous system – and indicates that transplantation of these cells represents a potential new avenue for the treatment of spinal cord injuries and other central nervous system disorders.

Working together closely, research teams at the University of Colorado School of Medicine and University of Rochester Medical Center have made a major breakthrough in the use of human astrocytes for repairing injured spinal cords in rats.

"We've shown in previous research that the right types of rat astrocytes are beneficial, but this study brings it up to the human level, which is a huge step," said Chris Proschel, Ph.D., lead study author and assistant professor of Genetics at the University of Rochester Medical Center. "What's really striking is the robustness of the effect. Scientists have claimed repair of spinal cord injuries in rats before, but the benefits have been variable and rarely as strong as what we've seen with our transplants."

There is one caveat to the finding – not just any old astrocyte will do. Using stem cells known as human fetal glial precursor cells, researchers generated two types of astrocytes by switching on or off different signals in the cells. Once implanted in the animals, they discovered that one type of human astrocyte promoted significant recovery following spinal cord injury, while another did not.

"Our study is unique in showing that different types of human astrocytes, derived from the exact same population of human precursor cells, have completely different effects when it comes to repairing the injured spinal cord," noted Stephen Davies, Ph.D., first author and associate professor in the Department of Neurosurgery at the University of Colorado School of Medicine. "Clearly, not all human astrocytes are equal when it comes to promoting repair of the injured central nervous system."

The research teams from Rochester and Colorado also found that transplanting the original stem cells directly into spinal cord injured rats did not aid recovery. Researchers believe this approach – transplanting undifferentiated stem cells into the damaged area and hoping the injury will cause the stem cells to turn into the most useful cell types – is probably not the best strategy for injury repair.

According to Mark Noble, director of the University of Rochester Stem Cell and Regenerative Medicine Institute, "This study is a critical step toward the development of improved therapies for spinal cord injury, both in providing very effective human astrocytes and in demonstrating that it is essential to first create the most beneficial cell type in tissue culture before transplantation. It is clear that we cannot rely on the injured tissue to induce the most useful differentiation of these precursor cells."

To create the different types of astrocytes used in the experiment, researchers isolated human glial precursor cells, first identified by Margot Mayer-Proschel, Ph.D., associate professor of Genetics at the University of Rochester Medical Center, and exposed these precursor cells to two different signaling molecules used to instruct different astrocytic cell fate – BMP (bone morphogenetic protein) or CNTF (ciliary neurotrophic factor).

Transplantation of the BMP human astrocytes provided extensive benefit, including up to a 70% increase in protection of injured spinal cord neurons, support for nerve fiber growth and recovery of locomotor function, as measured by a rat's ability to cross a ladder-like track.

In contrast, transplantation of the CNTF astrocytes, or of the stem cells themselves, failed to provide these benefits. Researchers are currently investigating why BMP astrocytes performed so much better than CNTF astrocytes, but believe multiple complex cellular mechanisms are probably involved.

"It is estimated that astrocytes make up the vast majority of all cell types in the human brain and spinal cord, and provide multiple different types of support to neurons and other cells of the central nervous system," said Jeannette Davies, Ph.D., assistant professor at the University of Colorado School of Medicine and co-lead author of the study. "These multiple functions are likely to all be contributing to the ability of the right human astrocytes to repair the injured spinal cord."

With these results, the Proschel and Davies teams are moving forward on the necessary next steps before they can implement the approach in humans, including testing the transplanted human astrocytes in different injury models that resemble severe, complex human spinal cord injuries at early and late stages after injury.

"Studies like this one bring increasing hope for our patients with spinal cord injuries," said Jason Huang, M.D., associate professor of Neurosurgery at the University of Rochester Medical Center and Chief of Neurosurgery at Highland Hospital. "Treating spinal cord injuries will require a multi-disciplinary approach, but this study is a promising one showing the importance of modifying human astrocytes prior to transplantation and has significant clinical implications."

In addition to Proschel and Noble, Davies and Davies, Mayer-Proschel and Chung-Hsuan Shih from the University of Rochester Medical Center contributed to the research. Portions of this research were funded by the New York State Spinal Cord Injury Research Program, the Carlson Stem Cell Fund and private donations by the international spinal cord injury community.

http://www.eurekalert.org/pub_releases/2011-03/cfe-eow022811.php

Effectiveness of wastewater treatment may be damaged during a severe flu pandemic
Existing plans for antiviral and antibiotic use during a severe influenza pandemic could reduce wastewater treatment efficiency prior to discharge into receiving rivers, resulting in water quality deterioration at drinking water abstraction points.

These conclusions are published this week (2 March 2011) in a new paper in the journal *Environmental Health Perspectives*, which reports on a study designed to assess the ecotoxicologic risks of a pandemic influenza medical response. The research was carried out by a team from the Centre for Ecology & Hydrology (UK), the Institute for Scientific Interchange (Italy), Utrecht University (Netherlands), the University of Sheffield (UK), and Indiana University (USA).

The global public health community closely monitored the unfolding of the 2009 H1N1 influenza pandemic to best mitigate its impact on society. However, little attention was given to the impact that the medical response might have on the environment.

In order to evaluate this risk, the research team coupled a global spatially-structured epidemic model that simulates the quantities of antiviral and antibiotics used during an influenza pandemic of varying severity, with a water quality model applied to the Thames catchment in southern England to predict their environmental concentrations. An additional model was then used to assess ecotoxicologic effects of antibiotics and antiviral in wastewater treatment plants (WWTP) and rivers.

The research team concluded that, consistent with expectations, a mild pandemic (as in 2009) was projected to exhibit a negligible ecotoxicologic hazard. However in a moderate and severe pandemic nearly all WWTPs (80-100%) were projected to exceed the threshold for microbial growth inhibition, potentially reducing the capacity of the plant to treat wastewater. In addition, a proportion (5-40%) of the River Thames was similarly projected to exceed key thresholds for environmental toxicity, resulting in potential contamination and eutrophication at drinking water abstraction points.

Lead author Dr Andrew Singer, from the Centre for Ecology & Hydrology, said, "Our results suggest that existing plans for drug use during an influenza pandemic could result in discharge of inefficiently treated wastewater into the UK's rivers. The potential widespread release of antivirals and antibiotics into the environment may hasten the development of resistant pathogens with implications for human health during and potentially well after the formal end of the pandemic."

Dr Singer added, "We must develop a better understanding of wastewater treatment plants ecotoxicity before the hazards posed by a pandemic influenza medical response can be reliably assessed. However, the production and successful distribution of pre-pandemic and pandemic influenza vaccines could go a long way towards alleviating all of the identified environmental and human health problems highlighted in our paper, with the significant added benefit of reducing morbidity and mortality of the UK population.

This latter challenge of vaccination is probably society's greatest challenge, but also where the greatest gains can be made."

http://www.eurekalert.org/pub_releases/2011-03/slri-sft022811.php

Scientists from Toronto and Helsinki discover genetic abnormalities after creation of stem cells

Discovery sheds new light on the process of stem cell generation, and will help promote safer stem-cell based studies and future clinical trials

Toronto, ON and Helsinki, Finland Dr. Andras Nagy's laboratory at the Samuel Lunenfeld Research Institute of Mount Sinai Hospital and Dr. Timo Otonkoski's laboratory at Biomedicum Stem Cell Center (University of Helsinki), as well as collaborators in Europe and Canada have identified genetic abnormalities associated with reprogramming adult cells to induced pluripotent stem (iPS) cells. The findings give researchers new insights into the reprogramming process, and will help make future applications of stem cell creation and subsequent use safer. The study was published online today in Nature.

The team showed that the reprogramming process for generating iPS cells (i.e., cells that can then be 'coaxed' to become a variety of cell types for use in regenerative medicine) is associated with inherent DNA damage.

This damage is detected in the form of genetic rearrangements and 'copy number variations,' which are alterations of DNA in which a region of the genome is either deleted or amplified on certain chromosomes. The variability may either be inherited, or caused by de novo mutation.

"Our analysis shows that these genetic changes are a result of the reprogramming process itself, which raises the concern that the resultant cell lines are mutant or defective," said Dr. Nagy, a Senior Investigator at the Lunenfeld. "These mutations could alter the properties of the stem cells, affecting their applications in studying degenerative conditions and screening for drugs to treat diseases. In the longer term, this discovery has important implications in the use of these cells for replacement therapies in regenerative medicine."

"Our study also highlights the need for rigorous characterization of generated iPS lines, especially since several groups are currently trying to enhance reprogramming efficiency," said Dr. Samer Hussein, a McEwen post-doctoral scientist who initiated these studies with Dr. Otonkoski, before completing them with Dr. Nagy. "For example, increasing the efficiency of reprogramming may actually reduce the quality of the cells in the long run, if genomic integrity is not accurately assessed."

The researchers used a molecular technique called single nucleotide polymorphism (SNP) analysis to study stem cell lines, and specifically to compare the number of copy number variations in both early and intermediate-stage human iPS cells with their respective parental, originating cells.

Drs. Nagy and Otonkoski and their teams found that iPS cells had more genetic abnormalities than their originating cells and embryonic stem cells. Interestingly, however, the simple process of growing the freshly generated iPS cells for a few weeks selected against the highly mutant cell lines, and thus most of the genetic abnormalities were eventually 'weeded out.'

"However, some of the mutations are beneficial for the cells and they may survive during continued growth," said Dr. Otonkoski, Director and Senior Scientist at the Biomedicum Stem Cell Center.

Stem cells have been widely touted as a source of great hope for use in regenerative medicine, as well as in the development of new drugs to prevent and treat illnesses including Parkinson's disease, spinal cord injury and macular degeneration. But techniques for generating these uniquely malleable cells have also opened a Pandora's Box of concerns and ethical quandaries. Health Canada, the U.S. Food and Drug Administration and the European Union consider stem cells to be drugs under federal legislation, and as such, subject to the same regulations.

"Our results suggest that whole genome analysis should be included as part of quality control of iPS cell lines to ensure that these cells are genetically normal after the reprogramming process, and then use them for disease studies and/or clinical applications," said Dr. Nagy.

"Rapid development of the technologies in genome-wide analyses will make this more feasible in the future," said Dr. Otonkoski. "In addition, there is a need to further explore if other methods might mitigate the amount of DNA damage generated during the generation of stem cells," both investigators agreed.

The present study received support from the Stem Cell Network of Canada, the Canadian Institutes of Health Research and Ontario Ministry of Research and Innovation (for Dr. Nagy), the McEwen Centre Fellowship program (for Dr. Hussein), and the ESTOOLS network funding from the 6th Framework Program of the European Union (for Dr. Otonkoski).

http://www.eurekalert.org/pub_releases/2011-03/oup-rsa030111.php

Research suggests alcohol consumption helps stave off dementia

Experts agree that long-term alcohol abuse is detrimental to memory function and can cause neuro-degenerative disease. However, according to a study published in Age and Ageing by Oxford University Press today, there is evidence that light-to-moderate alcohol consumption may decrease the risk of cognitive decline or dementia.

