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**Current blood transfusion practice in trauma centers feasible but wastes scarce plasma**  
*The use of a 1:1:1 blood transfusion protocol in patients with severe trauma is feasible in hospitals, although it is associated with higher waste of plasma, according to a randomized trial published in CMAJ (Canadian Medical Association Journal).*

Previous retrospective studies suggested that a 1:1:1 transfusion strategy or fixed-ratio transfusion could reduce the number of deaths from hemorrhage; therefore, the strategy has been widely adopted in trauma centres around the world and for nontrauma patients. It uses an equal ratio of red blood cells, plasma and platelets to transfuse patients and has been in use since 2007. However, 1:1:1 is associated with higher waste of blood plasma.

Researchers conducted a randomized trial to determine feasibility and safety of 1:1:1 in 78 patients presenting to Sunnybrook Health Sciences Centre, a large trauma centre in Toronto, Canada, with low blood pressure and substantial bleeding who were expected to need massive blood transfusion. About half the patients (40) were randomly assigned to the fixed-ratio transfusion, and the remaining (38) underwent the laboratory-guided transfusion protocol at the centre.

"These findings suggest that a fixed-ratio transfusion protocol is feasible, but it was associated with increased plasma wastage (about 2 units per patient)," writes Dr. Sandro Rizoli, Trauma Program Director, St Michael's Hospital, and Professor of Surgery and Critical Care Medicine, University of Toronto, with coauthors.

Thawed type AB plasma, a scarce resource, is needed for 1:1:1 transfusion which also involves delays because of the need to thaw the material.

However, deaths from all causes after 28 days was higher in the fixed-ratio group (32.5%) compared with 14% in the control group and there was a higher rate of respiratory distress in the patients receiving 1:1:1.

"Widespread adoption of the [1:1:1] strategy has significant resource and safety implications. Its full implementation requires access to thawed type AB plasma, which is chronically in short supply. ...the 1:1:1 transfusion protocol may lead to unnecessary exposure to blood components and an increased risk of acute respiratory distress syndrome, sepsis and multiple organ dysfunction," write the authors.

They caution that widespread implementation of the 1:1:1 transfusion strategy will be challenging because of an increased demand for plasma, a scarce resource, and higher wastage. Larger clinical trials should be conducted to provide more data.

[http://www.eurekalert.org/pub\\_releases/2013-07/twi-pf071013.php](http://www.eurekalert.org/pub_releases/2013-07/twi-pf071013.php)

**Prior flu exposure dictates your future immunity, allowing for new, rationally developed regiments**

*Findings offer alternative approach to creating a universal influenza vaccine*

A team of scientists, led by researchers at The Wistar Institute, has determined that it might be possible to stimulate the immune system against multiple strains of influenza virus by sequentially vaccinating individuals with distinct influenza strains isolated over the last century. Their results also suggest that world health experts might need to re-evaluate standard tests used for surveillance of novel influenza strains. Their findings are published in the Journal of Experimental Medicine, available online now.

According to the Wistar researchers, their analysis could lead to an alternative approach to creating a "universal" flu vaccine—a vaccine that would provide resistance to seasonal and pandemic influenza strains over many years, negating the need for an annual flu shot.

"Influenza vaccines are very safe and provide good protection. However, we need to continuously update seasonal flu vaccines because influenza viral proteins change over time," said Scott Hensley, Ph.D., an assistant professor at The Wistar Institute and corresponding author on the study. "Since influenza viruses are constantly changing, we all have unique pre-exposure histories that depend on when we were born and the specific types of viruses that circulated during our childhood."

Vaccines work by stimulating the immune system to produce antibody proteins against particles (called antigens) from an infectious agent, such as bacteria or a virus. The immune system saves the cells that produce effective antibodies, which then provide immunity against future attacks by the same or similar infectious agents. Despite the availability of a vaccine, seasonal influenza typically kills 36,000 Americans, alone, and nearly a half million individuals around the world, in total.

Most current efforts to create universal vaccines hinge on the idea of generating antibodies against a portion of the virus that is relatively unchanged year-to-year.

"Our studies demonstrate that individuals that are infected sequentially with dramatically different influenza strains mount antibody responses against a conserved region of influenza virus," Hensley said. "Since we now

know that pre-exposure events can influence vaccine responsiveness in a predictable way, we can begin to design vaccine regimens that preferentially elicit antibody responses against conserved regions of influenza virus." The researchers began their current work by studying human antibody responses against the 2009 pandemic H1N1 virus. The 2009 strain is antigenically distinct from recently circulating seasonal H1N1 strains, and a distant relative of the virus that caused the devastating "Spanish Flu" of the early 20th century. The most effective antibodies are those that bind to a particular portion (or "epitope") of hemagglutinin (HA), a protein produced by the influenza virus.

According to Hensley, however, their chief insight occurred when his team hit the "sort" button on a spreadsheet document, thereby arranging all samples by age of the donor. Different aged people, they found, mount vastly different antibody responses to pandemic H1N1, depending on whether or not they were exposed to a seasonal H1N1 years earlier. "We can now accurately predict how individuals will respond to the pandemic H1N1 strain based on the year that they were born," Hensley said.

Their investigation also suggests that ferrets with no prior influenza exposure might not be the most reliable predictor of human immune responses. Anti-sera—or blood containing antibodies—created in these "naïve" ferrets are commonly used for influenza surveillance. The researchers found that naïve ferrets mount a response to an epitope in a decidedly different portion of HA than do most humans, but subsequently infecting these ferrets with other historical influenza strains can shift the antibody response toward the epitope that human antibodies recognize. This shift might also be replicable in humans through multiple infections or vaccinations, the researchers believe.

According to Hensley, one strategy would be to sequentially vaccinate children with antigenically distinct viral strains. "Babies are born with an immunological blank slate," Hensley said. "We may be able to strategically vaccinate our children with antigenically diverse influenza strains to elicit antibodies against conserved viral epitopes."

*The portion of this research conducted at The Wistar Institute was funded by National Institute of Allergy and Infectious Diseases grant K22AI091651, the Commonwealth of Pennsylvania CURE Program, and a University of Pennsylvania Institute for Translational Medicine and Therapeutics grant.*

*Members of the Hensley laboratory that co-authored this study include Yang Li, Jaclyn L. Myers, Ph.D., Colleen B. Sullivan, Jonathan Madara, and Susanne Linderman. Additional co-authors also include Qin Liu, M.D., Ph.D., of Wistar; Joshua B. Plotkin, Ph.D., and David L. Bostick, Ph.D. of the University of Pennsylvania; Susanna Esposito, M.D., and Nicola Principi, M.D. from the University of Milan, Donald M. Carter, Ph.D., and Ted M. Ross, Ph.D., formerly of the University of Pittsburgh; Jens Wrammert, Ph.D., and Rafi Ahmed, Ph.D., of Emory University, and Patrick Wilson, Ph.D. of University of Chicago.*

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## **RI Hospital study: Lunar cycle affects cardiac patients undergoing acute aortic dissection**

### ***Waning and full moon cycles impact length of stay, mortality***

PROVIDENCE, R.I. – If you need cardiac surgery in the future, aortic dissection in particular, reach for the moon. Or at least try to schedule your surgery around its cycle. According to a study at Rhode Island Hospital, acute aortic dissection (AAD) repair performed in the waning full moon appears to reduce the odds of death, and a full moon was associated with shorter length of stay (LOS). The study is published online in advance of print in the journal *Interactive Cardiovascular and Thoracic Surgery*.

The purpose of the study was to assess the effect of natural time variations of both the season and the lunar cycle phase on hospital survival and length of stay (number of days a patient is in the hospital) following acute aortic dissection repair.

"While there has been previous research of seasonal impacts on cardiovascular disease, there has not been any data about the effect of the lunar cycles on cardiac cases, until now," said senior author Frank Sellke, M.D., chief of cardiothoracic surgery and co-director of the Cardiovascular Institute at Rhode Island, The Miriam and Newport hospitals. "We focused the study on patients having aortic dissection and found that the odds of dying following this procedure were greatly reduced during the waning full moon, and that length of stay was also reduced during the full moon."

Researchers studied the relationship of lunar cycles and seasonal variation on two surgical groups: Group A: Patients having repair of ascending aortic dissection, and Group B: Patients having aortic dissection and either aortic valve surgery, coronary bypass surgery, or both. They also studied the relationship of the lunar cycle on patients' length of stay. The study indicates that aortic dissection performed during the full moon phase had a significantly shorter length of stay than two other moon phases – 10 days for the full moon cycle vs. 14 days for the other phases.

"Can we always plan for such procedures to be performed around lunar cycles? Of course not," Sellke said.

"But better understanding the effects of the environment – including seasonal and lunar cycles – on our health can help us to better understand these rhythms, and ultimately provide better care for our patients."

*The study was not funded. Sellke's principal affiliation is Rhode Island Hospital, a member hospital of the Lifespan health system in Rhode Island. He also has an academic appointment at The Warren Alpert Medical School of Brown University.*

*Other Lifespan researchers involved in the study are Joseph L. Fava, Ph.D, of The Miriam Hospital; Taiho Shin, MD; Nikolas Dobrilovic, M.D.; Afshin Ehsan, M.D.; Arthur Bert, M.D., all of Rhode Island Hospital and the Alpert Medical School. Lead research Jeffrey Shuhaiber, formerly with Rhode Island Hospital, is now affiliated with the Cleveland Clinic.*

[http://www.eurekalert.org/pub\\_releases/2013-07/uocd-cas071513.php](http://www.eurekalert.org/pub_releases/2013-07/uocd-cas071513.php)

## **Common autism supplement affects endocrine system**

### ***Study of luteolin shows progesterone-blocking effects***

Plant-based diets are healthy. Plants are high in flavonoids. So flavonoids are healthy. At least that's the reasoning of many manufacturers of flavonoid-based nutritional supplements. But a University of Colorado Cancer Center study published this week in the journal *Hormones & Cancer* shows that may not be the case. Flavonoids tested in the study affected the endocrine system in ways that in one case promoted cancer and in another repressed it.

"Even outside these specific findings with cancer, what we're saying is that flavonoids are active and not always in good or even predictable ways," says Steven K. Nordeen, PhD, investigator at the CU Cancer Center and professor emeritus in the Department of Pathology at the CU School of Medicine.

His study explored the effects of the flavonoids luteolin and quercetin on cell models of breast and endometrial cancer. In over-the-counter supplement form, the first compound, luteolin, is commonly recommended for the treatment of pediatric autism spectrum disorders.

Nordeen and colleagues show that luteolin blocks some of the endocrine effects of the hormone progesterone. Work from another CU Cancer Center investigator, Carol Sartorius, PhD, had previously shown that progesterone expands a population of therapy-resistant, stem cell-like cells in some breast cancers. In the present work, Nordeen showed that luteolin blocked this increase – a beneficial effect. But then in an endometrial cancer cell model, luteolin had two deleterious effects. First, it acted like estrogen to directly stimulate cancer cell growth and second, by again blocking progesterone's action, luteolin disabled the brake that progesterone puts on estrogen-dependent endometrial cancer growth.