Estimates from various studies have suggested the prevalence of alcohol-related dementia to be about 10% of all cases of dementia. Now researchers have found after analyzing 23 longitudinal studies of subjects aged 65 years and older that the impact of small amounts of alcohol was associated with lower incidence rates of overall dementia and Alzheimer dementia, but not of vascular dementia and cognitive decline. It is still an open question whether different alcoholic beverages, such as beer, wine, and spirits, all have a similar effect. Some studies have shown a positive effect of wine only, which may be due either to the level of ethanol, the complex mixture that comprises wine, or to the healthier life-style ascribed to wine drinkers.

A total of 3,327 patients were interviewed in their homes by trained investigators (physicians, psychologists, gerontologists) and reassessed one and a half years and three years later. Information on the cognitive status of those who had died in the interim was collected from family members, caregivers or primary care physicians.

Among the 3,327 patients interviewed at baseline, 84.8% (n=2,820) could be personally interviewed one and a half years later and 73.9% (n=2,460) three years later. For the vast majority of subjects who could not be personally interviewed, systematic assessments (follow-up 1: 482; follow-up 2: 336) focusing particularly on dementia could be obtained from GPs, relatives or caregivers. Within three years, follow-up assessments were unavailable for only 49 subjects (1.5%). Proxy information could be obtained for 98.0% (n=295) of the 301 patients who had died in the interim. Since dementia is associated with a higher mortality rate, proxy information is particularly important in order to avoid underestimation of incident dementia cases.

At baseline there were 3,202 persons without dementia. Alcohol consumption information was available for 3,180 subjects:

- * 50.0% were abstinent
- * 24.8% consumed less than one drink (10 grams of alcohol) per day
- * 12.8% consumed 10-19 grams of alcohol per day
- * 12.4% consumed 20 or more grams per day
- * A small subgroup of 25 participants fulfilled the criteria of harmful drinking (>60 grams of alcohol per day for men, respectively >40 grams for women)
- * One man (>120 grams of alcohol per day) and one woman (>80 grams of alcohol per day) reported an extremely high consumption of alcohol
- * Among the consumers of alcohol almost half (48.6%) drank wine only
- * 29.0% drank beer only
- * 22.4% drank mixed alcohol beverages (wine, beer, or spirits)

Alcohol consumption was significantly associated with male gender, younger age, higher level of education, not living alone, and not being depressed. The calculation of incident cases of dementia is based on 3,202 subjects who had no dementia at baseline. Within the follow-up period of three years:

* 217 cases of dementia (6.8%) were diagnosed, whereby 111 subjects (3.5%) suffered from Alzheimer dementia. Due to the relatively small numbers, other subgroups of dementia (vascular dementia: n=42; other specific dementia, e.g. dementia in Parkinson's disease, Lewy body dementia, alcohol dementia: n=14; dementia with unknown aetiology: n=50) were not considered in the following analyses.

Univariate and multivariate analyses revealed that alcohol consumption was significantly associated with a lower incidence of overall dementia and Alzheimer dementia. In line with a large-scale study also based on GP attenders aged 75 years and older, the study found that light-to-moderate alcohol consumption was associated with relatively good physical and mental health. This three-year follow-up study included, at baseline, only those subjects 75 years of age and older, the mean age was 80.2 years, much higher than that in most other studies.

***Acknowledgements** This study is part of the German Research Network on Dementia (KND) and the German Research Network on Degenerative Dementia (KNDD) and was funded by the German Federal Ministry of Education and Research (grants KND: 01GI0102, 01GI0420, 01GI0422, 01GI0423, 01GI0429, 01GI0431, 01GI0433, 01GI0434; grants KNDD: 01GI0710, 01GI0711, 01GI0712, 01GI0713, 01GI0714, 01GI0715, 01GI0716). The funding bodies have had no influence on the paper or the decision to publish.*

http://www.eurekalert.org/pub_releases/2011-03/hsop-ssi022811.php

Study shows ibuprofen may reduce risk of developing Parkinson's disease

Boston, MA – A new study by Harvard School of Public Health (HSPH) researchers shows that adults who regularly take ibuprofen, a non-steroidal anti-inflammatory drug (NSAID), have about one-third less risk of developing Parkinson's disease than non-users.

"There is no cure for Parkinson's disease, so the possibility that ibuprofen, an existing and relatively non-toxic drug, could help protect against the disease is captivating," said senior author Alberto Ascherio, professor

of epidemiology and nutrition at HSPH. The study will be published online March 2, 2011, in *Neurology* and is scheduled to appear in the March 8, 2011, print issue.

Parkinson's disease, a progressive nervous disease occurring generally after age 50, affects at least half a million Americans, according to the National Institute of Neurological Disorders and Stroke. About 50,000 new cases are reported each year, with the number expected to increase as the U.S. population ages. It is hypothesized that ibuprofen may reduce inflammation in the brain that may contribute to the disease.

Prior studies showed a reduced Parkinson's disease risk among NSAIDs users, but most did not differentiate between ibuprofen and other non-aspirin NSAIDs.

In the new study, Ascherio, lead author Xiang Gao, research scientist at HSPH and associate epidemiologist in the Channing Laboratory at Brigham and Women's Hospital, and colleagues analyzed data from nearly 99,000 women enrolled in the Brigham and Women's Hospital-based Nurses' Health Study and over 37,000 men in the Health Professionals Follow-Up Study. The researchers identified 291 cases (156 men and 135 women) of Parkinson's disease during their six-year follow-up study (1998-2004 in women; 2000-2006 in men). Based on questionnaires, the researchers analyzed the patients' use of ibuprofen (e.g. Advil, Motrin, Nuprin), aspirin or aspirin-containing products, other anti-inflammatory pain relievers (e.g., Aleve, Naprosyn), and acetaminophen (e.g., Tylenol). (Although not an NSAID, acetaminophen was included because it's similarly used to treat pain.) Age, smoking, diet, caffeine, and other variables also were considered.

"We observed that men and women who used ibuprofen two or more times per week were about 38% less likely to develop Parkinson's disease than those who regularly used aspirin, acetaminophen, or other NSAIDs," Gao said. "Our findings suggest that ibuprofen could be a potential neuroprotective agent against Parkinson's disease, however, the exact mechanism is unknown."

These findings raise hope that a readily available, inexpensive drug could help to treat Parkinson's disease. "Because the loss of brain cells that leads to Parkinson's disease occurs over a decade or more, a possible explanation of our findings is that use of ibuprofen protects these cells. If so, use of ibuprofen could help slow the disease's progression," Gao said.

The findings do not mean that people who already have Parkinson's disease should begin taking ibuprofen, Ascherio added. "Although generally perceived as safe, ibuprofen can have side effects, such as increased risk of gastrointestinal bleeding. Whether this risk is compensated by a slowing of the disease progression should be investigated under rigorous supervision in a randomized clinical trial," he said.

Support for the study was provided by the National Institutes of Health's (NIH) National Institute of Neurological Disorders and Stroke and the Intramural Research Program of NIH's National Institute of Environmental Health Sciences.

"Use of Ibuprofen and Risk of Parkinson's Disease," Xiang Gao, Honglei Chen, Michael A. Schwarzschild, and Alberto Ascherio. Neurology, March 8, 2011. Online March 2, 2011.

http://www.eurekalert.org/pub_releases/2011-03/nios-uac030211.php

Using artificial, cell-like 'honey pots' to entrap deadly viruses

Researchers from the National Institute of Standards and Technology (NIST) and the Weill Cornell Medical College have designed artificial "protocells" that can lure, entrap and inactivate a class of deadly human viruses - think decoys with teeth.

The technique offers a new research tool that can be used to study in detail the mechanism by which viruses attack cells, and might even become the basis for a new class of antiviral drugs.

A new paper* details how the novel artificial cells achieved a near 100 percent success rate in deactivating experimental analogs of Nipah and Hendra viruses, two emerging henipaviruses that can cause fatal encephalitis (inflammation of the brain) in humans. "We often call them honey pot protocells," says NIST materials scientist David LaVan, "The lure, the irresistibly sweet bait that you can use to capture something."

Henipaviruses, LaVan explains, belong to a broad class of human pathogens - other examples include parainfluenza, respiratory syncytial virus, mumps and measles - called enveloped viruses because they are surrounded by a two-layer lipid membrane similar to that enclosing animal cells. A pair of proteins embedded in this membrane act in concert to infect host cells. One, the so-called "G" protein, acts as a spotter, recognizing and binding to a specific "receptor" protein on the surface of the target cell.

The G protein then signals the "F" protein, explains LaVan, though the exact mechanism isn't well understood. "The F protein cocks like a spring, and once it gets close enough, fires its harpoon, which penetrates the cell's bilayer and allows the virus to pull itself into the cell. Then the membranes fuse and the payload can get delivered into the cell and take over." It can only do it once, however.

The "honey pot" protocells have a core of nanoporous silica - inert but providing structural strength - wrapped in a lipid membrane like a normal cell. In this membrane the research team embedded bait, the protein Ephrin-B2, a known target of henipaviruses. To test it, they exposed the protocells to experimental analogs of

the henipaviruses developed at Weill Cornell. The analogs are nearly identical to henipaviruses on the outside, but instead of henipaviral RNA, they bear the genome of a nonpathogenic virus that is engineered to express a fluorescent protein upon infection. This enables counting and visualizing infected cells.

In controlled experiments, the team demonstrated that the protocells are amazingly effective decoys, essentially clearing a test solution of active viruses, as measured by using the fluorescent protein to determine how many normal cells are infected by the remaining viruses.

The immediate benefit, LaVan says, is a powerful research tool for studying how enveloped viruses work. "This is a nice system to study this sort of choreography between a virus and a cell, which has been very hard to study. A normal cell will have tens of thousands of membrane proteins. You might be studying this one, but maybe it's one of the others that are really influencing your experiment. You reduce this essentially impossibly complicated natural cell to a very pure system, so you now can vary the parameters and try to figure out how you can trick the viruses."

In the long run, say the researchers, the honey pot protocells could become a whole new class of antiviral drugs. Viruses, they point out, are notorious for rapidly evolving to become resistant to drugs, but because the honey pots use the virus's basic infection mechanism, any virus that evolved to avoid them likely would be less effective at infecting normal cells as well.

M. Porotto, F. Yi, A. Moscona and D.A. LaVan. Synthetic protocells interact with viral nanomachinery and inactivate pathogenic human virus. PLoS ONE published online on March 1, 2011. <http://dx.plos.org/10.1371/journal.pone.0016874>.

http://www.eurekalert.org/pub_releases/2011-03/jhmi-nss030211.php

New study suggests ALS could be caused by a retrovirus Viruses that are natural part of human genome may be culprit

A retrovirus that inserted itself into the human genome thousands of years ago may be responsible for some cases of the neurodegenerative disease amyotrophic lateral sclerosis (ALS), also known as Lou Gherig's disease. The finding, made by Johns Hopkins scientists, may eventually give researchers a new way to attack this universally fatal condition.

While roughly 20 percent of ALS cases appear to have a genetic cause, the vast majority of cases appear to arise sporadically, with no known trigger. Research groups searching for a cause of this so-called sporadic form had previously spotted a protein known as reverse transcriptase, a product of retroviruses such as HIV, in ALS patients' serum samples, suggesting that a retrovirus might play a role in the disease. However, these groups weren't able to trace this reverse transcriptase to a specific retrovirus, leaving some scientists in doubt whether retroviruses are involved in ALS.