What helps in breast cancer hurts in endometrial cancer. But Nordeen says the most important issue is the simple fact that these flavonoids are active and we don't yet know how the body responds to the blood levels of flavonoids reached when taking supplements. In the case of luteolin supplements for autism/spectrum, "You're giving prepubescent kids a supplement that affects the endocrine system and that's dangerous," Nordeen says. He points out that "nutraceuticals" – which include flavonoid and other active-ingredient supplements – aren't FDA regulated to the degree that are medicines. This allows manufacturers to market supplements without fully testing nutraceutical products for efficacy or potential side effects. "I'm not saying that flavonoids in a normal, plant-rich diet are bad," Nordeen says, "but caution is warranted when consuming additional flavonoids via supplements.

Detrimental effects of flavonoids are not without precedent. A diet of red clover can affect development and reproduction in livestock. And the *New England Journal of Medicine* documented breast development in prepubescent boys that was linked to the use of shampoos and balms containing lavender or tea tree oils containing flavonoids.

"Because flavonoid supplements are widely used, we need to do the research necessary to understand their effects, both desirable and undesirable, in consumers using these products. We shouldn't be taking this stuff blindly because, just like prescription medicines, there can be unanticipated consequences," Nordeen says.

<http://bit.ly/16E7UiF>

## **Prickly Painkiller**

### ***An experimental plant extract may end intractable pain with a single injection***

By Arlene Weintraub | Monday, July 15, 2013 | 6

Although medicine has advanced far enough to treat basic headaches, strained muscles and the agony of having a cavity filled, inflammatory pain—the kind that results from osteoarthritis, bone cancer and back injuries—has proved to be a far more elusive target. Current remedies, including morphine and other opiates, flood all the nerves of the body, causing dangerous side effects. More localized remedies, such as steroid injections, wear off over time. Recently researchers have begun working with a toxin found in a Moroccan cactuslike plant that may be able to deliver permanent, local pain relief with a single injection.

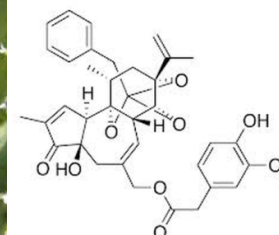
The compound, called resiniferatoxin (RTX), works by destroying the neurons specifically responsible for inflammatory pain. These neurons extend from the body's periphery (including the skin and internal organs) to the spinal cord, carrying pain signals along their axons. The signals eventually travel up to the brain. When injected directly into spinal fluid, RTX homes in on and kills only those neurons that produce a protein called TRPV1, which transmits the sensation of noxious heat and inflammation. It does not harm normal tissue and other pain-sensing nerves, such as those that produce the feeling of pinpricks or pinches.

RTX has been tested in pet dogs that suffer from debilitating pain, and the studies have shown promising results. Unlike rodents, dogs experience pain much the way people do. "And they have personalities," says Andrew Mannes, chief of the department of perioperative medicine at the National Institutes of Health. "We can get insight into their psyches that we can't with rats."

The NIH is now running a trial of RTX in people with advanced cancer. Although Mannes and his colleagues cannot predict how soon they will have data, pain experts are watching the trial with interest. David Maine, director of the Center for Interventional Pain Medicine at Mercy Medical Center in Baltimore, says there are other ways to kill pain fibers, such as using alcohol to destroy nerves, but they sometimes cause the pain to come roaring back, far worse than before. "When you can streamline where a drug acts and avoid consequences outside of that, you potentially have a winner," Maine says.



*Euphorbia resinifera*  
(Resin spurge)



resiniferatoxin

<http://news.discovery.com/human/health/randy-travis-heart-condition-130715.htm#mkcpgn=rssnws1>

### **Randy Travis Heart Crisis: Could It Happen to You?**

***Diagnosed with acquired viral cardiomyopathy, a life threatening condition that strikes with surprising frequency***

Jul 15, 2013 12:00 PM ET // by Paul Greenberg

More than a week after being rushed to the hospital with a heart ailment, Grammy-award-winning country singer Randy Travis remains sedated and in critical condition, although reportedly slowly improving. Travis was diagnosed with acquired viral cardiomyopathy, a life threatening condition that strikes with surprising frequency, although it is not clearly understood by the general population. The widespread publicity surrounding Travis' condition has caused many to wonder: How common is cardiomyopathy, and what causes it?

According to Dr. Thierry H. Le Jemtel, director of the Heart Failure and Cardiac Transplantation Program at Tulane Heart and Vascular Institute, it's almost impossible to know how many people have this condition.

"We really don't know for sure how common it is because many people can have this condition and not even know it," said Le Jemtel. "That means we never see them and they go undiagnosed. They may not even realize they have symptoms, because they are really only using a small percentage of their heart muscle's potential."

Further complicating the diagnosis is the fact that there is a spectrum of viruses that can cause cardiomyopathy, a condition that can cause the heart to become enlarged, thick or rigid. However, those that do exhibit pronounced symptoms will generally experience extreme shortness of breath and fatigue, Le Jemtel said.

"In America people rarely walk more than five or six blocks. People do not climb a lot of stairs, so overall the peak function of your heart decreases. Unless you're active in sports, you probably only use about 20 percent of your reserves. That means a lot of patients only find out they have the condition when the symptoms become extreme."

Once that happens, doctors are left to determine the diagnosis through process of elimination. First, coronary artery disease must be ruled out, as well as other common conditions including genetic problems, hypertension and diabetes. Once those possibilities are eliminated, a catheter may be inserted to perform a biopsy on a small piece of the left ventricle of the heart. This procedure will allow doctors to determine if the condition is viral, said Le Jemtel.

Travis's symptoms were so extreme that he was implanted with a left ventricular assist device that helps pump blood from the lower chambers of the heart to the rest of the body. His condition worsened when he suffered a blood clot that caused a stroke, which led to surgery to relieve pressure on his brain.

Not all patients suffer such dire consequences. Terry Merlenbach, 61, was diagnosed with acquired viral cardiomyopathy 10 years ago. "For two nights, I couldn't sleep because I was so short of breath I was literally panting," Merlenbach said. "It got worse and finally I ended up in the emergency room. They did an angiogram to find out if my arteries were clogged, but eventually they told me I had a virus that had weakened my heart."

Living with the condition for a decade has severely limited Merlenbach's lifestyle, although she is able to lead a relatively normal life.

"I can't work a full time job any longer because I tire out very easily, and I'm told this is pretty common in people that have what I have. I have limited stamina, but I have adjusted my activities to accommodate it. I'm actually doing pretty well, all things considered." Merlenbach sees a cardiologist every six months to monitor the condition and must take a beta-blocker drug every day. Beta-blockers reduce blood pressure.

Travis's condition may be complicated by his alcoholism, even though he went through a rehab program in late 2012. "Long term alcohol use definitely weakens the heart," Le Jemtel said. "There is a condition called alcoholic cardiomyopathy, which leads to progressive and chronic cardiac dysfunction."

Although it is not known if Travis had the condition prior to his most recent health crisis, Le Jemtel said it is possible the alcohol abuse may have been a contributing factor.

<http://www.medscape.com/viewarticle/807822?src=rss>

### Inadequate Sleep May in Itself Up Odds of Diabetes Onset

*Troubled sleep, short sleep, and sleep apnea predicted the onset of type 2 diabetes, independent of mental-health disorders, in a prospective study of young, healthy military personnel.*

Marlene Busko

This is the first study to clearly show that lack of a good night's sleep may be an independent risk factor for subsequent diabetes, rather than merely a surrogate marker for a mental-health disorder such as depression or posttraumatic stress disorder (PTSD), the researchers say.

"Since mental-health conditions and sleep disorders seem to be independently related to diabetes, [this research suggests that] there could be different pathways leading to diabetes," lead author Edward J. Boyko, MD, from the Department of Veterans Affairs Puget Sound Health Care System in Seattle, Washington, told *Medscape Medical News*. However, since this was an observational study, it is too early to establish a causal relationship between inadequate sleep and incident diabetes, he cautioned, adding that further research is needed.

The paper was [published online](#) July 8 in *Diabetes Care*.

#### Sleep-Deprived Citizens, Diabetes Epidemic

In the United States, the incidence of diabetes has risen dramatically over the past 30 years, while the average hours of nightly sleep have declined over that time, the authors report. A recent study showed that close to a third of full-time workers in the United States get 6 or fewer hours of sleep each night, they note. Poor sleep, depression, and PTSD have all been reported to predict a higher risk for type 2 diabetes, but it was unclear whether sleep disturbances merely reflected mental-health disorders.

The researchers examined data from 47,093 members of the US military service who enrolled in the [Millennium Cohort Study](#) in 2001 to 2003 and replied to survey questions 3 years and 6 years later.

The population was "younger [and healthier] than a population you would typically study for risk of diabetes; [at baseline] the mean age was only 34.9 years, and they were only slightly overweight, with an average [body mass index] BMI of 26," Dr. Boyko noted.

The participants replied to questions asking about the average number of hours they slept each day, whether they often had trouble falling or staying asleep, and whether they had been told by a doctor that they had sleep apnea.

From baseline to year 3, there were 383 cases of new, self-reported diabetes, and from year 3 to year 6 there were 488 cases of newly occurring diabetes. Compared with individuals who did not develop new-onset diabetes, those who did were more likely to be nonwhite and older (age 42.6 vs 36.6 years)

and have a higher mean BMI (29.4 vs 26.3) at baseline. They were also significantly more likely to have reported mental-health and sleep disorders at baseline.

After adjustment for demographic and mental health characteristics, measures of inadequate sleep were still linked with a 1.21-fold to a 1.78-fold increased risk of being diagnosed with type 2 diabetes.

#### Percentage of Participants With Baseline Mental-Health and Sleep Disorders, No Diabetes Onset vs Diabetes Onset (Within 6 Years)\*

Baseline Characteristic	No Diabetes Onset (n = 46,710)	With Diabetes Onset (n = 871)
Depression	2.6	5.1
Panic disorder	1.2	3.4
Other anxiety disorder	1.8	4.1
PTSD	3.7	8.4
Sleep apnea	2.6	10.3
Trouble sleeping	23.4	31.9
Sleeping ≤ 5 hours a night	14.7	19.8

\*P ≤ 0.01 for all

#### Sleep-Related Risk Factors for Incident Type 2 Diabetes

Risk Factor	Odds Ratio (95% CI)
Trouble sleeping	1.21 (1.03–1.42)
Sleep apnea	1.78 (1.39–2.28)
Sleeping < 5 hours a night*	1.52 (1.09–2.14)
Sleeping 5 hours a night*	1.28 (1.01–1.62)

\*Compared with sleeping 7 hours a night

Although the survey looked at military personnel, "I think the results really apply to a working population of younger individuals," Dr. Boyko said.

Based on these outcomes, "it is unlikely that sleep simply serves as a surrogate marker for associated mental-health conditions previously shown to predict diabetes risk," according to the authors.

"Confirmation of these findings through further analyses may advance our understanding of diabetes pathophysiology and create new opportunities for prevention," they conclude.

*The study was supported by the Department of Defense. The Millennium Cohort Study is funded through the Military Operational Medicine Research Program of the US Army Medical Research and Materiel Command. The Department of Veterans Affairs Puget Sound supported Dr. Boyko's involvement in this research. The authors have reported no relevant financial relationships.*

*Diabetes Care. Published online July 8, 2013. [Abstract](#)*

<http://www.sciencedaily.com/releases/2013/07/130715151059.htm>

## **Computer as Smart as a 4-Year-Old? Researchers IQ Test New Artificial Intelligence System**

***Artificial and natural knowledge researchers IQ-tested one of the best available artificial intelligence systems and learned that it's about as smart as the average 4-year-old.***

**By Jeanne Galatzer-Levy.**

Artificial and natural knowledge researchers at the University of Illinois at Chicago have IQ-tested one of the best available artificial intelligence systems to see how intelligent it really is. Turns out it's about as smart as the average 4-year-old, they will report July 17 at the U.S. Artificial Intelligence Conference in Bellevue, Wash. The UIC team put ConceptNet 4, an artificial intelligence system developed at M.I.T., through the verbal portions of the Weschsler Preschool and Primary Scale of Intelligence Test, a standard IQ assessment for young children. They found ConceptNet 4 has the average IQ of a young child. But unlike most children, the machine's scores were very uneven across different portions of the test.

"If a child had scores that varied this much, it might be a symptom that something was wrong," said Robert Sloan, professor and head of computer science at UIC, and lead author on the study. Sloan said ConceptNet 4 did very well on a test of vocabulary and on a test of its ability to recognize similarities.

"But ConceptNet 4 did dramatically worse than average on comprehension-the 'why' questions," he said.

One of the hardest problems in building an artificial intelligence, Sloan said, is devising a computer program that can make sound and prudent judgment based on a simple perception of the situation or facts-the dictionary definition of commonsense.

Commonsense has eluded AI engineers because it requires both a very large collection of facts and what Sloan calls implicit facts-things so obvious that we don't know we know them. A computer may know the temperature at which water freezes, but we know that ice is cold.

"All of us know a huge number of things," said Sloan. "As babies, we crawled around and yanked on things and learned that things fall. We yanked on other things and learned that dogs and cats don't appreciate having their tails pulled." Life is a rich learning environment. "We're still very far from programs with commonsense-AI that can answer comprehension questions with the skill of a child of 8," said Sloan. He and his colleagues hope the study will help to focus attention on the "hard spots" in AI research.

Study coauthors are UIC professors Stellan Ohlsson of psychology and Gyorgy Turan of mathematics, statistics and computer science; and UIC mathematical computer science undergraduate student Aaron Urasky.

*The study was supported by award N00014-09-1-0125 from the Office of Naval Research and grant CCF-0916708 from the National Science Foundation.*

<http://www.sciencedaily.com/releases/2013/07/130715151156.htm>

## **Chemical Compound Shows Promise as Alternative to Opioid Pain Relievers**

***A drug targeting a protein complex containing two different types of opioid receptors may be an effective alternative to morphine and other opioid pain medications, without any of the side effects or risk of dependence, according to research led by the Icahn School of Medicine at Mount Sinai.***

The findings are published in July in the journal Proceedings of the National Academy of Sciences.

Morphine is still the most widely-used pain reliever, or analgesic, in people with severe pain, but chronic use can lead to addiction and negative side effects such as respiratory issues, constipation, or diarrhea.

In a previous study published in Science Signaling by Lakshmi Devi, PhD, Professor of Pharmacology and Systems Therapeutics at Mount Sinai, researchers identified a therapeutic target called a GPCR heteromer, which is a protein complex that is made up of two opioid receptors called mu and delta. They also showed that

the heteromer is abundant in the area of the brain that processes pain, and is the likely cause of morphine tolerance and side effects.

In the current study, Dr. Devi carried out high throughput screening in collaboration with researchers at the National Institutes of Health (NIH) to identify which small molecules might act on the signaling pathway associated with this protein complex. Researchers found one compound called CYM51010 that was as potent as morphine, but less likely to result in tolerance and negative side effects. Dr. Devi's team is currently developing modified versions of this compound that may have potential as analgesics with reduced side effects.

"GPCR heteromers have been suggested to represent powerful targets for improved, novel therapeutics with reduced adverse effects in people with severe pain," said Dr. Devi. "However, there are presently no chemical tools that allow us to investigate their role in vivo. Our work represents a promising step in this direction, providing results that pave the way towards a new understanding of the function and pharmacology of opioid receptor heteromers."

Dr. Devi and her team are currently working with co-author Marta Filizola, PhD, Associate Professor of Structural and Chemical Biology at Mount Sinai, to learn how CYM51010 binds to the protein complex. Armed with this information, they hope to modify the compound to treat pain without the development of dependency. They also plan to restrict their benefit to the gastrointestinal system and treat diarrhea associated with irritable bowel disease that is unresponsive to existing therapies.

*This study was supported by National Institute on Drug Abuse Grants R01-008863 and K05-019521.*

*I. Gomes, W. Fujita, A. Gupta, A. S. Saldanha, A. Negri, C. E. Pinello, E. Roberts, M. Filizola, P. Hodder, L. A. Devi.*

*Identification of a - opioid receptor heteromer-biased agonist with antinociceptive activity. Proceedings of the National Academy of Sciences, 2013; DOI: 10.1073/pnas.1222044110*

<http://www.sciencedaily.com/releases/2013/07/130715202458.htm>

## **People Who Eat Nuts More Than Three Times a Week Have Reduced Risk of Dying from Cancer or Cardiovascular Disease**

***People who eat nuts, particularly walnuts, are more likely to live longer, finds research in BioMed Central's open access journal BMC Medicine.***

In a longitudinal study, researchers suggest that those who eat nuts more than three times a week have a reduced risk of dying from cancer or cardiovascular disease than non-nut eaters.

The PREDIMED nutrition trial based in Spain looked at the effect on the primary prevention of cardiovascular disease of over 7000 older people (aged 55 to 90) randomized to a Mediterranean Diet supplemented with extra virgin olive oil or nuts, compared to a control group following a low fat diet. In Mediterranean regions, nut consumption is relatively high compared to other countries. People who ate nuts tended to have a lower BMI and smaller waist. They were also less likely to smoke and were more physically active than those who rarely or never ate nuts. Nut eating was associated with a better diet in general as these people ate more vegetables, fruit and fish.

There were fewer people with type 2 diabetes or people taking medicine for hypertension in the group of people who ate the most nuts. Overall, nut eaters had a 39% lower mortality risk and walnut eaters 45% lower -- meaning that they were less likely to die than the non-nut eaters.

People eating more than 3 servings (1 serving -- 28 g) a week of nuts reduced risk of death due to cardiovascular disease by 55% and cancer by 40%. A similar effect was demonstrated for walnuts.

Prof Jordi Salas-Salvadó, from the Universitat Rovira i Virgili who led this study explained, "Quite how nuts are able prevent premature mortality is not entirely clear, nor why walnut should be better for you than other nuts. Walnuts have particularly high content of alpha-linoleic acid and phytochemicals, especially in their 'skin' both of which, along with fibre and minerals such as calcium, magnesium and potassium, may contribute to their healthy effect."

*Marta Guasch-Ferré, Mònica Bulló, Miguel Ángel Martínez-González, Emilio Ros, Dolores Corella, Ramon Estruch, Montserrat Fitó, Fernando Arós, Julia Wärnberg, Miquel Fiol, José Lapetra, Ernest Vinyoles, Rosa Lamuela-Raventós, Lluís Serra-Majem, Xavier Pintó, Valentina Ruiz-Gutierrez, Josep Basora and Jordi Salas-Salvado. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. BMC Medicine, 2013; 11: 164 DOI: 10.1186/1741-7015-11-164*

*Sabine Rohrmann and David Faeh. Should we go nuts about nuts? BMC Medicine, 2013; 11: 165 DOI: 10.1186/1741-7015-11-165*

[http://www.eurekalert.org/pub\\_releases/2013-07/uoc--urf071613.php](http://www.eurekalert.org/pub_releases/2013-07/uoc--urf071613.php)

## **UCLA researchers find link between intestinal bacteria and white blood cell cancer**

***Researchers from UCLA's Jonsson Comprehensive Cancer Center have discovered that specific types of bacteria that live in the gut are major contributors to lymphoma, a cancer of the white blood cells.***

Published online ahead of press today in the journal *Cancer Research*, the study was led by Robert Schiestl, member of the Jonsson Cancer Center and professor of pathology and laboratory medicine, environmental health sciences, and radiation oncology.

In rodents, intestinal bacteria influence obesity, intestinal inflammation and certain types of epithelial cancers. (Epithelial cancers affect the coverings of the stomach, liver or colon.) However, little is known about the identity of the bacterial species that promote the growth of, or protect the body from, cancer — or about their effect on lymphoma.

Up to 1,000 different species of bacteria (intestinal microbiota) live in the human gut. Intestinal microbiota number 100 trillion cells; over 90 percent of the cells in the body are bacteria. The composition of each person's microbiome — the body's bacterial make-up — is very different, due to the types of bacteria people ingest early in their lives, as well as the effects of diet and lifestyle.

Schiestl's group wanted to determine whether differences in peoples' microbiomes affect their risk for lymphoma, and whether changing the bacteria can reduce this risk. They studied mice with ataxia-telangiectasia (A-T), a genetic disease that in humans and mice is associated with a high rate of B-cell lymphoma. They discovered that, of mice with A-T, those with certain microbial species lived much longer than those with other bacteria before developing lymphoma, and had less of the gene damage (genotoxicity) that causes lymphoma. "This study is the first to show a relationship between intestinal microbiota and the onset of lymphoma," Schiestl said. "Given that intestinal microbiota is a potentially modifiable trait, these results hold considerable promise for intervention of B-cell lymphoma and other diseases."

The scientists also were able to create a detailed catalog of bacteria types with promoting or protective effects on genotoxicity and lymphoma, which could be used in the future to create combined therapies that kill the bacteria that promote cancer (as antibiotics do) and increase the presence of the bacteria that protect from cancer (as probiotics do).

*The work was supported by the National Institutes of Health, Jonsson Cancer Center, the Crohn's and Colitis Foundation of America, the Eli & Edythe Broad Center of Regenerative Medicine & Stem Cell Research, the Austrian Federal Ministry of Science and Research, NASA, University of California Toxic Substances Research and Teaching Program, and the UCLA Graduate Division.*

[http://www.eurekalert.org/pub\\_releases/2013-07/jhm-pwp071613.php](http://www.eurekalert.org/pub_releases/2013-07/jhm-pwp071613.php)

## **People with pre-diabetes who drop substantial weight may ward off type 2 diabetes**

***People with pre-diabetes who lose roughly 10 percent of their body weight within six months of diagnosis dramatically reduce their risk of developing type 2 diabetes over the next three years, according to results of research led by Johns Hopkins scientists.***

The findings, investigators say, offer patients and physicians a guide to how short-term behavior change may affect long-term health.

"We have known for some time that the greater the weight loss, the lower your risk of diabetes," says study leader Nisa Maruthur, M.D., M.H.S., an assistant professor in the Division of General Internal Medicine at the Johns Hopkins University School of Medicine. "Now we understand that we can see much of the benefit of losing that weight in those first six months when people are adjusting to a new way to eating and exercising. Substantial weight loss in the short term clearly should go a long way toward preventing diabetes."

Preventing pre-diabetes from becoming full-blown diabetes is critical, Maruthur says. Uncontrolled diabetes — marked by excess sugar in the blood — can lead to eye, kidney and nerve damage, as well as cardiovascular disease. The new research suggests that if people with pre-diabetes don't lose enough weight in those first months, physicians may want to consider more aggressive treatment, such as adding a medication to push blood sugar levels lower.

A report on the research is published online today in the *Journal of General Internal Medicine*.