Seeking to verify whether a culprit retrovirus indeed exists, Avindra Nath, M.D., a professor of neurology at the Johns Hopkins University School of Medicine, and colleagues examined brain samples from 62 people: 28 who died from ALS, 12 who died from chronic, systemic diseases such as cancer, 10 who died from accidental causes and 12 who had another neurodegenerative disease, Parkinson's disease, at the time of their deaths. Using a technique known as polymerase chain reaction, the researchers searched for messenger RNA (mRNA) transcripts from retroviruses, a chemical signature that retroviruses were active in these patients.

In samples from the ALS and chronic disease patients, the search turned up mRNA transcripts that came from human endogenous retrovirus K (HERV-K). This retrovirus is one of thousands that became a part of the human genome after infecting our ancestors long ago. Nowadays, these retroviruses are no longer contagious, but are instead passed along through inheritance in part of the genome that scientists consider "junk" DNA.

When Nath and his colleagues took a closer look at the mRNA, they saw that the transcripts seemed to originate from different parts of the genome in the samples from ALS and systemic disease patients. The transcripts also came from different tissues in the brain. While patients with ALS tended to have HERV-K transcripts present in areas surrounding the motor cortex of the brain - the area affected by the disease - the other patients' transcripts were spread more diffusely through the brain.

Although the researchers express caution, the findings, reported in the January *Annals of Neurology*, suggest that HERV-K might be the ALS retrovirus that researchers have been looking for.

"This paper doesn't establish causation beyond the level of doubt, but it does provide some promising links between HERV-K and ALS," Nath says. "We've never found a putative retrovirus for this disease before, so this opens up a whole new area."

He and his colleagues plan to study whether HERV-K might cause neuronal damage, a step closer to linking this retrovirus to ALS. They also plan to study what factors may cause HERV-K to reactivate in some people and lead to ALS symptoms. Researchers might eventually be able to fight ALS, Nath adds, using antiretroviral drugs specific to HERV-K.

The only vertebrate that eats with its mouth shut

* 10:09 02 March 2011 by Colin Barras

The Pacific hagfish is the only vertebrate that can obey the cardinal rule of the dinner table: don't eat with your mouth open. Uniquely among the 50,000 vertebrate species alive today, it can absorb nutrients through its skin.

Vertebrate skin is impermeable to minimise chemical exchanges between the body and its surroundings. This is why backboned animals can live in salty or fresh water – and how they avoid excess water loss on land.

But the primitive hagfish, thought to be as close as we can get in a living animal to the first vertebrate, has an internal salinity that matches its surroundings. So Chris Glover at the University of Canterbury in Christchurch, New Zealand, and colleagues reasoned that the animal might have a permeable skin.

In the Pacific hagfish (*Eptatretus stoutii*) this could double as a gut, as it likes to dine inside carcasses, exposing its skin to a nutrient-rich soup.



No biting (Image: Norbert Wu/Getty)

To find out, the team placed Pacific hagfish skin samples in between nutrient-rich seawater and a solution mimicking the hagfish's bodily fluids. They found that amino acids from the seawater passed through the skin – and the stronger the amino acid concentration, the higher the rate of uptake. Such a non-linear relationship is strong evidence that nutrients are actively transported across the skin, says Glover.

The hagfish's dining habits may have led to the adaptation, but as some invertebrates also possess a "gut skin", Glover thinks it may be a transitory state in the evolution of the vertebrate digestive system.

Robert Sansom, a palaeontologist at the University of Leicester, UK, says that data from related animal groups could help fill the gaps in our understanding of how vertebrate feeding evolved.

Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2010.2784

<http://www.physorg.com/news/2011-03-drug-brain-function-cardiac.html>

Study: Drug could help preserve brain function after cardiac arrest

(PhysOrg.com) -- An experimental drug that targets a brain system that controls inflammation might help preserve neurological function in people who survive sudden cardiac arrest, new research suggests.

Survival rates for sudden cardiac arrest are low, but recent medical advancements have improved the chances for recovery. Many people who do survive suffer a range of disorders that relate to neurological deficits caused by loss of blood flow to the brain when their heart stops.

The researchers, led by a team at Ohio State University, believe these neurological problems might relate to inflammation and brain-cell death. The study revealed how the brain is damaged during cardiac arrest, as well as how a drug might counter those effects.

The scientists identified in a mouse model how the loss of blood in the brain sets off a process that attracts inflammatory compounds and kills brain cells. The study showed that these damaging effects were associated with alteration of the cholinergic system – an area of the brain that sends signals using the neurotransmitter acetylcholine to regulate inflammation.

Mice that were treated with an experimental drug called GTS-21, which activates acetylcholine, had lower levels of inflammatory chemicals and reduced damage to brain cells in the days following a surgically induced cardiac arrest and subsequent resuscitation.

“This is a drug that has been used safely in humans in clinical trials, so we think our findings have significant clinical potential,” said Courtney DeVries, professor of neuroscience and psychology at Ohio State University and senior author of the study. “Another very important aspect of the study is that the drug was not given until 24 hours after resuscitation, and yet it was successful at reversing inflammatory effects in the brain. So there would be a large therapeutic window of time if this could eventually be used clinically.”

The research is published in the March 2 issue of *The Journal of Neuroscience*.

Cardiac arrest is not the same as a heart attack, which occurs when blood flow to the heart is interrupted. In sudden cardiac arrest, the heart's electrical system malfunctions and blood flow stops altogether. The American Heart Association estimates that fewer than 8 percent of people who suffer cardiac arrest in a home or community setting will survive, and that brain damage can occur within four to six minutes after the heart has stopped. Lasting effects of this brain damage can include physiological problems as well as memory loss and increased anxiety and depression.

In this study, the researchers surgically induced cardiac arrest in groups of anesthetized mice and then revived them eight minutes later using cardiopulmonary resuscitation. The scientists then analyzed brain tissue in mice three and seven days after the heart stoppage. Some mice received the drug beginning 24 hours after resuscitation, and some did not.

Within three days after the cardiac arrest, the untreated animals' brain tissue showed increased levels of immune cells in the central nervous system that indicate neurons are under attack. In addition, there were signs of high activity in the brain associated with the creation of compounds linked to inflammation.

These compounds included tumor necrosis factor-alpha, interleukin-1 beta and interleukin-6 (IL-6) – all members of a family of proteins called cytokines, chemical messengers that cause inflammation, most often to fight infection or repair injury. When these proteins are circulating without an infection to fight, the body part hosting them – in this case, the brain – experiences excess inflammation.

By day seven after cardiac arrest, some untreated mice also had elevated levels of IL-6 in their bloodstream, a sign that excessive inflammation was present in other parts of the body.

“The higher IL-6 levels in the blood are important, because this cytokine is also a marker of inflammation in humans,” DeVries said.

The researchers also observed reduced activity levels of the enzyme that generates the neurotransmitter acetylcholine, suggesting that chemical signaling that protects the brain by regulating inflammation had been severely altered in mice that had experienced cardiac arrest.

“The cholinergic system is important for maintaining an appropriate balance between inflammation in the central nervous system and throughout the body,” said DeVries, also an investigator in Ohio State's Institute for Behavioral Medicine Research. “Though the presence of cytokines can be beneficial in limited amounts, the huge inflammatory response in these mouse brains became detrimental to the survival of the neurons.”

Twenty-four hours after cardiac arrest and resuscitation, some of the mice received daily treatments of the experimental drug GTS-21. This drug can reverse these signaling malfunctions and restore the anti-inflammatory properties of the cholinergic system.

Mice that received this treatment had lower levels of pro-inflammatory compounds in their brains three days later and fewer inflammation markers in their blood seven days later than did untreated mice. In addition, fewer brain cells died in these mice compared to mice that did not receive any treatment after cardiac arrest and resuscitation. When the researchers simultaneously introduced a drug that can counter the GTS-21, the mice showed none of the improvements associated with the treatment.

“This confirmed for us that we were targeting the appropriate system to reduce inflammation in the brain,” DeVries said. “Essentially, what we were trying to do is provide balance to the cholinergic system. GTS-21 replaced a signal that was missing, which in turn reduced the inflammatory response to levels that are not as damaging to neurons.” DeVries also noted, however, that cardiac arrest disrupts the cholinergic signaling at multiple points. So restoration of one part of the system appears to reduce damaging effects on some, but not all, responses to the blood loss in the brain.

She also said her lab is continuing research in this area to further explore the link between inflammation in the brain that follows cardiac arrest and resulting neurological problems.

“The cognitive effects are one of the biggest patient concerns. If these symptoms are related to increased inflammation that occurs after cardiac arrest, this drug might have potential benefits that go far beyond control of inflammation; they might also help improve other symptoms,” DeVries said.

GTS-21 is currently being tested by other researchers as a potential treatment for Alzheimer's disease, schizophrenia and nicotine addiction. It can cross the blood-brain barrier, so it can be given intravenously.

More information: <http://www.jneurosci.org/> Provided by The Ohio State University

<http://www.newscientist.com/article/dn20191-zoologger-the-hairy-beast-with-seven-fuzzy-sexes.html>

Zoologger: The hairy beast with seven fuzzy sexes

*** 17:33 02 March 2011 by Michael Marshall**

Species: Tetrahymena thermophila

Habitat: fresh water around the world, having way more sex than you

Finding someone to have sex with can be a trial. There are plenty of humans in the world, but the proportion who are desirable, live nearby and – crucially – are willing to have sex with you can be prohibitively small. Most of us make the quest still harder by ruling out half the population before we even start looking.

At first glance it looks like the single-celled organism *Tetrahymena thermophila* has cracked this problem in spectacular fashion. It has not two but seven sexes, and each one can mate with any of the others, which opens up the field considerably. Unfortunately, they all look alike. What's more, the different sexes are not equally common – thanks to the peculiar way each individual's sex is determined.

Fuzzy sex

Tetrahymena thermophila is a single cell covered with a coat of hairs called cilia. The cilia wave back and forth, powering it through the water. Its seven sexes are rather prosaically named I, II, III, IV, V, VI and VII. An individual of a given sex can mate with individuals of any except its own, so there are 21 possible orientations.

In most animals, what sex you are is straightforward. A human with two X chromosomes is female, while someone with an X and a Y is male. Other species use different systems, but they are all clear cut when it comes to sex determination and mating.



Young healthy VII WLTM I, II, III, IV, V, VI for conjugation (Image: Volker Steger/E. Cole/SPL)

Not so for *Tetrahymena*. Its sex is controlled by a gene called *mat*, but it is not as simple as one version of the gene encoding one sex. Instead, each allele of the gene sets out a series of probabilities. For instance, an individual born with the *mat2* allele has zero chance of being type I, a 0.15 chance of being type II, a 0.09 chance of being type III, and so on. There are at least 14 of these alleles, each offering a different set of probabilities. They are divided into two major groups called A and B: A alleles produce every sex except IV and VII, while B alleles produce everything except I.

Skewed sex

As if that weren't enough, sex itself is different for this animal. Most cells have a single nucleus that contains all their DNA, but *Tetrahymena* has two: a large macronucleus and a small micronucleus. The macronucleus controls the everyday functions of the cell, while the micronucleus deals with its complicated sex life. Mating is called conjugation, and involves swapping genes from the micronuclei. Each animal's rejigged micronucleus then builds a new macronucleus.