Maruthur and her colleagues based their conclusions on analysis of data from the Diabetes Prevention Program (DPP), the largest diabetes prevention study in the United States. Overweight, hyperglycemic people were recruited between 1996 and 1999 and followed for an average of 3.2 years. More than 3,000 participants at 27 academic medical centers were assigned at random either to receive an intense lifestyle intervention, doses of the diabetes drug metformin designed to reduce blood glucose (sugar) levels, or a placebo. Maruthur and her colleagues searched the study information for links among short-term weight loss, reduction of blood glucose levels and impact on the longer-term risk of developing diabetes.



Patients with pre-diabetes have blood sugar levels higher than normal but not yet high enough to be classified as type 2 diabetes. Although not all people with pre-diabetes develop full-blown type 2 disease, without intervention the risk of getting it within 10 years is substantially increased and damage to health may already have begun.

The good news, Maruthur says, is that studies like hers show that the progression from pre-diabetes to type 2 diabetes is not inevitable and lifestyle changes can bring blood sugar levels back to normal.

Participants in the lifestyle arm of the DPP were advised about better eating habits, directed to exercise 150 minutes a week, and given one-on-one counseling for the first six months and group counseling thereafter. Researchers found that those in the lifestyle intervention arm who lost 10 percent or more of their body weight had an 85 percent reduction in risk of developing diabetes within three years. Even more moderate weight loss showed positive effects. Those who lost 5 to 7 percent of their body weight reduced their risk of developing diabetes by 54 percent three years later.

Those who were given metformin, a drug that prevents the liver from producing too much glucose, did not lose significant amounts of weight on average. But those whose blood sugar levels were significantly lowered in six months of taking the medication saw their future risk of developing diabetes fall as well.

The lowest risk, Maruthur says, occurred in patients who lost weight and also lowered the amount of glucose in their blood, as measured by a blood test taken after fasting.

"I'm usually thrilled if a patient loses 3 to 5 percent of his or her body weight after six months, but based on this new knowledge, if patients aren't losing more weight and if their glucose remains elevated, it might be time to escalate treatment by prescribing metformin," she says.

Maruthur says few doctors use metformin in patients with pre-diabetes, but given what her new study shows, it might make sense for them to consider prescribing the drug to patients who are unable or unwilling to lose substantial weight in the short term.

When blood tests indicate pre-diabetes, doctors like Maruthur often discuss with their patients the changes they can make to hopefully stave off type 2 diabetes. "Right now, the doctor and patient discuss this and may not discuss it again until the next appointment, which may be six months away or even longer," she says. "This routine isn't getting us anywhere." She says doctors don't effectively provide behavior modification programs, in part because insurance rarely covers them. The new research suggests just how valuable — and potentially cost-effective — such interventions could be, she says.

*Maruthur's work is supported by a grant from the National Institutes of Health's National Center for Research Resources (1KL2RR025006-01). Other Johns Hopkins researchers involved in the study include Frederick L. Brancati, M.D., M.H.S., and Jeanne M. Clark, M.D., M.P.H. For more information: <http://tinyurl.com/n6nbnrv>*

[http://www.eurekalert.org/pub\\_releases/2013-07/uops-hra071513.php](http://www.eurekalert.org/pub_releases/2013-07/uops-hra071513.php)

## **Highest risk Alzheimer's genetic carriers take positive steps after learning risk status**

*No signs of increased distress, anxiety after learning Alzheimer's risk status, Penn-led study shows*

BOSTON - People who found out they carried an uncommon genetic risk for Alzheimer's disease did not experience more anxiety, depression or distress than non-carriers, and were more active in efforts to reduce their risk of Alzheimer's disease - by exercising, eating a healthy diet and taking recommended vitamins and medications - report researchers from the Perelman School of Medicine at the University of Pennsylvania today at the 2013 Alzheimer's Association International Conference (AAIC). Researchers note that this study will inform how research studies and clinical practices reveal genetic and other risk factors to people interested in being tested in the future.

"This study informs our understanding of the impact of people finding out their genetic risk for Alzheimer's in the absence of any treatments to prevent dementia," said lead study author Jason Karlawish, MD, professor of Medicine and Medical Ethics and Health Policy in Penn's Perelman School of Medicine. "We saw that, following their genetic counseling session, people took positive steps to mitigate their Alzheimer's risk, such as following a healthy diet and exercising. They might also be willing to join an Alzheimer's dementia prevention trial."

As part of the NIH-funded REVEAL study led by Robert Green, MD, at Boston's Brigham and Women's Hospital, an analysis of 648 people tested for the Alzheimer's disease genetic risk marker APOe4 was conducted, where participants learned their risk estimate, based on genotype, gender, ethnicity and family history. Only 4 percent of participants (28 people) were in the highest risk group, carrying two copies of APOe4, while 34 percent (221) had a single copy of the gene and 62 percent (399) carried no genetic risk marker. After a year of following the three groups, there was no inflated perceived risk of getting Alzheimer's disease, nor was there any significant difference between groups for scores on anxiety, depression and test-related distress. "What is the experience of being an APOE4 homozygote?"

*Findings from the REVEAL Study" by Karlawish et al will be presented on Tuesday, July 16 at 12:00pm ET. The study was supported by grants from the National Institutes of Health (HG002213, HG005092, HG006500 and AG027841.*

[http://www.eurekalert.org/pub\\_releases/2013-07/jhm-ssm071613.ph](http://www.eurekalert.org/pub_releases/2013-07/jhm-ssm071613.ph)

## **Self-perpetuating signals may drive tumor cells to spread**

***Self-perpetuating signaling circuit inside connective tissue cells allows these cells to propel themselves in a particular direction***

Singapore - A team of international researchers from Duke-NUS Graduate Medical School Singapore and the Johns Hopkins University School of Medicine (USA) has identified a self-perpetuating signaling circuit inside connective tissue cells that allows these cells to form a front and a back and propel themselves in a particular direction over a long period of time. This propulsion is the same movement that tumor cells use to invade healthy tissue during cancer metastasis so cracking the code to this signaling network may lead to new therapeutic strategies against cancer and other devastating diseases.

Many different types of cells in our body can crawl and migrate to distinct locations, sometimes over long distances. Immune system cells, for example, move to a wound site to kill microorganisms during an infection, and connective tissue cells (fibroblasts) move there to repair damaged areas. Cell migration is essential to a variety of biological processes, such as the development of an organism, wound healing, and immune surveillance, but also the invasion of tumor cells during cancer metastasis.

Cell migration is an extraordinarily complex process which depends on the ability of a cell to form a front and a back (called polarization) and generate force in one preferred direction. Migrating cells are able to do this spontaneously, without assistance from the environment. How they do this is a question that has kept cell biologists busy for the last three decades.

These latest results shed light on the migratory mechanism of cells. In particular, the team found that the signaling network involved has an interesting property, well known to engineers and bankers: it is self-perpetuating. A classic analogy to this type of circuit is a bank run, which occurs when a large number of customers withdraw their money from a bank due to concerns about the bank's solvency. As more people withdraw their funds, the probability of default increases, prompting more people to withdraw their money, in a kind of self-fulfilling prophecy (or positive feedback loop).

The team went on to show that this positive feedback circuit is switched on in very specific regions in the connective tissue cells, causing proteins to push against only one side of the outer envelope of the cell, eventually causing movement in one preferred direction. Predictably, two important protein components of this signaling circuit, called Ras and PI3K, are often mutated in cancer. This suggests that misregulation of this circuit may increase the invasiveness of cancer cells. It also highlights the need to understand how signaling proteins interact with each other inside cells, hopefully leading one day to new therapies for cancer and other deadly diseases.

This study, entitled "The small GTPase HRas shapes local PI3K signals through positive feedback and regulates persistent membrane extension in migrating fibroblasts" was published online in *Molecular Biology of the Cell* on May 15. It is supported by a grant from the Ministry of Education.

[http://www.eurekalert.org/pub\\_releases/2013-07/aabu-sdo071613.php](http://www.eurekalert.org/pub_releases/2013-07/aabu-sdo071613.php)

## **Single dose of ADHD drug can reduce fall risk in older adults -- Ben-Gurion U researchers**

***Single dose of methylphenidate helps to improve balance control during walking, reducing the risk of falls***  
BEER-SHEVA, ISRAEL - Ben-Gurion University of the Negev (BGU) researchers have discovered that a single dose of methylphenidate (MPH), used to treat Attention Deficit Hyperactivity Disorder (ADHD) and narcolepsy, helps to improve balance control during walking, hence reducing the risk of falls among elderly adults. Falls in older adults are the leading cause of hip fractures and other injury-related visits to emergency rooms and of accidental death. Age-related deterioration in gait and balance is a major contributor to falls in older adults.

According to a study published in *The Journals of Gerontology*, the BGU researchers found that a single dose of MPH improves walking by reducing the number of step errors and the step error rate in both single and dual tasks.

"Our results add to a growing body of evidence showing that MPH may have a role as a therapeutic option for improving gait and reducing fall risk in older adults," said Itshak Melzer of BGU's Schwartz Movement Analysis and Rehabilitation Laboratory, Department of Physical Therapy, Faculty of Health Sciences. "This is especially true in real-life situations, where the requirement to walk commonly occurs under more complicated,

'dual task' circumstances with cognitive attention focused elsewhere (e.g., watching traffic, talking) and not on performing a specific motor task."

The study participants were 30 healthy older adults who were at least 70 years-old and had the ability to walk 70 feet (20 meters) without personal assistance or an assistive device. The participants were given a single dose (10 mg.) of MPH and were assessed under four task conditions of single and combined motor and cognitive tasks."The enhanced attention that comes about as a result of MPH may lead to improved balance control during walking, especially in dual task conditions," Meltzer explains.

"Our findings that MPH improves gait can be explained not just by its effect of attentional improvements, but also by indications that it has a direct influence on areas of the brain that deal with motor and balance control." Other BGU researchers involved in the study include Yaakov Bachner, M.A Program in Gerontology, Department of Public Health; Tal Guy, Schwartz Movement Analysis and Rehabilitation Laboratory, Department of Physical Therapy, Faculty of Health Sciences; and Zamir Shorer, Pediatric Neurology Unit, Soroka University Medical Center and the BGU's Faculty of Health Sciences.

The study was supported by a grant from Myers-JDC-Brookdale Institute of Gerontology and Human Development and Eshel-The Association for the Planning and Development of Services for the Aged in Israel.

<http://bit.ly/12u5RwB>

### **First Lab-Grown Burger To Be Served**

***Burger made of meat grown in a lab will set a hungry person back \$325,000***

Jul 16, 2013 09:14 AM ET // by Jesse Emspak

Science fiction writers have been writing about artificial meats for decades — often the trope is that poorer people eat the vat-grown stuff, while the idle rich get real cows. For now though, the reality has been reversed: a burger made of meat grown in a lab will set a hungry person back \$325,000 (£216,000).

That's one expensive burger, some 100,000 times more expensive than usual. The price is the amount of funding that Mark Post, a vascular physiologist at the University of Maastricht, got for his project of growing meat in a Petri dish rather than a cow. (The source of the funding hasn't been revealed yet).

To make his meat, Post harvested stem cells from the waste of slaughterhouses. That doesn't alter the fact that the cells themselves are still the same ones that are in a cow in any case.

Post added nutrients to the cells, causing them to grow into muscle tissue, which he then stretched out to "exercise" and keep it from atrophying. Lacking blood, the meat doesn't have any color. And so far, the strips he's made are only an inch or so long and very thin. But packing enough of them together produces a reasonable meat patty. That's what Post plans to offer on Aug. 5: a taste of a burger made with the lab-grown meat at an invitation-only event.