With all this going on it should come as no surprise that *Tetrahymena* populations look a little weird. Unlike many animals, the sexes are not equally common. According to Rebecca Zufall and colleagues at the University of Houston in Texas, that is all down to the fuzzy way it chooses its sex.

They built mathematical models of populations of animals with different kinds of sex determination. So long as the populations were no bigger than about 1000, fuzzy sex determination always led to skewed sex ratios. This was true even if the different alleles complemented each other – one of them boosting sexes I, II and III, say, while another boosted IV, V, VI and VII.

Their model also showed that alleles supporting several sexes outcompeted alleles that only supported one, because they coped better with wild swings in the sex ratio caused by mass deaths and the like. Zufall says there are probably more animals with fuzzy sex determination than anyone suspects.

Journal reference: *Evolution*, DOI: 10.1111/j.1558-5646.2011.01266.x

http://www.eurekalert.org/pub_releases/2011-03/jhmi-ffo030311.php

Feet first? Old mitochondria might be responsible for neuropathy in the extremities Long journey of organelles to feet and hands leads to dysfunction, pain

The burning, tingling pain of neuropathy may affect feet and hands before other body parts because the powerhouses of nerve cells that supply the extremities age and become dysfunctional as they complete the long journey to these areas, Johns Hopkins scientists suggest in a new study. The finding may eventually lead to new ways to fight neuropathy, a condition that often accompanies other diseases including HIV/AIDS, diabetes and circulatory disorders.

Neuropathies tend to hit the feet first, then travel up the legs. As they reach the knees, they often start affecting the hands. This painful condition tends to affect people who are older or taller more often than younger, shorter people. Though these patterns are typical of almost all cases of neuropathy, scientists have been stumped to explain why, says study leader Ahmet Hoke, M.D., Ph.D., a professor of neurology and neuroscience at the Johns Hopkins University School of Medicine.

He and his colleagues suspected that the reason might lie within mitochondria, the parts of cells that generate energy. While mitochondria for most cells in the body have a relatively quick turnover - replacing themselves every month or so - those in nerve cells often live much longer to accommodate the sometimes long journey from where a cell starts growing to where it ends. The nerve cells that supply the feet are about 3 to 4 feet long in a person of average height, Hoke explains. Consequently, the mitochondria in these nerve cells take about two to three years to travel from where the nerve originates near the spine to where it ends in the foot.

To investigate whether the aging process during this travel might affect mitochondria and lead to neuropathy, Hoke and his colleagues examined nerve samples taken during autopsies from 11 people who had HIV-associated neuropathy, 13 who had HIV but no neuropathy, and 11 HIV-negative people who had no signs

of neuropathy at their deaths. The researchers took two matched samples from each person - one from where the nerves originated near the spine and one from where the nerves ended near the foot.

They then examined the DNA from mitochondria in each nerve sample. Mitochondria have their own DNA that's separate from the DNA in a cell's nucleus.

The researchers report in the January Annals of Neurology that in patients with neuropathy, DNA from mitochondria in the nerve endings at the ankle had about a 30-fold increase in a type of mutation that deleted a piece of this DNA compared to mitochondrial DNA from near the spine. The difference in the same deletion mutation between the matched samples in people without neuropathy was about threefold.

Since mitochondria quit working upon a person's death, the scientists looked to a monkey model of HIV neuropathy to see whether these deficits affected mitochondrial function. Tests showed that the mitochondria from the ankles of these animals didn't function as well as those from near their spines, generating less energy and producing faulty proteins and damaging free radicals.

Hoke explains that as mitochondria make the trek from near the spine to the feet, their DNA accumulates mutations with age. These older mitochondria might be more vulnerable to the assaults that come with disease than younger mitochondria near the spine, leading older mitochondria to become dysfunctional first. The finding also explains why people who are older or taller are more susceptible to neuropathies, Hoke says.

"Our mitochondria age as we age, and they have even longer to travel in tall people," he says. "In people who are older or taller, these mitochondria in the longest nerves are in even worse shape by the time they reach the feet."

Hoke notes that if this discovery is confirmed for other types of neuropathy, it could lead to mitochondria-specific ways to treat this condition. For example, he says, doctors may eventually be able to give patients drugs that improve the function of older mitochondria, in turn improving the function of nerve cells and relieving pain.

For more information, go to: <http://neuroscience.jhu.edu/AhmetHoke.php>

http://www.hopkinsmedicine.org/neurology_neurosurgery

http://www.eurekalert.org/pub_releases/2011-03/sri-srs030311.php

Scripps Research study points to liver, not brain, as origin of Alzheimer's plaques **Results could lead to new strategies for prevention and therapy**

LA JOLLA, CA – Unexpected results from a Scripps Research Institute and ModGene, LLC study could completely alter scientists' ideas about Alzheimer's disease - pointing to the liver instead of the brain as the source of the "amyloid" that deposits as brain plaques associated with this devastating condition. The findings could offer a relatively simple approach for Alzheimer's prevention and treatment. The study was published online today in The Journal of Neuroscience Research.

In the study, the scientists used a mouse model for Alzheimer's disease to identify genes that influence the amount of amyloid that accumulates in the brain. They found three genes that protected mice from brain amyloid accumulation and deposition. For each gene, lower expression in the liver protected the mouse brain. One of the genes encodes presenilin - a cell membrane protein believed to contribute to the development of human Alzheimer's.

"This unexpected finding holds promise for the development of new therapies to fight Alzheimer's," said Scripps Research Professor Greg Sutcliffe, who led the study. "This could greatly simplify the challenge of developing therapies and prevention."

An estimated 5.1 million Americans have Alzheimer's disease, including nearly half of people age 85 and older. By 2050, the number of people age 65 and over with this disease will range from 11 million to 16 million unless science finds a way to prevent or effectively treat it. In addition to the human misery caused by the disease, there is the unfathomable cost. A new report from the Alzheimer's Association shows that in the absence of disease-modifying treatments, the cumulative costs of care for people with Alzheimer's from 2010 to 2050 will exceed \$20 trillion.

A Genetic Search-and-Find Mission

In trying to help solve the Alzheimer's puzzle, in the past few years Sutcliffe and his collaborators have focused their research on naturally occurring, inherited differences in neurological disease susceptibility among different mouse strains, creating extensive databases cataloging gene activity in different tissues, as measured by mRNA accumulation. These data offer up maps of trait expression that can be superimposed on maps of disease modifier genes.

As is the case with nearly all scientific discovery, Sutcliffe's research builds on previous findings. Several years ago, researchers at Case Western Reserve mapped three genes that modify the accumulation of pathological beta amyloid in the brains of a transgenic mouse model of Alzheimer's disease to large

chromosomal regions, each containing hundreds of genes. The Case Western scientists used crosses between the B6 and D2 strains of mice, studying more than 500 progeny.

Using the results from this study, Sutcliffe turned his databases of gene expression to the mouse model of Alzheimer's, looking for differences in gene expression that correlated with differences in disease susceptibility between the B6 and D2 strains. This intensive work involved writing computer programs that identified each genetic difference that distinguished the B6 and D2 genomes, then running mathematical correlation analysis (known as regression analysis) of each difference. Correlations were made between the genotype differences (B6 or D2) and the amount of mRNA product made from each of the more than 25,000 genes in a particular tissue in the 40 recombinant inbred mouse strains. These correlations were repeated 10 times to cover 10 tissues, the liver being one of them.

"A key aspect of this work was learning how to ask questions of massive data sets to glean information about the identities of heritable modifier genes," Sutcliffe said. "This was novel and, in a sense, groundbreaking work: we were inventing a new way to identify modifier genes, putting all of these steps together and automating the process. We realized we could learn about how a transgene's pathogenic effect was being modified without studying the transgenic mice ourselves."

Looking for a Few Good Candidates

Sutcliffe's gene hunt offered up good matches, candidates, for each of the three disease modifier genes discovered by the Case Western scientists, and one of these candidates - the mouse gene corresponding to a gene known to predispose humans carrying particular variations of it to develop early-onset Alzheimer's disease - was of special interest to his team.

"The product of that gene, called Presenilin2, is part of an enzyme complex involved in the generation of pathogenic beta amyloid," Sutcliffe explained. "Unexpectedly, heritable expression of Presenilin2 was found in the liver but not in the brain. Higher expression of Presenilin2 in the liver correlated with greater accumulation of beta amyloid in the brain and development of Alzheimer's-like pathology."

This finding suggested that significant concentrations of beta amyloid might originate in the liver, circulate in the blood, and enter the brain. If true, blocking production of beta amyloid in the liver should protect the brain.

To test this hypothesis, Sutcliffe's team set up an in vivo experiment using wild-type mice since they would most closely replicate the natural beta amyloid-producing environment. "We reasoned that if brain amyloid was being born in the liver and transported to the brain by the blood, then that should be the case in all mice," Sutcliffe said, "and one would predict in humans, too."

The mice were administered imatinib (trade name Gleevec, an FDA-approved cancer drug), a relatively new drug currently approved for treatment of chronic myelogenous leukemia and gastrointestinal tumors. The drug potently reduces the production of beta amyloid in neuroblastoma cells transfected by amyloid precursor protein (APP) and also in cell-free extracts prepared from the transfected cells. Importantly, Gleevec has poor penetration of the blood-brain barrier in both mice and humans.

"This characteristic of the drug is precisely why we chose to use it," Sutcliffe explained. "Because it doesn't penetrate the blood-brain barrier, we were able to focus on the production of amyloid outside of the brain and how that production might contribute to amyloid that accumulates in the brain, where it is associated with disease."

The mice were injected with Gleevec twice a day for seven days; then plasma and brain tissue were collected, and the amount of beta amyloid in the blood and brain was measured. The findings: the drug dramatically reduced beta amyloid not only in the blood, but also in the brain where the drug cannot penetrate. Thus, an appreciable portion of brain amyloid must originate outside of the brain, and imatinib represents a candidate for preventing and treating Alzheimer's.

As for the future of this research, Sutcliffe says he hopes to find a partner and investors to move the work into clinical trials and new drug development.

In addition to Sutcliffe, the authors of the study, titled "Peripheral reduction of β -amyloid is sufficient to reduce brain $A\beta$: implications for Alzheimer's disease," include Peter Hedlund and Elizabeth Thomas of Scripps Research, and Floyd Bloom and Brian Hilbush of ModGene, LLC, which funded the project. For more information, see <http://onlinelibrary.wiley.com/doi/10.1002/jnr.22603/abstract> .

http://www.eurekalert.org/pub_releases/2011-03/jhmi-sat030311.php

Solving a traditional Chinese medicine mystery

Discovery of molecular mechanism reveals antitumor possibilities

Researchers at the Johns Hopkins School of Medicine have discovered that a natural product isolated from a traditional Chinese medicinal plant commonly known as thunder god vine, or lei gong teng (雷公藤), and used for hundreds of years to treat many conditions including rheumatoid arthritis works by blocking gene control

machinery in the cell. The report, published as a cover story of the March issue of Nature Chemical Biology, suggests that the natural product could be a starting point for developing new anticancer drugs.