Eating lab-grown meat isn't just for people who are squeamish about eating animals (it seems unlikely that many vegetarians will be mollified by its vat-grown status). The real issue is that cow and pig meat is land and energy-intensive. And the demand for meat worldwide is going up as people become wealthier. Between the deforestation for pasture and the contribution to greenhouse gas emissions, more meat production isn't looking like a sustainable option.

On the other hand, there's a lot of work that goes into growing stem cells into muscle, and when you add up the inputs it's not clear culturing meat uses any less energy or generates less carbon, even if it is more indirect.

<http://bit.ly/12vqd8A>

### **Red Planet Riviera: Ancient Mars Ocean Found?**

***With the help of rover Curiosity, we now know that ancient Mars had large quantities of liquid water flowing across its surface.***

Jul 16, 2013 04:09 PM ET // by Ian O'Neill

However, evidence for large bodies of water - i.e. oceans - has been hard to come by. But using high-resolution orbital data, Caltech scientists now think they've found a long-dry river delta that once flowed into a very large body of water. Welcome to the Aeolis Riviera - the strongest evidence yet for a Martian coastline.

PHOTOS: The Psychedelic Landscape of Mars

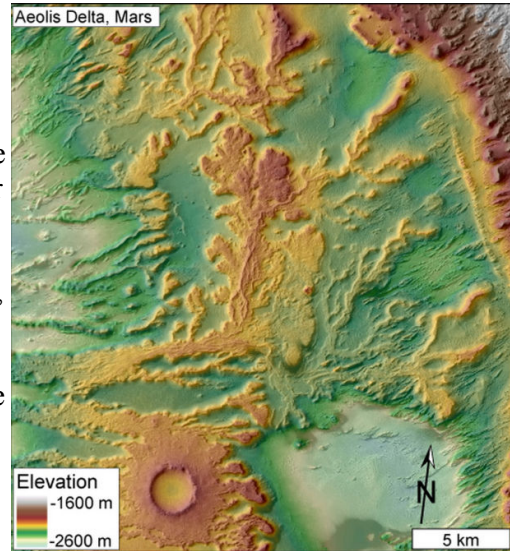
Aeolis Dorsa is a vast plain about 1,000 kilometers (620 miles) east of Gale Crater, where NASA's rover Curiosity is currently exploring. Using high-resolution observations from NASA's Mars Reconnaissance Orbiter's High-Resolution Imaging Science Experiment (HiRISE) camera, the Caltech team spotted what appears to be a river delta leading to a large depression, a candidate for the basin of an ancient ocean.

"Scientists have long hypothesized that the northern lowlands of Mars are a dried-up ocean bottom, but no one yet has found the smoking gun," said Mike Lamb, assistant professor of geology at Caltech and a co-investigator of this research, in a news release. The research has been published in the Journal of Geophysical Research.

It is thought that large regions of the Red Planet's northern hemisphere was once covered in water as the majority of the landmass is at a lower elevation than the southern hemisphere. This is exactly where you'd expect to see evidence of ancient large bodies of water. But over the aeons, the evidence has weathered away, making any positive identification of such features difficult.

While analyzing an area inside Aeolis Dorsa, however, the researchers noticed a collection of inverted channels. On Mars, these raised ridges were likely caused by the deposition of rocks and other material by the flow of water down river channels. Long after the rivers ran dry, the rocky deposits remained behind. The softer sediment surrounding the river channels eventually weathered away, blasted by the Martian wind and other erosion processes. However, the deposited rocks, once found at the bottom of the rivers, were immune to this weathering, causing them to rise out of the landscape as ridges, tracing the paths of ancient riverbeds.

Looking down from its orbit, the MRO has been able to image these veined, raised structures and found what appears to be an ancient river delta leading into the depressed portion of Aeolis Dorsa.



*The river delta candidate leading into Aeolis Dorsa. DiBiase et al./Journal of Geophysical Research/NASA/JPL-Caltech/USGS/NASA Landsat*

On Earth, river deltas form at the mouths of rivers connecting to seas and oceans. The Nile Delta is a classic example, where the water from the river flows into the Mediterranean Sea. Sediment has built up at the Nile's mouth to create fanned, multichannel features, leading to a sudden drop-off — i.e. the sea.

However, understanding which way the water would have been flowing in an ancient Mars "river delta candidate" can be challenging. Could the water actually have been flowing the other way? Perhaps this isn't a delta at all; it could be reversed — several streams and small river tributaries flowing into a larger channel. Because of HiRISE's precision, high-resolution 3D images could be created to map which direction the landscape is sloping, revealing the direction of water flow. Indeed, the water would have been flowing downhill, creating a fan-like delta and the drop-off at the end of this Mars delta could be the beginning of an ocean basin. Therefore this could be the strongest evidence yet of a Martian coastline.

"This is probably one of the most convincing pieces of evidence of a delta in an unconfined region — and a delta points to the existence of a large body of water in the northern hemisphere of Mars," said Roman DiBiase, Caltech postdoctoral scholar and lead author of the paper.

Although more work is needed, the researchers estimate that the "ocean" would have, at least, covered Aeolis Dorsa, all 100,000 square kilometers (39,000 square miles) of it. To compare with a terrestrial mass of water, this is larger than Lake Superior (82,414 square kilometers or 31,820 square miles).

In the year since Curiosity landed inside Gale Crater, the mission has uncovered incredible insights to the water history of the Red Planet inside a comparatively small impact crater. Imagine what a long-duration rover mission to a river delta would reveal. I for one would love to see a robotic mission clawing through the exposed ridges of ancient riverbed, hunting down evidence for the past habitability of an ancient Mars coastline.

<http://www.sciencedaily.com/releases/2013/07/130716173807.htm>

### **'Brown Ocean' Can Fuel Inland Tropical Cyclones**

*Hurricane Sandy in 2012 was a cold-core extratropical cyclone, a storm type known to derive energy over land from the clashes between different air masses.*

In the summer of 2007, Tropical Storm Erin stumped meteorologists. Most tropical cyclones dissipate after making landfall, weakened by everything from friction and wind shear to loss of the ocean as a source of heat energy. Not Erin. The storm intensified as it tracked through Texas. It formed an eye over Oklahoma. As it spun over the southern plains, Erin grew stronger than it ever had been over the ocean.

Erin is an example of a newly defined type of inland tropical cyclone that maintains or increases strength after landfall, according to NASA-funded research by Theresa Andersen and J. Marshall Shepherd of the University of Georgia in Athens.

Before making landfall, tropical storms gather power from the warm waters of the ocean. Storms in the newly defined category derive their energy instead from the evaporation of abundant soil moisture -- a phenomenon that Andersen and Shepherd call the "brown ocean." "The land essentially mimics the moisture-rich environment of the ocean, where the storm originated," Andersen said.

The study is the first global assessment of the post-landfall strength and structure of inland tropical cyclones, and the weather and environmental conditions in which they occur.

"A better understanding of inland storm subtypes, and the differences in the physical processes that drive them, could ultimately improve forecasts," Andersen said. "Prediction and earlier warnings can help minimize damage and loss of life from severe flooding, high winds, and other tropical cyclone hazards."

The study was published March 2013 in the *International Journal of Climatology*.

To better understand tropical cyclones that survive beyond landfall, Andersen and Shepherd accessed data archived by the National Oceanic and Atmospheric Administration's National Climatic Data Center for tropical cyclones from 1979 to 2008. Storms had to meet the criteria of retaining a measureable central pressure by the time they tracked at least 220 miles (350 kilometers) inland, away from the maritime influence of the nearest coast. Next they obtained atmospheric and environmental data for before and after the storms from NASA's Modern Era Retrospective-Analysis for Research and Applications.

Of the 227 inland tropical cyclones identified, 45 maintained or increased strength, as determined by their wind speed and central pressure. The researchers show, however, that not all such storms are fueled equally.

In October 2012, Hurricane Sandy demonstrated the destructive power of extratropical cyclones -- a well-studied storm type that undergoes a known physical and thermal transition. These systems begin as warm-core tropical cyclones that derive energy from the ocean. Over land, the storms transition to cold-core extratropical cyclones that derive energy from clashes between different air masses. Of the study's 45 inland storms that maintained or increased strength, 17 belonged to this category.

Tropical Storm Erin, however, is among the newly described storm category that accounted for 16 of the 45 tropical cyclones. Instead of transitioning from a warm-core to cold-core system, these storms maintain their tropical warm-core characteristics. The storm type, which Andersen and Shepherd call tropical cyclone maintenance and intensification events, or TCMIIs, have the potential to deliver much more rainfall than their extratropical counterparts.

"Until events like Erin in 2007, there was not much focus on post-landfall tropical cyclones unless they transitioned," Andersen said. "Erin really brought attention to the inland intensification of tropical cyclones."

"This is particularly critical since a study by former National Hurricane Center Deputy Director Ed Rappaport found that 59 percent of fatalities in landfalling tropical cyclones are from inland freshwater flooding," Shepherd said.

While most inland tropical cyclones occur in the United States and China, the hotspot for TCMIIs during the 30-year study period turned out to be Australia. The uneven geographic distribution led Andersen and Shepherd to investigate the environment and conditions surrounding the brown ocean phenomenon that gives rise to the storms.

Andersen and Shepherd show that a brown ocean environment consists of three observable conditions. First, the lower level of the atmosphere mimics a tropical atmosphere with minimal variation in temperature. Second, soils in the vicinity of the storms need to contain ample moisture. Finally, evaporation of the soil moisture releases latent heat, which the team found must measure at least 70 watts averaged per square meter. For comparison, the latent heat flux from the ocean averages about 200 watts per square meter.

Indeed, all three conditions were present when Erin tracked across the U.S. Gulf Coast and Midwest. Still, questions remain about the factors -- such as variations in climate, soil and vegetation -- that make Australia the region where brown ocean conditions most often turn up. The research also points to possible implications for storms' response to climate change. "As dry areas get drier and wet areas get wetter, are you priming the soil to get more frequent inland tropical cyclone intensification?" asked Shepherd.

*Theresa K. Andersen, J. Marshall Shepherd. A global spatiotemporal analysis of inland tropical cyclone maintenance or intensification. International Journal of Climatology, 2013; DOI: 10.1002/joc.3693*

[http://www.eurekalert.org/pub\\_releases/2013-07/miot-ndf071613.php](http://www.eurekalert.org/pub_releases/2013-07/miot-ndf071613.php)

## **Newly discovered flux in the Earth may solve missing-mantle mystery**

***MIT research points to large reservoirs of material deep in the mantle that may help to explain Earth's origins.***

**Written by Jennifer Chu, MIT News Office**

CAMBRIDGE, MA -- It's widely thought that the Earth arose from violent origins: Some 4.5 billion years ago, a maelstrom of gas and dust circled in a massive disc around the sun, gathering in rocky clumps to form asteroids. These asteroids, gaining momentum, whirled around a fledgling solar system, repeatedly smashing into each other to create larger bodies of rubble - the largest of which eventually cooled to form the planets.

Countless theories, simulations and geologic observations support such a scenario. But there remains one lingering mystery: If the Earth arose from the collision of asteroids, its composition should resemble that of meteoroids, the small particles that break off from asteroids.

But to date, scientists have found that, quite literally, something doesn't add up: Namely, the Earth's mantle — the layer between the planet's crust and core — is missing an amount of lead found in meteorites whose composition has been analyzed following impact with the Earth.