"Extracts of this medicinal plant have been used to treat a whole host of conditions and have been highly lauded for anti-inflammatory, immunosuppressive, contraceptive and antitumor activities," says Jun O. Liu, Ph.D., a professor of pharmacology and molecular sciences at Johns Hopkins. "We've known about the active compound, triptolide, and that it stops cell growth, since 1972, but only now have we figured out what it does."

Triptolide, the active ingredient purified from the plant *Tripterygium wilfordii* Hook F, has been shown in animal models to be effective against cancer, arthritis and skin graft rejection. In fact, says Liu, triptolide has been shown to block the growth of all 60 U.S. National Cancer Institute cell lines at very low doses, and even causes some of those cell lines to die. Other experiments have suggested that triptolide interferes with proteins known to activate genes, which gives Liu and colleagues an entry point into their research.

The team systematically tested triptolide's effect on different proteins involved with gene control by looking at how much new DNA, RNA and protein is made in cells. They treated HeLa cells with triptolide for one hour, compared treated to untreated cells and found that triptolide took much longer to have an effect on the levels of newly made proteins and DNA, yet almost immediately blocked manufacture of new RNA. The researchers then looked more closely at the three groups of enzymes that make RNA and found that low doses of triptolide blocked only one, RNAPII.

But the RNAPII enzyme complex actually requires the assistance of several smaller clusters of proteins, according to Liu, which required more investigative narrowing down. Using a small gene fragment in a test tube, the researchers mixed in RNAPII components and in some tubes included triptolide and some not to see which combinations resulted in manufacture of new RNA. Every combination of proteins that included a cluster called TFIIF stopped working in the presence of triptolide.

But again, TFIIF is made of 10 individual proteins, many of which, according to Liu, have distinct and testable activities. Using information already known about these proteins and testing the rest to see if triptolide would alter their behaviors, the research team finally found that triptolide directly binds to and blocks the enzymatic activity of one of the 10, the XPB protein.

"We were fairly certain it was XPB because other researchers had found triptolide to bind to an unknown protein of the same size, but they weren't able to identify it," says Liu. "

To convince themselves that the interaction between triptolide and XPB is what stops cells from growing, the researchers made 12 chemicals related to triptolide with a wide range of activity and treated HeLa cells with each of the 12 chemicals at several different doses. By both counting cells and testing XPB activity levels, the team found that the two correlate; chemicals that were better at decreasing XPB activity were also better at stopping cell growth and vice versa.

"Triptolide's general ability to stop RNAPII activity explains its anti-inflammatory and anticancer effects," says Liu. "And its behavior has important additional implications for circumventing the resistance that some cancer cells develop to certain anticancer drugs. We're eager to study it further to see what it can do for future cancer therapy."

This research was supported in part by discretionary funds from the Johns Hopkins Department of Pharmacology and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Authors on the paper include Denis Titov, Qing-Li He, Shridhar Bhat, Woon-Kai Low, Yongjun Dang, Michael Smeaton and Jun O. Liu of Johns Hopkins; Benjamin Gilman, Jennifer Kugel and James Goodrich of the University of Colorado, Boulder; and Arnold Demain of Drew University, Madison, N.J.

<http://www.physorg.com/news/2011-03-world-artificial-bronchus-graft-france.html>

Lung cancer: 'Artificial airway' transplant is world first

French doctors said on Thursday they were delighted at a medical first in which a 78-year-old man was given a section of artificial airway to save a lung afflicted by bronchial cancer.

The bronchi are the main tubes for taking air from the trachea to the two sides of the lung.

In cases of early, non-metastasizing cancer of the bronchus, surgeons typically remove a whole lung, as well as the bronchus itself, if the tumour is located in the centre of the organ. In more than a quarter of cases, this leads to death within three months of the operation.

A team led by thoracic and vascular surgeon Emmanuel Martinod removed the diseased part of the bronchus and grafted a replacement, thus saving the lung. The transplant, carried out in a three-hour on October 28 2009, entailed a small metal tube-shaped frame, or stent, which supported a section of artery taken from a deceased donor and frozen in a tissue bank. The advantage of aortal tissue is that it does not require anti-rejection drugs, which are not recommended for cancer patients, whose weakened immune system is less able to combat infection.

"The patient is doing very well," Martinod, a professor at the Avicenne Hospital in eastern Paris, told a press conference. "He needs regular monitoring, but he's doing fine, he's walking, he goes to his house in the country." The patient "has the respiratory capacity of an 80-year-old man with a history of smoking," he said.

Alain Carpentier, a professor of bio-surgery who is also president of France's Academy of Sciences, said the tissue regrowth was "magical. The bronchus is regenerating," he said, explaining that the transplanted aortal tissue had become a "matrix" which was now being recolonised by bronchial cells. They were rebuilding the epithelium, a mucal lining of the bronchus that cleanses the airways. The surgery culminated 10 years of research.

Between 20 and 30 similar operations are being scheduled in an investigation to see whether the transplant should be enlisted in routine surgery for treating this form of lung cancer.

<http://www.scientificamerican.com/article.cfm?id=new-aids-treatment-immune-cell-genes>

Giving HIV a Poor Reception: New AIDS Treatment Tinkers with Immune Cell Genes
Researchers have found new ways to interfere with a co-receptor important to HIV infection, and the outcomes so far are encouraging

By Bob Roehr | Thursday, March 3, 2011 | 0

BOSTON - A novel treatment for HIV could involve changing the genes in a person's immune cells and, ultimately, in his or her stem cells, as well. It might even lead to a cure for that deadly disease. Promising advances in that direction were presented here Monday at the 18th Conference on Retroviruses and Opportunistic Infections. The pieces have been coming together for some time. First came the understanding that HIV enters a cell by grabbing on to a CD4 receptor molecule on the surface, and then on to a co-receptor molecule - the one most commonly used is called CCR5.

Then came discovery of the delta-32 mutation to the gene that encodes CCR5. Individuals who inherits a copy from one parent have fewer CCR5 receptors on their cells, are more resistant to becoming infected with HIV, and if infected, have a slower disease progression than a people without the mutation.

Inherit a mutant gene from both parents and the result is no CCR5 receptors at all, which makes it almost impossible for HIV to enter a cell. About 1 percent of Europeans have this double variant.

Pharmaceutical companies took this as a cue to develop a way to chemically block the CCR5 receptor, thereby artificially denying HIV entry into the cell. The result was the small molecule drug maraviroc, which has been on the market since 2007.

"The Berlin patient"

That same year, German researcher Gero Hütter was treating a patient on therapy for HIV infection who had developed acute myeloid leukemia. Treatment for leukemia involves effectively eradicating the immune system with radiation and chemotherapy, followed by a bone marrow transplant containing stem cells to build a new immune system. He was intrigued by the possibility of using a bone marrow graft from a donor who carried the double CCR5 mutation. His patient, who would initially request anonymity and become known as the "Berlin Patient," embraced the experiment.

Good fortune was with them; among the German registry of donors who were a good HLA (human leukocyte antigen) tissue match to the patient (necessary to prevent transplant rejection), was a single donor with the rare CCR5 double mutation. Treatment moved forward: A recurrence of the leukemia required a second round of radiation and chemotherapy, and then bone marrow transplantation of the CCR5 delta-32-carrying stem cells. The new stem cells were given time to establish a new immune system before all anti-HIV drugs were stopped.

And nothing happened. Typically when a person with HIV stops therapy even undetectable virus quickly rebounds to very high levels, generally within a few weeks. The doctor and patient waited as the months ticked by, and still no virus reappeared. They came to the conclusion that they had proved their hypothesis; the patient had apparently been cured of HIV.

They avoided the glare of public disclosure throughout the experiment but finally were confident enough with the outcome to publish a paper on the case study in 2009 in The New England Journal of Medicine.

Zinc fingers

This proof of principle was intriguing but it was difficult to see how it might apply to more than a handful of patients. One could not destroy a patient's immune system with radiation and chemotherapy unless there was a medically justified reason for doing so, such as treatment for cancer. Finding a compatible bone marrow match is difficult enough for many patients. Adding the requirement of the rare double CCR5 mutation exponentially multiplied the problem.

One possible option was to narrow the focus of research from stem cells and their pluripotent capacity to generate a broad array of cells to specific immune cells that are important to HIV. CD4+ T cells were the

natural choice. These T cells express the CD4 receptor and are a key component of the immune system as well as the favorite target for HIV to infect and reproduce.

Sangamo BioSciences, a Richmond, California–based pharmaceutical company, has developed a "zinc fingers" technology that can home in on the CCR5 section of cellular DNA and artificially create a functional equivalent of the delta-32 mutation. They backed the study announced on Monday, along with the nonprofit California Institute for Regenerative Medicine, which was set up by the state in 2004 via a \$3-billion bond issue to promote stem cell research.

This first-of-its-kind study involved six male patients aged 48 to 55 at the University of California in Los Angeles and San Francisco. All of them had been infected with HIV for 20 to 30 years but were on therapy and suppressing HIV below the level of detection. But those decades of infection had taken a toll; their CD4+ T-cell counts were between 200 and 500, less than half what is considered normal.

The study gathered circulating CD4+ T cells from the patient's blood via a process called apheresis. At a central processing facility, the cells were modified with the zinc finger process, then those that were successfully changed to carry the delta-32 mutation were expanded, or grown in very large numbers. Finally, 30 billion of them were infused back into the patient.

The results, which were part of a phase I safety study (rather than phase II efficacy study) were soon apparent. Study leader Jay Lalezari of Quest Clinical Research says there was "a significant engraftment and expansion of the cells, a three-fold increase over what would have been predicted." The total CD4+ T cell count increased by at least 100 in five of the six patients. The changes persisted, with 67 percent of cells showing the modification in the blood three months after treatment.

The researchers took myriad other measures during the study and all seemed to move in a positive direction. Lalezari says it is "probably as good as we could have hoped for in this population."

One subject's experience

Matt Sharp is a veteran HIV treatment activist who was concerned with his low CD4+ T cell count. It meant he had to take various drugs as prophylaxis to prevent the development of opportunistic infections. It also meant having to live with the side effects of those drugs. So, he chose to enroll in the zinc finger study.

He is pleased that his CD4+ T cell count roughly doubled to more than 500 and has remained there so far for six months. It meant he was able to discontinue the prophylaxis drugs.

Scott Hammer, an AIDS researcher at Columbia University's College of Physicians and Surgeons and a vice chair of the retroviral conference where the results were presented Monday, says, "This is early work that takes molecular biology into the clinic.... We shouldn't be raising the flag to say we've solved the problem yet."

Lalezari agreed, emphasizing that this is proof-of-concept study demonstrates that it is technically feasible to do the work, and it is safe. The procedure's real test will come when patients stop their therapies. Will the virus remain suppressed or will they have to go back on a drug regimen?

Another step that may be required for a "cure" is developing a parallel genetic "fix" for CXCR4, another co-receptor HIV sometimes uses to enter cells. And it may be that the modified CD4+ T cells will run their life course and have to be replenished periodically. Perhaps it would make sense to modify stem cells as a more permanent source of protection from HIV infection. That, however, raises another set of issues.

Sharp is wary about stopping his HIV drug regimen. He feels his immune system is fragile and is waiting to see how successful the treatment is for other patients who started the program with a higher CD4+ T cell counts. But he does look forward to the day when future developments might bring a cure and allow him to completely stop his HIV medications.

<http://www.newscientist.com/article/dn20195-found-fine-american-fishing-tackle-12-millennia-old.html>

Found: fine American fishing tackle, 12 millennia old

*** 19:00 03 March 2011 by Ferris Jabr**

A treasure trove of finely crafted fishing spearheads from 12,000 years ago has been discovered on the Channel Islands of California.

They are a clue to the lifestyles of some of the earliest American settlers, and suggest that two separate cultures lived in North America at the time: one, the well-known Clovis culture, lived inland and feasted on mammoths, mastodons and other mammals; the other was a coastal culture with a taste for seafood.

The archaeologists who made the find believe that the two groups were distinct, but shared trade links.

Jon Erlandson of the University of Oregon in Eugene and his team poked around caves, springs and likely sites of ancient human settlement on the islands of Santa Rosa and San Miguel, and found more than 50 shell middens – large trash heaps of discarded seashells, chipped stone tools and animal bones – which they dated to between 10,000 and 12,000 years ago.

They think that during this period early Americans used the islands for seasonal hunting camps, most likely in the winter when fresh water would have been plentiful. The remains suggest that early colonisers hunted birds such as overwintering Canada geese, snow geese, albatross and cormorants – and possibly marine mammals like otters and seals – but also harvested a variety of shellfish from kelp forests, including mussels, red abalone and crabs.

Such a diet contrasts with the big-game hunters who lived on the mainland at the time and liked to chase camels, horses and mastodons.

Delicate work

But what astonished Erlandson and his colleagues were the tools they found near the middens.



High-tech tackle, scale bar: 1 centimetre per square (Image: J. Erlandson)

Team member Todd Braje of Humboldt State University in Arcata, California, describes finely crafted barbed spearheads. "We found very thin, expertly made projectile points and it blew us away that these delicate flint-knapped points are this old," he says. Such tools are generally only found at more recent sites. These fine, barbed points are markedly different from those previously found at Clovis sites, which tend to be simple, fluted points. This hints at the coexistence of two separate groups of people in North America at the time.

However, Loren Davis of Oregon State University in Corvallis points out that the team also found Clovis-like spearheads on the islands: he says that tools he has dug up on the North American mainland look nearly identical to some of the ones Erlandson and his team found.

"That means peoples on the Channel Islands and people in western Idaho, for example, were at one point exposed to the same ideas about how to make technology," Davis says. A likely explanation is that the two groups shared some kind of trade.

By land or sea?

That Erlandson and his teams found the remains on what was once a single island off the coast of modern-day California is also significant. There are many hypotheses for how humans colonised North America: one popular scenario is that they crossed over from Asia across a land bridge that once linked Siberia and Alaska.

But some historians believe at least some of the early settlers were seafarers, and either dropped down along the coast from Alaska or even crossed over from Japan. Erlandson and his colleagues say their new finds support the idea that the first people to inhabit the Americas were mariners, or perhaps that land and sea-based migrations occurred in tandem.

It's too early to say for sure. Davis points out – and Braje concedes – that the Channel Island sites are not the oldest in the Americas, so they do not tell us about the very first pioneers. Still, Braje says, "this pushes back the chronology of New World seafaring to 12,000, maybe 13,000 years ago. It gets us a big step closer to showing that a coastal migration route happened, or was at least possible."

Journal reference: Science, DOI: 10.1126/science.1201477

<http://www.scientificamerican.com/article.cfm?id=enzyme-strengthen-old-memories>

Enzyme Can Strengthen Old Memories

Research paves way to adjusting recall of events.

By Amy Maxmen

Precious memories need not fade if a report today bears fruit. Neuroscientists have successfully strengthened old memories in rats, according to research published today in *Science*.

A handful of substances can strengthen memories as they're being made. But a greater aim for neuroscientists is to learn how to enhance existing, older memories, such as where you live or your grandson's name -- memories often lost because of dementia or amnesia.

"Finding out what perpetuates long-term memory has been a real challenge," says Todd Sacktor, a neuroscientist at SUNY Downstate Medical Center in New York and an author on the paper. "What's special here is we've found a way to make old memories stronger without interfering with them as they're formed or recalled."

When a memory is made, new connections, or synapses, form between brain cells. To keep the memory, that synapse must endure. Scientists don't yet know exactly what strengthens these synapses to keep memories

stable over time, but there are some clues. In 2007, Sacktor and his colleagues erased long-term memories that rats had formed weeks earlier using a drug that inhibited the enzyme protein kinase Mzeta (PKMzeta).

Doubts laid to rest

In the current study, the researchers alleviated some neuroscientists' concerns about the specificity of the PKMzeta-blocking drug by using genetic tools in rats to disrupt PKMzeta and also boost the enzyme in the neocortex, a presumed repository for long-term memory storage in the brain.

One week after rats fell ill from drinking sweet, lithium-laced water, they were given injections containing genetic elements that would either block or increase the activity of PKMzeta. Rats with abundant PKMzeta in their neocortices seemed to remember that sweet water caused illness. They hardly touched the sweet water when they were served it again a week after the injection -- far less so than untreated rats. Meanwhile, rats with reduced PKMzeta activity drank thirstily. The same thing happened with salty, lithium-laced water given a week before the treatment and again a week after.

"I'm a believer now," says David Glanzman, a neuroscientist at the University of California, Los Angeles. "I was cautious at first, but this study is impressive because they've specifically altered levels of the kinase."

Lead author Yadin Dudai, a neuroscientist at the Weizmann Institute of Science in Rehovot, Israel, says that PKMzeta is persistently active for months -- or longer -- after animals learn. Without it, memories of those lessons won't stick. The enzyme seems to modify proteins at synapses that receive information from chemical messengers called neurotransmitters. In doing so, says Dudai, PKMzeta probably increases the sensitivity of the synapse to neurotransmitters and facilitates memory recall.

Other established memories were probably also strengthened by the PKMzeta boost, says Dudai. Thus, targeting the enzyme could one day lead to long-sought treatments for diseases in which established memories grow dim. Conversely, blocking it might help people with post-traumatic stress disorder to forget a damaging experience.

However, neuroscientists must first find ways to target only good memories or only the bad. "Treatments that will enhance or inhibit memories are just around the corner," says Glanzman. "What will be tough is finding the needle of a specific memory in the synaptic haystack of a human brain."

http://www.eurekalert.org/pub_releases/2011-03/nu-hsc030211.php

Human stem cells transformed into key neurons lost in Alzheimer's

Discovery may lead to new drugs and neuron transplantation for Alzheimer's

CHICAGO --- Northwestern Medicine researchers for the first time have transformed a human embryonic stem cell into a critical type of neuron that dies early in Alzheimer's disease and is a major cause of memory loss. This new ability to reprogram stem cells and grow a limitless supply of the human neurons will enable a rapid wave of drug testing for Alzheimer's disease, allow researchers to study why the neurons die and could potentially lead to transplanting the new neurons into people with Alzheimer's. The paper will be published March 4 in the journal *Stem Cells*.

These critical neurons, called basal forebrain cholinergic neurons, help the hippocampus retrieve memories in the brain. In early Alzheimer's, the ability to retrieve memories is lost, not the memories themselves. There is a relatively small population of these neurons in the brain, and their loss has a swift and devastating effect on the ability to remember.

"Now that we have learned how to make these cells, we can study them in a tissue culture dish and figure out what we can do to prevent them from dying," said senior study author Jack Kessler, M.D., chair of neurology and the Davee Professor of Stem Cell Biology at Northwestern University Feinberg School of Medicine and a physician at Northwestern Memorial Hospital. The lead author of the paper is Christopher Bissonnette, a former doctoral student in neurology who labored for six years in Kessler's lab to crack the genetic code of the stem cells to produce the neurons. His research was motivated by his grandfather's death from Alzheimer's.

"This technique to produce the neurons allows for an almost infinite number of these cells to be grown in labs, allowing other scientists the ability to study why this one population of cells selectively dies in Alzheimer's disease," Bissonnette said. The ability to make the cells also means researchers can quickly test thousands of different drugs to see which ones may keep the cells alive when they are in a challenging environment. This rapid testing technique is called high-throughput screening.

Kessler and Bissonnette demonstrated the newly produced neurons work just like the originals. They transplanted the new neurons into the hippocampus of mice and showed the neurons functioned normally. The neurons produced axons, or connecting fibers, to the hippocampus and pumped out acetylcholine, a chemical needed by the hippocampus to retrieve memories from other parts of the brain.

Human skin cells transformed into stem cells and then neurons

In new, unpublished research, Northwestern Medicine scientists also have discovered a second novel way to make the neurons. They made human embryonic stem cells (called induced pluripotent stem cells) from human skin cells and then transformed these into the neurons.

Scientists made these stem cells and neurons from skin cells of three groups of people: Alzheimer's patients, healthy patients with no family history of Alzheimer's, and healthy patients with an increased likelihood of developing the disease due to a family history of Alzheimer's because of genetic mutations or unknown reasons.

"This gives us a new way to study diseased human Alzheimer's cells," Kessler said. "These are real people with real disease. That's why it's exciting."

Researcher motivated by his grandfather's Alzheimer's disease

Bissonnette's persistence in the face of often frustrating research was fueled by the childhood memory of watching his grandfather die from Alzheimer's.

"I watched the disease slowly and relentlessly destroy his memory and individuality, and I was powerless to help him," Bissonnette recalled. "That drove me to become a scientist. I wanted to discover new treatments to reverse the damage caused by Alzheimer's disease." "My goal was to make human stem cells become new healthy replacement cells so that they could one day be transplanted into a patient's brain, helping their memory function again," he said. Bissonnette had to grow and test millions of cells to figure out how to turn on the exact sequence of genes to transform the stem cell into the cholinergic neuron.

"A stem cell has the potential to become virtually any cell in the body, from a heart cell to a layer of skin," he explained. "Its development is caused by a cascade of things that slowly bump it into a final cell type."

But it wasn't enough just to develop the neurons. Bissonnette then had to learn how to stabilize them so they lived for at least 20 days in order to prove they were the correct cells.

"Since this was brand new research, people didn't know what kind of tissue culture mature human neurons would like to live in," he said. "Once we figured it out, they could live indefinitely."

The research was supported by the National Institutes of Health.

<http://www.latimes.com/health/la-na-unapproved-drugs-20110303,0,4370223.story>

FDA orders 500 cough and cold drugs off the market

The prescription medications came onto the market before a law that required makers to prove their effectiveness. Many of the unapproved drugs, however, are already discontinued, a pharmacist says.

By Andrew Zajac, Washington Bureau Reporting from Washington

The Food and Drug Administration on Wednesday ordered the makers of about 500 unapproved prescription cough and cold medicines to get them off the market because they have not been proven safe and effective.

The drugs have been linked to a few relatively minor problems, such as drowsiness and irritability, but the FDA is concerned that medical problems associated with them may be significantly underreported.

"We have some specific safety concerns with some of them," Deb Autor, head of compliance in the FDA's drug office, said in a telephone news conference.

Some of the targeted drugs are labeled as suitable for infants and children but contain ingredients covered by a 2008 FDA advisory that warned against using over-the-counter medications in children under age 2.