Much of the Earth is composed of rocks with a high ratio of uranium to lead (uranium naturally decays to lead over time). However, according to standard theories of planetary evolution, the Earth should harbor a reservoir of mantle somewhere in its interior that has a low ratio of uranium to lead, to match the composition of meteorites. But such a reservoir has yet to be discovered — a detail that leaves Earth's origins hazy.

Now researchers in MIT's Department of Earth, Atmospheric and Planetary Sciences have identified a "hidden flux" of material in the Earth's mantle that would make the planet's overall composition much more similar to that of meteorites. This reservoir likely takes the form of extremely dense, lead-laden rocks that crystallize beneath island arcs, strings of volcanoes that rise up at the boundary of tectonic plates.

As two massive plates push against each other, one plate subducts, or slides, under the other, pushing material from the crust down into the mantle. At the same time, molten material from the mantle rises up to the crust, and is ejected via volcanoes onto the Earth's surface.

According to the MIT researchers' observations and calculations, however, up to 70 percent of this rising magma crystallizes into dense rock — dropping, leadlike, back into the mantle, where it remains relatively undisturbed. The lead-heavy flux, they say, puts the composition of the Earth's mantle on a par with that of meteorites.

"Now that we know the composition of this flux, we can calculate that there's tons of this stuff dropping down from the base of the crust into the mantle, so it is likely an important reservoir," says Oliver Jagoutz, an assistant professor of geology at MIT. "This has a lot of implications for understanding how the Earth evolved through history."

Jagoutz and his colleague Max Schmidt, of the Swiss Federal Institute of Technology in Zurich, have detailed their results in a paper published in *Earth and Planetary Science Letters*.

### **A mantle exposed**

Measuring the composition of material that has dropped into the mantle is a nearly impossible task. Jagoutz estimates that such dense rocks would form at a depth of 40 to 50 kilometers below the surface, beyond the reach of conventional sampling techniques.

There is, however, one place on earth where such a depth of the crust and mantle is exposed: a region of northern Pakistan called the Kohistan arc. Forty million years ago, this island arc was crushed between India and Asia as the two plates collided.

"When India came in, it slammed into the arc, and the arc extended and rotated itself," Jagoutz says. "Because of that, we now have a cross-section of the mantle-to-crust transition. This is the only place on Earth where this exists."

On various trips from 2000 to 2007, Jagoutz trekked through the Kohistan arc region, collecting rocks from various parts of the arc's crust and mantle. Bringing them back to the lab, he analyzed the rocks' density and composition, discovering that some were "density-unstable" — much denser than the mantle. These denser rocks could potentially sink into the mantle, creating a hidden reservoir.

### **Adding up to an asteroid origin**

The researchers measured the rocks' composition, and found that the denser rocks contained much more lead than uranium — exactly the ratio predicted for the missing reservoir of material. Jagoutz then performed a mass balance (a simple conservation-of-mass calculation) to determine how much dense rock drops into the mantle, based on the composition of the region's crust, rocks and mantle: Essentially, the mass of the Kohistan arc, minus whatever material drops into the mantle, should equal the material that comes out of the mantle.

Jagoutz and Schmidt solved the equation for 10 common elements. From their calculations, they found that 70 percent of the magma that rises from the mantle must ultimately drop back down, relatively heavy with lead. Applying this statistic to other island arcs in the world — such as the Andean volcanic belt and the Cascade Range — they found that the amount of material dropped into the mantle globally equals the composition and quantity of the so-called missing reservoir — a finding that suggests that Earth did indeed form from the collision of meteorites.

"If we are right, one of the questions we have is: Why is the Earth capable of hiding something from us? Why is there never a volcano that brings up these rocks?" Jagoutz adds. "You'd think it'd come back up, but it doesn't. It's actually interesting."

[http://www.eurekalert.org/pub\\_releases/2013-07/hcfa-egc071713.php](http://www.eurekalert.org/pub_releases/2013-07/hcfa-egc071713.php)

## Earth's gold came from colliding dead stars

### *Colliding neutron stars produce produce rare heavy elements, including gold*

We value gold for many reasons: its beauty, its usefulness as jewelry, and its rarity. Gold is rare on Earth in part because it's also rare in the universe. Unlike elements like carbon or iron, it cannot be created within a star. Instead, it must be born in a more cataclysmic event - like one that occurred last month known as a short gamma-ray burst (GRB).

Observations of this GRB provide evidence that it resulted from the collision of two neutron stars - the dead cores of stars that previously exploded as supernovae. Moreover, a unique glow that persisted for days at the GRB location potentially signifies the creation of substantial amounts of heavy elements - including gold.

"We estimate that the amount of gold produced and ejected during the merger of the two neutron stars may be as large as 10 moon masses - quite a lot of bling!" says lead author Edo Berger of the Harvard-Smithsonian Center for Astrophysics (CfA).

Berger presented the finding today in a press conference at the CfA in Cambridge, Mass.

A gamma-ray burst is a flash of high-energy light (gamma rays) from an extremely energetic explosion. Most are found in the distant universe. Berger and his colleagues studied GRB 130603B which, at a distance of 3.9 billion light-years from Earth, is one of the nearest bursts seen to date.

Gamma-ray bursts come in two varieties - long and short - depending on how long the flash of gamma rays lasts. GRB 130603B, detected by NASA's Swift satellite on June 3rd, lasted for less than two-tenths of a second. Although the gamma rays disappeared quickly, GRB 130603B also displayed a slowly fading glow dominated by infrared light. Its brightness and behavior didn't match a typical "afterglow," which is created when a high-speed jet of particles slams into the surrounding environment.

Instead, the glow behaved like it came from exotic radioactive elements. The neutron-rich material ejected by colliding neutron stars can generate such elements, which then undergo radioactive decay, emitting a glow that's dominated by infrared light - exactly what the team observed.

"We've been looking for a 'smoking gun' to link a short gamma-ray burst with a neutron star collision. The radioactive glow from GRB 130603B may be that smoking gun," explains Wen-fai Fong, a graduate student at the CfA and a co-author of the paper.

The team calculates that about one-hundredth of a solar mass of material was ejected by the gamma-ray burst, some of which was gold. By combining the estimated gold produced by a single short GRB with the number of such explosions that have occurred over the age of the universe, all the gold in the cosmos might have come from gamma-ray bursts.

"To paraphrase Carl Sagan, we are all star stuff, and our jewelry is colliding-star stuff," says Berger.

<http://www.sciencedaily.com/releases/2013/07/130717051730.htm>

## Family Tree of Fish Yields Surprises

***The mighty tuna is more closely related to the dainty seahorse than to a marlin or sailfish.***

That is one of the surprises from the first comprehensive family tree, or phylogeny, of the "spiny-rayed fish," a group that includes about a third of all living vertebrate species. The work is published July 15 in the journal Proceedings of the National Academy of Sciences. The spiny-rayed fish are an incredibly diverse group, including tuna and billfish, tiny gobies and seahorses, and oddities such as pufferfish and anglerfish. The fish occupy every aquatic environment from coral reefs and open oceans to lakes and ponds. It includes all the major commercially fished species -- all of which are threatened. But until now, no one has had any idea exactly how more than 18,000 species in 650 families are related to each other, said Peter Wainwright, professor and chair of evolution and ecology at the University of California, Davis and senior author on the paper.



***The mighty tuna is more closely related to the dainty seahorse than to a marlin or sailfish. That is one of the surprises from the first comprehensive family tree, or phylogeny, of the "spiny-rayed fish," a group that includes about a third of all living vertebrate species. (Credit: © Melissa Fiene / Fotolia)***

"There has been a 'bush' at the top of the family tree leading to the rest of the vertebrates," Wainwright said.

"Now we have this beautiful phylogeny of one-third of all vertebrates."

The study also shows that after roaring along for their first 100 million years, the pace of evolution of the spiny-rayed fish downshifted about 50 million years ago.

Some groups of fish have gone along steadily for millennia; others have gone through bursts of rapid evolution. Overall, the researchers found that the rate at which new species formed was fairly constant across the group

from their origin to about 50 million years ago, then dropped about five-fold and has remained at that level since. That might mean that these fish have essentially filled the available spaces, Wainwright said.

"It's not uncommon in evolution to see a rapid diversification followed by a slowdown, but it's never been seen on such a scale before," he said.

Wainwright's laboratory worked with the lab of Tom Near, a former postdoctoral scholar at UC Davis now at Yale University, and colleagues at the University of Tennessee, The Field Museum in Chicago, Florida Atlantic University and CUNY Staten Island to construct the family tree. Matt Friedman, a paleontologist at the University of Oxford, England, added fossils that helped set dates for branches of the tree.

The researchers looked at 10 genes in more than 500 fish species representing most of the families of spiny-rayed fish. They used the genetic data to construct a tree, grouping related families together. They also looked at the pace of evolution -- the rate at which new species formed -- in different branches, and across the group as a whole.

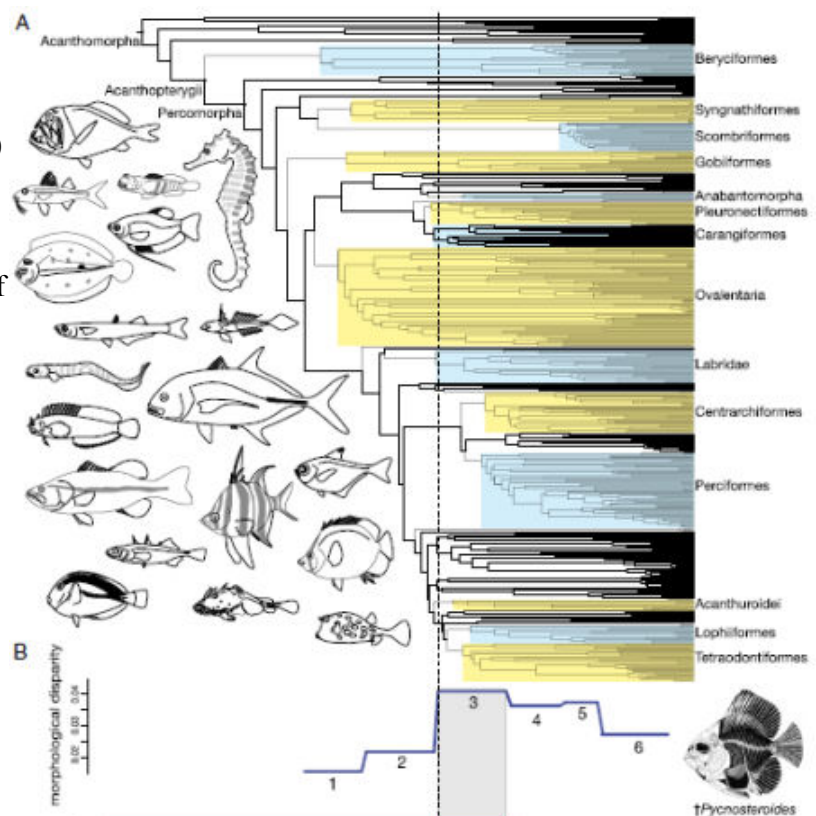
The spiny-rayed fish originated about 150 million years ago, separating from more primitive fish, such as lampreys, sharks and sturgeon, and from the ancestors of salmon and trout. Since then, they have spread into every aquatic habitat on Earth.

The tree shows some interesting relationships. For example, tuna are more closely related to seahorses than to swordfish or barracuda. The oddly shaped pufferfishes are related to anglerfish, the only fishes whose bodies are wider than they are deep.

Cichlids, a family that includes about 2,000 species of freshwater fish known for brooding their young in their mouths and a favorite for studies of evolution, are related to the engineer gobies, an obscure family of just two species that live on coral reefs and raise their young in a nest.

Wainwright's special interest is in the evolution of fish jaws. Fish have two sets of jawbones, an outer jaw and "pharyngeal jaws" in the throat that adapted to different functions. In some fish, the lower pharyngeal jaw is fused into a single solid bone that can be used to crush prey such as shellfish.

Biologists had assumed that this fused jaw had evolved once and then spread into different groups of fish. Instead, the new tree shows that this structure evolved at least six times in different groups of fish.



**Time-calibrated phylogenetic tree of Acanthomorpha with select major clades highlighted with alternating blue and yellow boxes that correspond with group names.**

Additional collaborators on the project were: Samantha Price at UC Davis; Alex Dornburg, Ron Eytan and Kristen Kuhn at Yale University; Leo Smith at the Field Museum; Jon Moore, Florida Atlantic University; and Frank Burbrink, College of Staten Island/CUNY, Staten Island. Funding was provided by the National Science Foundation.

T. J. Near, A. Dornburg, R. I. Eytan, B. P. Keck, W. L. Smith, K. L. Kuhn, J. A. Moore, S. A. Price, F. T. Burbrink, M. Friedman, P. C. Wainwright. [Phylogeny and tempo of diversification in the superradiation of spiny-rayed fishes](#). *Proceedings of the National Academy of Sciences*, 2013; DOI: 10.1073/pnas.1304661110

<http://bit.ly/15mVjkN>

## Chromosome that causes Down's silenced for first time

**HOPES that symptoms of Down's syndrome could be reversed have been raised by the silencing of the extra chromosome that causes the condition.**

17 July 2013 by Andy Coghlan

Jeanne Lawrence at the University of Massachusetts Medical School in Worcester took skin cells from men with the condition and "rewound" them into an embryonic state.

People with Down's have an extra copy of chromosome 21, altering the way they develop. Into this extra chromosome, her team inserted a copy of a gene called XIST. This gene has a silencing function and is



normally found on the X chromosome, where it is needed to suppress one of the two X chromosomes in females.

With XIST activated, the extra chromosome 21 seemed silenced. These cells developed normally, and within two weeks had formed neural rosettes, clusters of cells that form the central nervous system. None had done so in untreated cells.

XIST activation also prevented the expression of an APP gene present on the extra chromosome that makes beta-amyloid – a protein linked to Alzheimer's disease and which hastens the progression of Down's syndrome (Nature, DOI: 10.1038/nature12394).

Intervening in a live embryo is not likely, though. "I can't see how it could be done in all relevant cells in an embryo at the time Down's would be diagnosed," says Robin Lovell-Badge of London's National Institute of Medical Research.

Victor Tybulewicz, also at the NIMR, thinks the therapy's value will be in explaining what goes wrong. "It can be used to switch off the chromosome at different times, to understand if some consequences could be reversed," he says.

Elizabeth Fisher at University College London says it might be possible to treat some symptoms by silencing the chromosome in certain areas of the body.

[http://www.eurekalert.org/pub\\_releases/2013-07/e-sia071813.php](http://www.eurekalert.org/pub_releases/2013-07/e-sia071813.php)

### **Snow in an infant solar system**

#### *A frosty landmark for planet and comet formation*

Astronomers using the Atacama Large Millimeter/submillimeter Array (ALMA - <http://www.eso.org/alma>) have taken the first ever image of the snow line in an infant solar system. On Earth, snow lines form at high altitudes where falling temperatures turn the moisture in the air into snow. This line is clearly visible on a mountain, where the snow-capped summit ends and the rocky face begins.

The snow lines around young stars form in a similar way, in the distant, colder reaches of the dusty discs from which solar systems form. Starting from the star and moving outwards, water (H<sub>2</sub>O) is the first to freeze, forming the first snow line. Further out from the star, as temperatures drop, more exotic molecules can freeze and turn to snow, such as carbon dioxide (CO<sub>2</sub>), methane (CH<sub>4</sub>), and carbon monoxide (CO). These different snows give the dust grains a sticky outer coating and play an essential role in helping the grains to overcome their usual tendency to break up in collisions, allowing them to become the crucial building blocks of planets and comets. The snow also increases how much solid matter is available and may dramatically speed up the planetary formation process.

Each of these different snow lines -- for water, carbon dioxide, methane and carbon monoxide -- may be linked to the formation of particular kinds of planets<sup>[1]</sup>. Around a Sun-like star in a solar system like our own, the water snow line would correspond to a distance between the orbits of Mars and Jupiter, and the carbon monoxide snow line would correspond to the orbit of Neptune.

The snow line spotted by ALMA is the first glimpse of the carbon monoxide snow line, around TW Hydrae, a young star 175 light-years away from Earth. Astronomers believe this budding solar system shares many of the same characteristics of the Solar System when it was just a few million years old.

"ALMA has given us the first real picture of a snow line around a young star, which is extremely exciting because of what it tells us about the very early period in the history of the Solar System," said Chunhua "Charlie" Qi (Harvard-Smithsonian Center for Astrophysics, Cambridge, USA) one of the two lead authors of the paper. "We can now see previously hidden details about the frozen outer reaches of another solar system similar to our own."

But the presence of a carbon monoxide snow line could have greater consequences than just the formation of planets. Carbon monoxide ice is needed to form methanol, which is a building block of the more complex organic molecules that are essential for life. If comets ferried these molecules to newly forming Earth-like planets, these planets would then be equipped with the ingredients necessary for life.

Before now, snow lines had never been imaged directly because they always form in the relatively narrow central plane of a protoplanetary disc, so their precise location and extent could not be determined. Above and below the narrow region where snow lines exist, the star's radiation prevents ice formation. The dust and gas concentration in the central plane is necessary to insulate the area from the radiation so that carbon monoxide and other gases can cool and freeze.

This team of astronomers succeeded in peering inside this disc to where the snow has formed with the help of a clever trick. Instead of looking for the snow -- as it cannot be observed directly -- they searched for a molecule known as diazenylium (N<sub>2</sub>H<sup>+</sup>), which shines brightly in the millimetre portion of the spectrum, and so is a

perfect target for a telescope such as ALMA. The fragile molecule is easily destroyed in the presence of carbon monoxide gas, so would only appear in detectable amounts in regions where carbon monoxide had become snow and could no longer destroy it. In essence, the key to finding carbon monoxide snow lies in finding diazenylium.

ALMA's unique sensitivity and resolution has allowed the astronomers to trace the presence and distribution of diazenylium and find a clearly defined boundary approximately 30 astronomical units from the star (30 times the distance between the Earth and the Sun). This gives, in effect, a negative image of the carbon monoxide snow in the disc surrounding TW Hydrae, which can be used to see the carbon monoxide snow line precisely where theory predicts it should be -- the inner rim of the diazenylium ring.

"For these observations we used only 26 of ALMA's eventual full complement of 66 antennas. Indications of snow lines around other stars are already showing up in other ALMA observations, and we are convinced that future observations with the full array will reveal many more of these and provide further, exciting insights into the formation and evolution of planets. Just wait and see," concludes Michiel Hogerheijde from Leiden Observatory, the Netherlands.

<sup>[1]</sup> For instance dry rocky planets form on the inner side of the water snow line (nearest the star), where only dust can exist. At the other extreme are the icy giant planets which form beyond the carbon monoxide snow line.

<http://www.space.com/22005-comet-ison-risky-road-ahead.html>

### **Comet of the Century? Comet ISON Faces Risky Road**

*About 10,000 years ago, Comet ISON left our solar system's distant shell, a region known as the Oort cloud, and began streaking toward the sun.*

by Megan Gannon, News Editor | July 17, 2013 04:34pm ET

This November, the icy wanderer will reach the climax of its journey, potentially providing a stunning skywatching show here on Earth.

Comet ISON was discovered just last September by two Russian amateur astronomers. Scientists have since recognized ISON as a possible "comet of the century," but to live up to its promise, it will have to survive its dangerous perihelion, or closest approach to the sun.

ISON is what's known as a sungrazing comet. These suicidal objects have orbits that bring them within 850,000 miles (1.4 million kilometers) of the sun, and scientists estimate that ISON's closest pass will be about 730,000 miles (1.2 million km) above the surface of Earth's star.

Sometime this month or perhaps in August, ISON is set to cross what's called the frost line. At this boundary, which lies some 230 million to 280 million miles (370 to 450 million km) from the sun, our star's radiation will start taking its toll on the comet, driving off more of its water and making ISON appear brighter.

ISON's road will only get rockier from there.

After the comet flies by Mars in October and then Mercury in mid-November, intensifying solar radiation will boil more material off ISON; pressure from solar particles could break the comet into pieces; tidal forces will create great gravitational stress; and one ill-timed solar storm could rip the comet's tail right off.

All eyes will be on ISON as it makes this perilous journey.

The comet has already had its picture taken by NASA's Hubble Space Telescope and Swift spacecraft, and in the coming months, the agency has a slew of ISON observations planned for its solar telescopes in space and some instruments on the ground.

In September, NASA will even launch a comet-watching balloon almost 23 miles (37 km) above Earth's surface to capture images of ISON with minimal interference from the atmosphere.

If the sun is merciful to ISON when it whips around the star on Nov. 28 (Thanksgiving Day), the comet could light up the sky for weeks. In the Northern Hemisphere, it could be visible in the morning near the east-southeast horizon in early December. Later in the month, and into early January, the comet could be visible all night, according to NASA.

Even if ISON fizzles, tracking the comet's path and reaction to solar forces could shed light on the makeup of the early solar system, scientists say.

Sungrazing comets like ISON sometimes plunge into parts of the sun's fiery atmosphere where no spacecraft can go. Researchers can learn about the sun itself by watching how the comet and its tail interact with the solar atmosphere.

For example, Comet Lovejoy passed just 87,000 miles (140,000 km) above the solar surface in mid-December 2011. The strange wiggle of Lovejoy's tail as it dove through the sun's corona helped scientists map out the region's complex magnetic field.

<http://bit.ly/12LrR9H>

**War arose recently, anthropologists contend**  
*Study of hunter-gatherers finds few lethal raids on opposing groups*  
By Bruce Bower

A battle has broken out among scientists trying to untangle the origins of war.

The fighting is over whether hunter-gatherer communities in recent centuries have tended more toward war — defined as banding together in groups to kill people in other populations — than toward one-on-one attacks within their own communities. A second front has broken out over how to extrapolate from modern behavior to the Stone Age. Some anthropologists regard the nomadic groups as helpful if imperfect models of Stone Age human behavior. Others suspect that too much evolutionary change and irregular contact with outsiders make hunter-gatherers unreliable signposts of the past.

Lethal attacks on one community by another rarely occurred during the 19th and 20th centuries, according to a new analysis of data previously gathered from nomadic hunter-gatherer populations. Murders of one person by another in the same group accounted for a majority of intentionally caused deaths, anthropologists Douglas Fry and Patrik Söderberg of Åbo Akademi University in Vasa, Finland, report in the July 19 *Science*.

Ten of the hunter-gatherer groups had no recorded killings involving more than one attacker, effectively making those societies no-war zones, Fry and Söderberg say.