Others are billed as timed-release products. Such medications are difficult to manufacture and, if quality controls are inadequate, some may release drugs too slowly, too quickly or not at all, Autor said.

The FDA also moved against several unapproved products that contain possibly dangerous combinations of drugs, such as two antihistamines, which can cause oversedation. None of the drugs is a household name, though Autor listed Cardec, Lodrane 24D, Organidin and Pediahist as brands consumers may have encountered.

In addition, none of the drugs fills a unique niche. "There are multiple other [approved] products available," Autor said. Many of the drugs came on the market before a 1962 law that required makers to prove their effectiveness. It's not clear how much of a public health threat they may pose.

A pharmacist who reviewed the FDA's list of unapproved cough and cold drugs said many of them are already off the market. "A lot of these medications have been discontinued. They're no longer available," said Sophia DeMonte, speaking on behalf of the American Pharmacists Assn. Wednesday's announcement does not affect over-the-counter preparations, which are widely used to treat cough and cold symptoms.

A list of unapproved drugs and other information can be found

at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm245048.htm>

NASA Scientist Sees Signs of Life in Meteorites

By ANDREW C. REVKIN

The buzz is building over a paper by Richard Hoover, an award-winning astrobiologist at NASA's Marshall Space Flight Center, concluding that filaments and other features found in the interior of three specimens of a rare class of meteorite appear to be fossils of a life form strongly resembling cyanobacteria.

Chemical analysis, Hoover argues, shows no evidence that the fossils are of organisms that infiltrated the meteorites after they arrived on Earth.

Here's one image from a field emission scanning electron microscope, showing what Hoover describes as features "interpreted as morphotypes of the cyanobacterium *Calothrix* spp." (*Journal of Cosmology*):

Hoover, who has for decades studied life forms that endure extreme conditions, has been probing such meteorites for many years, with earlier analysis - in 2007 and 2004 - revealing such structures and proposing a biological origin. Other work pointing to microfossils in meteorites goes back decades.

If Hoover's new analysis and interpretations hold up to scrutiny, the work could powerfully influence longstanding debates over the origins of terrestrial life and rarity of life elsewhere in the universe. The grand conclusion, of course, would be that life is a widespread phenomenon - the concept known as panspermia - and life on this planet could be an immigrant. And of course there's still the grand question of what started it all.

These are very big ifs, and this effort clearly falls into the category of "extraordinary claims" that require extraordinary evidence (as widely noted today). This is recognized by the journal's editors, who say they sent the paper for review to 100

independent scientists working in related fields, along with an invitation to 5,000 more researchers to critique the paper.

Rudy Schild, the journal's editor in chief, said in a note accompanying the paper that reactions to the research, "both pro and con," will be published on the journal's Web site between March 7 and 10. I'll check back in then of course, and I'm reaching out to Hoover and others working in this field now.

Here's the editor's note on the research, followed by the abstract and a link to the paper:

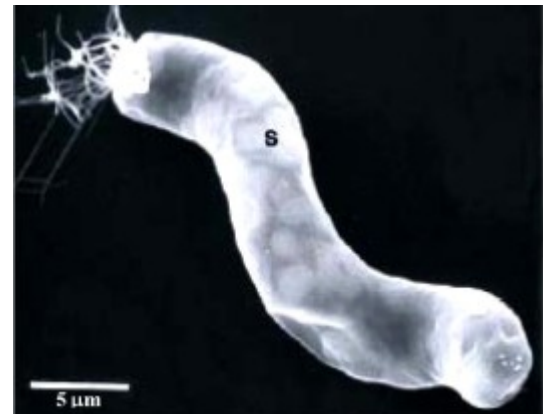
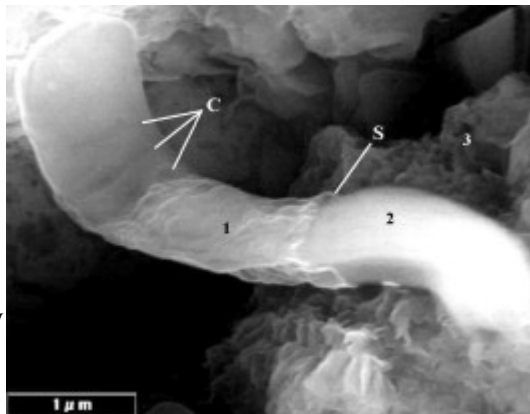
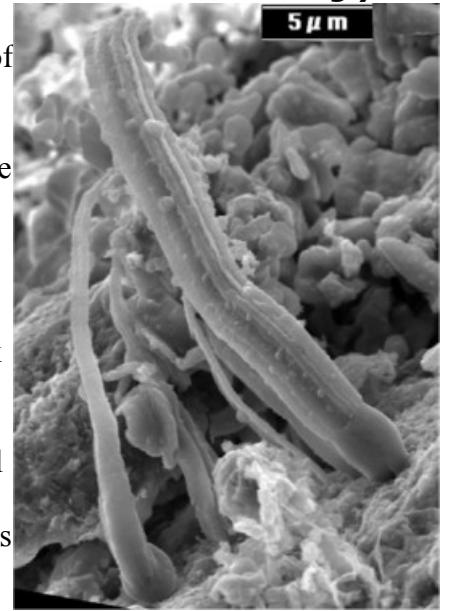
Fossils of Cyanobacteria in C11 Carbonaceous Meteorites

Richard B. Hoover, Ph.D. NASA/Marshall Space Flight Center

Synopsis

Dr. Hoover has discovered evidence of microfossils similar to Cyanobacteria, in freshly fractured slices of the interior surfaces of the Alais, Ivuna, and Orgueil C11 carbonaceous meteorites. Based on Field Emission Scanning Electron Microscopy (FESEM) and other measures, Dr. Hoover has concluded they are indigenous to these meteors and are similar to trichomic cyanobacteria and other trichomic prokaryotes such as filamentous sulfur bacteria. He concludes these fossilized bacteria are not Earthly contaminants but are the fossilized remains of living organisms which lived in the parent bodies of these meteors, e.g. comets, moons, and other astral bodies. The implications are that life is everywhere, and that life on Earth may have come from other planets.

Members of the Scientific community were invited to analyze the results and to write critical commentaries or to speculate about the implications. These commentaries will be published on March 7 through March 10, 2011.



*Is this ET? If it is, it resembles a distant cousin found here on Earth, a large bacteria aptly called *Titanospirillum velox*. Does this mean life is ubiquitous in the cosmos?*

Was life seeded on Earth from space?

*Spot the difference. An electron microscope image of an actual *Titanospirillum velox* – there's a strong resemblance with the "alien" fossil pictured top.*

**Official Statement from Dr. Rudy Schild,
Center for Astrophysics, Harvard-Smithsonian,
Editor-in-Chief, Journal of Cosmology.**

Dr. Richard Hoover is a highly respected scientist and astrobiologist with a prestigious record of accomplishment at NASA. Given the controversial nature of his discovery, we have invited 100 experts and have issued a general invitation to over 5000 scientists from the scientific community to review the paper and to offer their critical analysis. Our intention is to publish the commentaries, both pro and con, alongside Dr. Hoover's paper. In this way, the paper will have received a thorough vetting, and all points of view can be presented. No other paper in the history of science has undergone such a thorough analysis, and no other scientific journal in the history of science has made such a profoundly important paper available to the scientific community, for comment, before it is published. We believe the best way to advance science, is to promote debate and discussion.

Here's the abstract of the paper, which was published online Friday night in the March issue of the Journal of Cosmology:

[Fossils of Cyanobacteria in CI1 Carbonaceous Meteorites:](#)

Implications to Life on Comets, Europa, and Enceladus

Richard B. Hoover, Ph.D.

NASA/Marshall Space Flight Center, Huntsville, AL

Abstract

Environmental (ESEM) and Field Emission Scanning Electron Microscopy (FESEM) investigations of the internal surfaces of the CI1 Carbonaceous Meteorites have yielded images of large complex filaments. The filaments have been observed to be embedded in freshly fractured internal surfaces of the stones. They exhibit features (e.g., the size and size ranges of the internal cells and their location and arrangement within sheaths) that are diagnostic of known genera and species of trichomic cyanobacteria and other trichomic prokaryotes such as the filamentous sulfur bacteria. ESEM and FESEM studies of living and fossil cyanobacteria show similar features in uniseriate and multiseriate, branched or unbranched, isodiametric or tapered, polarized or unpolarized filaments with trichomes encased within thin or thick external sheaths. Filaments found in the CI1 meteorites have also been detected that exhibit structures consistent with the specialized cells and structures used by cyanobacteria for reproduction (baecocytes, akinetes and hormogonia), nitrogen fixation (basal, intercalary or apical heterocysts) and attachment or motility (fimbriae). Energy dispersive X-ray Spectroscopy (EDS) studies indicate that the meteorite filaments are typically carbon rich sheaths infilled with magnesium sulfate and other minerals characteristic of the CI1 carbonaceous meteorites. The size, structure, detailed morphological characteristics and chemical compositions of the meteorite filaments are not consistent with known species of minerals. The nitrogen content of the meteorite filaments are almost always below the detection limit of the EDS detector. EDS analysis of terrestrial minerals and biological materials (e.g., fibrous epsomite, filamentous cyanobacteria; mummy and mammoth hair/tissues, and fossils of cyanobacteria, trilobites, insects in amber) indicate that nitrogen remains detectable in biological materials for thousands of years but is undetectable in the ancient fossils. These studies have led to the conclusion that the filaments found in the CI1 carbonaceous meteorites are indigenous fossils rather than modern terrestrial biological contaminants that entered the meteorites after arrival on Earth. The $\delta^{13}\text{C}$ and D/H content of amino acids and other organics found in these stones are shown to be consistent with the interpretation that comets represent the parent bodies of the CI1 carbonaceous meteorites. The implications of the detection of fossils of cyanobacteria in the CI1 meteorites to the possibility of life on comets, Europa and Enceladus are discussed.

http://www.eurekalert.org/pub_releases/2011-03/sp-rwa030211.php

Rehabilitation within a day of knee replacement pays off

Starting rehabilitation sooner following knee arthroplasty surgery could pay dividends - for both patients and hospitals.

Commencing physical therapy within 24 hours of surgery can improve pain, range of joint motion and muscle strength as well as cut hospital stays, according to new research in the journal *Clinical Rehabilitation*, published by SAGE.

Mindful of the trend towards discharging patients from hospital more rapidly after surgery in recent years, physical therapy and public health researchers from Almeria, Malaga and Granada in Spain set out to investigate whether an early start to physical therapy would improve recovery from knee arthroplasty surgery. They compared patients who began treatment within 24 hours of surgery with those who began 48-72 hours after their operation in a random, controlled clinical trial. Each group comprised over 150 patients aged 50-75.

The post-operative treatment began with a series of leg exercises, breathing exercises, and tips on posture. By the second day walking short distances with walking aids was added, and in subsequent days this was built up towards adapting to daily life activities, such as beginning to climb stairs on day four.

On average, those beginning treatment earlier stayed in hospital two days less than the control group and had five fewer rehabilitation sessions before they were discharged. An early start also lead to less pain, a greater range of joint motion both in leg flexion and extension, improved muscle strength and higher scores in tests for gait and balance.

Health systems are currently subjected to strong economic pressures, and a cutting the length of hospital stays has become a priority. Other benefits of early mobilization after this surgery are fewer complications such as deep vein thrombosis, pulmonary embolism, chest infection, and urinary retention. With hospital-acquired infections such as MRSA also a serious concern, a shorter hospital stay might also lower the risk to patients of contracting this type of secondary infection.

"Orthopaedics, especially knee replacement surgery, is one area that may lend itself to accelerated discharge," says author Adelaida M^a Castro Sánchez, from the University of Almeria. "We therefore postulated that early rehabilitation after total knee arthroplasty could accelerate the capacity of patients for daily life activities, and reduce their hospital stay."

Osteoarthritis is estimated to affect around three quarters of over 65s in developed countries, and when it affects the knees it can be intensely painful, affecting the gait and leading to deformity. As a result, replacing the knee joint with a surgical implant has now become a routine, but major, surgical procedure.

Benefits of starting rehabilitation within 24 hours of primary total knee arthroplasty: randomised clinical trial by Nuria Sánchez Labraca, Adelaida Maria Castro-Sánchez, Guillermo A. Matarán-Peñarrocha, Manuel Arroyo-Morales, María del Mar Sánchez-Joya and Carmen Moreno-Lorenzo is published today, 7th March 2011, in Clinical Rehabilitation.

http://www.eurekalert.org/pub_releases/2011-03/nu-cct030411.php

Cardiac catheter that can do it all

New stretchable electronics device promises to make cardiac ablation therapy simpler

In an improvement over open-heart surgery, cardiologists now use catheters to eliminate damaged heart tissue in certain patients, such as those with arrhythmias. But this, too, can be a long and painful procedure as many catheters, with different functions, need to be inserted sequentially.

Now an interdisciplinary team including researchers from Northwestern University has developed one catheter that can do it all. This tool for cardiac ablation therapy has all necessary medical devices printed on a standard balloon catheter: a device for eliminating damaged tissue using heat, temperature and pressure sensors, an LED and an electrocardiogram (EKG) sensor.

The multifunctional catheter makes a minimally invasive technique for heart surgery even better. Both diagnostic and treatment capabilities are combined in one. The stretchable electronics developed by Yonggang Huang of Northwestern and John Rogers of the University of Illinois at Urbana-Champaign make it possible.

The research will be published March 6 by the journal Nature Materials.

"The use of one catheter to achieve all these functions will significantly improve clinical arrhythmia therapy by reducing the number of steps in the procedure, thereby saving time and reducing costs," said Huang, Joseph Cummings Professor of Civil and Environmental Engineering and Mechanical Engineering at Northwestern's McCormick School of Engineering and Applied Science. He led the Northwestern portion of the work.

In conversation with collaborating cardiologists, Moussa Mansour, M.D., of Harvard Medical School; Marvin Slepian, M.D., of the University of Arizona; and Joshua Moss, M.D., and Brian Litt, M.D., of the University of Pennsylvania, Huang and Rogers recognized that their stretchable electronics could improve the surgical tools currently used in cardiac ablation therapy. This procedure is used to cure or control a variety of arrhythmias, or irregular heartbeats.

The electronics Huang and Rogers use in this study are based on a "pop-out" design of interconnects, similar to their early design for stretchable electronics but with much larger -- approximately 130 percent -- stretchability. The type of arrhythmia the team focuses on is tachycardia, when the heart beats too fast; the tissue that induces this condition is the target of their ablation therapy.

This ability of the electronics to stretch is important because the researchers print all the necessary medical devices on a section of a standard endocardial balloon catheter (a thin, flexible tube) where the wall is thinner than the rest. (This section is slightly recessed from the rest of the catheter's surface.) There the sensitive devices and actuators are protected during the catheter's trip through the body to the heart. Once the catheter reaches the heart, the catheter is inflated, and the thin section expands significantly; the electronics are now exposed and in contact with the heart.

"Our challenge was how to make the electronics sustain such a large stretch when the thin wall expands under pressure," Huang said. "We devised what we call a 'pop-out interconnect' that performs very well. We didn't expect the electronics to sustain a stretch nearly three times the section's length."

Once the catheter is in place, the individual devices can perform their specific tasks when needed. The pressure sensor determines the pressure on the heart; the EKG sensor monitors the heart's condition during the procedure; the LED sheds light for imaging and also provides the energy for ablation therapy to eliminate (ablate) the tachycardia-inducing tissue; and the temperature sensor controls the temperature so as not to damage other, good tissue.

The entire system is designed to operate reliably without any changes in properties as the balloon inflates and deflates. "It demands all the features and capabilities that we've developed in stretchable electronics over the years in a pretty aggressive way," Rogers said. "It also really exercises the technology in an extreme, and useful, manner -- we put everything on the soft surface of a rubber balloon and blow it up without any of the devices failing."

These devices can deliver critical high-quality information, such as temperature, mechanical force, blood flow and electrogram, to the surgeon in real time. While the multifunctional catheter has not been used with humans, the researchers have demonstrated the utility of the device with anesthetized animals.

The fabrication techniques the engineers used in developing the balloon device could be exploited for integrating many classes of advanced semiconductor devices on a variety of surgical instruments. For example, the team also demonstrated surgical gloves with sensor arrays mounted on the fingertips to show that the electronics could be applied to other biomedical platforms.

Huang led the theory and mechanical and thermal design work at Northwestern. He and his colleagues' contribution was to ensure the mechanical integrity of the device so there was no failure during significant stretching and to control temperature during cardiac ablation therapy. Rogers, the Lee J. Flory Founder Chair in Engineering and professor of materials science and engineering at the University of Illinois at Urbana-Champaign, led the design, experimental and fabrication work.

The paper is titled "Materials for Multifunctional Balloon Catheters with Capabilities in Cardiac Electrophysiological Mapping and Ablation Therapy." The senior authors of the paper are from Northwestern University, the University of Illinois at Urbana-Champaign, Harvard Medical School, the University of Arizona and the Hospital of the University of Pennsylvania.

http://www.eurekalert.org/pub_releases/2011-03/waeh-nic030411.php

Newly identified cell population key to immune response

Scientists from the Walter and Eliza Hall Institute have identified the key immune cell population responsible for regulating the body's immune response.

The finding could have wide-ranging repercussions for the treatment of autoimmune diseases, organ transplantation and cancer, and change how the efficacy of newly developed drugs is measured.

The discovery was made by Dr Erika Cretney, Dr Axel Kallies and Dr Stephen Nutt from the institute's Molecular Immunology division. It centred on a population of immune cells called regulatory T cells.

Regulatory T cells (T-regs) are responsible for limiting the immune response. Disorders that decrease T-reg activity can lead to autoimmune disorders such as type 1 diabetes or coeliac disease, while increased T-reg activity can suppress the immune system when it should be actively killing cancerous or infected cells.

Dr Kallies said the research team had used molecular signatures to identify which cells within the regulatory T cell population were responsible for suppressing immune responses.

"It turns out that the bulk of cells which are classified as regulatory T cells may not do much," Dr Kallies said. "In this study we have identified a distinct group of effector regulatory T cells, or 'active T-regs', which are the key drivers of immune response regulation."

Dr Nutt said the research had implications for clinical trial outcomes.

"Researchers often measure regulatory T cell numbers in clinical trials as a parameter for establishing whether there has been a positive immune response," Dr Nutt said. "We have shown that the absolute number of regulatory T cells isn't as important as the presence of this particular active regulatory T cell population."

Dr Nutt said the research showed that mice without active T-reg cell populations developed severe autoimmune inflammatory bowel disease, which is fatal.

"Not having this T cell population in the gut causes the immune response to go into overdrive and attack the body's own cells," he said. "A lack of the factor that is needed to generate active T-reg cells has also been implicated in human genome-wide studies of Crohn's disease. So it would seem that this cell population is strongly linked to the development of autoimmunity."

Dr Cretney said that re-defining the active subset of the T-reg population would give researchers the ability to develop new ways to increase or block their activity in the body. "The next step for my research is to look at the function of this active T-reg population in autoimmunity and in cancer."

Dr Kallies said that for these reasons, there was a lot of excitement in the medical community about regulatory T cells. "Clinicians have shown that regulatory T cell activity impacts on many therapies," he said. "Many research teams are trying to manipulate and expand these cells for therapeutic use. Our finding will transform the way that researchers look at immune responses and open new avenues for treating diseases such as autoimmunity and cancer."

The research appears on the cover of today's edition of Nature Immunology. It was supported by the National Health and Medical Research Council, the Australian Research Council and Pfizer Australia.

<http://www.physorg.com/news/2011-03-role-molecule-brain-epileptic-seizures.html>

New role for an old molecule: protecting the brain from epileptic seizures

For years brain scientists have puzzled over the shadowy role played by the molecule putrescine, which always seems to be present in the brain following an epileptic seizure, but without a clear indication whether it was there to exacerbate brain damage that follows a seizure or protect the brain from it.

A new Brown University study unmaskes the molecule as squarely on the side of good: It seems to protect against seizures hours later.

Putrescine is one in a family of molecules called "polyamines" that are present throughout the body to mediate crucial functions such as cell division. Why they surge in the brain after seizures isn't understood. In a lengthy set of experiments, Brown neuroscientists meticulously traced their activity in the brains of seizure-laden tadpoles. What they found is that putrescine ultimately converts into the neurotransmitter GABA, which is known to calm brain activity. When they caused a seizure in the tadpoles, they found that the putrescine produced in a first wave of seizures helped tadpoles hold out longer against a second wave of induced seizures.

Carlos Aizenman, assistant professor of neuroscience and senior author of a study published in the journal Nature Neuroscience, said further research could ultimately produce a drug that targets the process, potentially helping young children with epilepsy. Tadpoles and toddlers aren't much alike, but this basic aspect of their brain chemistry is. "Overall, the findings presented in this study may have important therapeutic implications," Aizenman and co-authors wrote. "We describe a novel role for polyamine metabolism that results in a protective effect on seizures induced in developing animals."

Detective work

The result that "priming" the tadpoles with a seizure led to them being 25 percent more resistant to a subsequent seizure four hours later was "puzzling," said Aizenman, who is affiliated with the Brown Institute for Brain Science. It took about a dozen more experiments before his team, led by graduate student Mark Bell, could solve the mystery. First they hindered polyamine synthesis altogether and found that not only did the protection against seizures disappear, but it also left the tadpoles even more vulnerable to seizures. Then they interrupted the conversion of putrescine into other polyamines and found that this step enhanced the protection, indicating that putrescine was the beneficial member of the family.

Going with those results, they administered putrescine directly to the tadpoles and found that it took 65 percent longer to induce a seizure than in tadpoles that didn't get a dose of putrescine.

Further experiments showed that the protective effect occurs after putrescine is metabolized, with at least one intermediary step, into GABA, and GABA receptors are activated in brain cells.

"Potentially by manipulating this pathway we may be able to harness an ongoing protective effect against seizures," Aizenman said. "However I should caution that this is basic research and it is premature to predict how well this would translate into the clinic." In the meantime, the research may also help explain a bit more about young brains in general, Aizenman said. "Our findings may also tell us how normal brains, especially developing brains, may regulate their overall levels of activity and maybe keep a type of regulatory check on brain activity levels," he said.