The new evidence suggests that humans have evolved a tendency to avoid killing in general, the researchers contend. War originated only within the past 10,000 years, in their view, with armed conflicts intensifying as the first states expanded between 6,000 and 4,000 years ago. “Fry and Söderberg go against the popular tide in science ... and win hands down,” says anthropologist R. Brian Ferguson of Rutgers University in Newark, N.J. Archaeological evidence from Europe, the Middle East and western Asia contains relatively few signs of murder and war until after 10,000 years ago, he says.

But the new study has attracted fire from other investigators. “Fry and Söderberg use the hunter-gatherer record inappropriately to push the idea that because many modern hunter-gatherers were not seen to have war, ancestral hunter-gatherers also did not often have war,” says Harvard anthropologist Richard Wrangham.

Wrangham and others say that the new paper ignores relatively high homicide rates previously documented in hunter-gatherer groups, including some in the study. Critics also point to reports of regular fighting among neighboring hunter-gatherer communities; the groups that Fry and Söderberg studied were largely isolated. From critics’ perspective, war probably goes back tens of thousands of years and stoked the evolution of intense cooperation within, but not between, human groups.

Murders cause more deaths than war in both traditional and modern societies, with exceptions coming during the 20th century’s two world wars, says Harvard University psychologist Steven Pinker. Given war’s rarity, researchers are unlikely to observe raids and other attacks on rival groups when studying small hunter-gatherer samples such as those in the new study, he says. Rates of violent death are higher among hunter-gatherers and in other non-state societies than in state societies, he adds.

Fry and Söderberg’s finding that mobile hunter-gatherer bands infrequently organize warlike attacks does not surprise anthropologist Polly Wiessner of the University of Utah. But raiding and war does take place in a few such groups, as well as among sedentary hunter-gatherers that live year-round in bountiful settings near coasts or rivers. The great unanswered question, Wiessner says, concerns “how different societies harnessed and tamed aggression to build larger societies throughout human evolution.”

Fry and Söderberg identified data on 148 killings in 21 mobile hunter-gatherer groups. Just over half of those killings were committed by lone perpetrators. Almost two-thirds resulted from disputes within families, executions of group members, competition among men over women and other conflicts within groups.

About one-third of killings involved attacks by one group on another. Reasons included disputes over resources, thefts of women and revenge attacks for past stealing or other offenses. Australia’s Tiwi had an exceptionally large number of killings, 69, and accounted for most of the lethal attacks across groups.

Economist Samuel Bowles of New Mexico’s Santa Fe Institute criticizes Fry and Söderberg for choosing relatively peaceful groups, including the Tiwi, that mostly live in places where state-run armies discourage intergroup conflict. In his 2009 analysis of eight hunter-gatherer societies, the Tiwi ranked near the bottom in estimated rates of war-related deaths. None of the other seven groups he studied were part of Fry and Söderberg’s work.

A handful of reports have likewise found fairly regular, usually low-level warfare among neighboring hunter-gatherer societies, Wrangham says. In those cases, hunter-gatherers had little or no contact with more powerful farming communities that could have discouraged fighting. Warring groups had different customs and spoke different languages or dialects. Fry and Söderberg mainly addressed conflicts between bands of hunter-

gatherers with common customs and languages, which reveal little about the evolution of war, Wrangham contends.

Wrangham considers periodically warring hunter-gatherer groups to be the best available models of Stone Age practices. In a 2012 paper, he and a colleague proposed that ancient people in groups such as these evolved a tendency for males to band together and opportunistically kill members of rival groups — much as chimpanzees do.

*D. Fry and P. Söderberg. Lethal aggression in mobile forager bands and implications for the origins of war. Science. Vol. 341, July 19, 2013, p. 270. doi:10.1126/science.1235675. [Go to]*

<http://www.scientificamerican.com/article.cfm?id=h7n9-risk-human-to-human>

## **Risk of Human-to-Human Spread of Deadly New Bird Flu Virus Higher Than Previously Thought**

*Mounting evidence suggests lethal H7N9 bird flu poses “worrisome” threat*

By Dina Fine Maron | Thursday, July 18, 2013 | 9

Before this year the H7N9 bird flu virus linked to 133 human infections and 43 deaths was never seen in people. All the available evidence suggests that an effective biological barrier apparently kept a pandemic at bay—humans only contracted the novel virus via direct contact with poultry or environments such as live bird markets rather than by human-to-human transmission. New analysis from the Chinese Academy of Agricultural Sciences (CAAS), however, suggests that the virus is closer to becoming a disease transmitted among humans than previously thought.

A large study comparing the genomes of the five reported human H7N9 strains with 37 H7N9 viruses isolated from more than 10,000 poultry market, farm and slaughterhouse samples from across China suggests that the virus would only need small mutations in its protein structure in order to become easily transmissible among humans. Moreover, testing in ferrets—widely considered to be the best proxy for humans in flu testing—finds that one lethal strain of the virus that killed the first H7N9 victim in China is transmissible via respiratory droplet, meaning that it could conceivably be spread by coughing and sneezing. The new results are published in *Science* today. “Our findings indicate nothing to reduce the concern that these viruses can transmit between humans,” says study author Hualan Chen of the CAAS.

The new findings are “worrisome,” says Charles Chiu, an infectious disease expert at the University of California, San Francisco. “For this particular virus, for H7N9, whether or not there is human-to-human transmission is a critical question.”

Since April the number of H7N9 cases has abruptly dropped, but public health officials are concerned that, like other avian influenza viruses that have seasonal infection patterns, H7N9 could mount a resurgence in the fall. With more cases of H7N9 there would be more opportunities for the virus to mutate among humans and, consequently, make the necessary amino acid changes to create human-to-human transmissible H7N9. The H7N9 viruses isolated from birds and humans are already closely genetically related. In the *Science* analysis researchers found the viruses can bind to human airway receptors, but they maintain the ability to bind to avian airway receptors, too. In order for the virus to be transmissible among humans, it must further mutate to lose its ability to bind to avian airway receptors—a genetic re-sorting the authors say might be possible with only a few amino acid changes.

The *Science* paper’s results diverge somewhat from earlier research. A study from the U.S. Centers for Disease Control published in *Nature* last week also considered H7N9 transmission in ferrets and found that although ferrets housed together transmit the flu, when the animals were physically separated but shared the same air via a net between their cages, the healthy ferrets only rarely contracted the virus. In that work CDC researchers looked at respiratory droplet transmission in two different strains of H7N9 and found that in a strain originating in Anhui Province, China, only two out of six ferrets contracted the virus whereas in a strain from Shanghai, only one out of three ferrets contracted the virus. (*Scientific American* is part of Nature Publishing Group.) In the new study researchers also looked at multiple H7N9 strains and found the virus was similarly transmitted via direct contact. But in contrast to the authors of the *Nature* reports, they found that all three ferrets exposed to the Anhui H7N9 strain contracted the virus when exposed via respiratory droplets. The *Science* study authors ran the experiment twice and received the same results.

The significance of the conflicting airborne infection figures from the two studies is unclear because both studies looked at very small numbers of ferrets. Some of the discrepancy could have stemmed from differences in the lab environments. Alternatively, the virus may have changed slightly as the samples grew in the labs. What these studies, along with other existing research, make clear is that H7N9 can indeed spread via airborne transmission, but that this mode of transmission is not very effective compared with direct contact, says Richard Webby, an influenza expert at Saint Jude Children’s Research Hospital in Memphis. The new *Science* report

“adds a whole lot of data to the growing list of evidence that this virus is something we need to be worried about,” he says.

Adding to the virus transmission concerns is the fact that chickens, ducks and mice experimentally infected with avian strains of H7N9 show no visible disease symptoms. In outbreaks of H5N1, another flu strain, severely infected poultry served as a warning knell for human infection. But H7N9 could silently spread in poultry markets and there would be no easy way to detect it.

Chiu says that the new findings should prompt more robust surveillance of poultry populations. Other public health measures to combat the virus in humans include washing hands, avoiding touching the eyes, nose and mouth, and coughing into the elbow to help stop the spread of transmission. “Replication in humans,” the authors wrote, “will provide further opportunities for the virus to acquire more mutations and become more virulent and transmissible in the human population.”

<http://www.bbc.co.uk/news/science-environment-23366318>

## Neutrino 'flavour' flip confirmed

*An important new discovery has been made in Japan about neutrinos.*

By Jonathan Amos Science correspondent, BBC News

These are the ghostly particles that flood the cosmos but which are extremely hard to detect and study.

Experiments have now established that one particular type, known as the muon "flavour", can flip to the electron type during flight. The observation is noteworthy because it allows for the possibility that neutrinos and their anti-particle versions might behave differently. If that is the case, it could be an explanation for why there is so much more matter than antimatter in the Universe.

Theorists say the counterparts would have been created in equal amounts at the Big Bang, and should have annihilated each other unless there was some significant element of asymmetry in play. "The fact that we have matter in the Universe means there have to be laws of physics that aren't in our Standard Model, and neutrinos are one place they might be," Prof Dave Wark, of the UK's Science and Technology Facilities Council (STFC) and Oxford University, told BBC News. The confirmation

that muon flavour neutrinos can flip, or oscillate, to the electron variety comes from T2K, an international collaboration involving some 500 scientists.

The team works on a huge experimental set-up that is split across two sites separated by almost 300km.

At one end is the Japan Proton Accelerator Research Centre (J-Parc) located on the country's east coast.

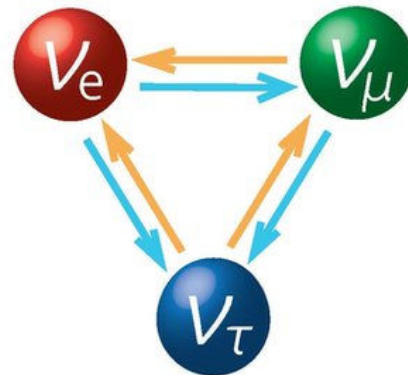
It generates a beam of muon neutrinos that it fires under the ground towards the Super-Kamiokande facility on the west coast. The Super-K, as it is sometimes called, is a tank of 50,000 tonnes of ultra-pure water surrounded by sensitive optical detectors. These photomultiplier tubes pick up the very rare, very faint flashes of light emitted when passing neutrinos interact with the water.

In experiments in early 2011, the team saw an excess of electron neutrinos turning up at Super-K, suggesting the muon types had indeed changed flavour en route. But just as the collaboration was about to verify its findings, the Great Tohoku Earthquake damaged key pieces of equipment and took T2K offline.

Months of repairs followed before the project was able then to gather more statistics and show the muon-electron oscillation to be a formal discovery.

Details are being reported on Friday at the [European Physical Society Conference on High Energy Physics](#) in Stockholm, Sweden. "Up until now the oscillations have always been measured by watching the types disappear and then deducing that they had turned into another type. But in this instance, we observe muon neutrinos disappearing and we observe electron neutrinos arriving - and that's a first," said Prof Alfons Weber, another British collaborator on T2K from the STFC and Oxford. Neutrino oscillations are

### The 'ghostly' neutrino particle



*Second most abundant particle in the Universe, after photons of light*

*Means 'small neutral one' in Italian; was first proposed by Wolfgang Pauli in 1930*

*Uncharged, and created in nuclear reactions and some radioactive decay chains*

*Shown to have a tiny mass, but hardly interacts with other particles of matter*

*Comes in three flavours, or types, referred to as muon, tau and electron*

*These flavours are able to oscillate - flip from one type to another - during flight*

*Could be a Majorana particle - that is a particle that is equal to its anti-particle*

governed by a matrix of three angles that can be thought of as the three axes of rotation in an aeroplane - roll, pitch and yaw.

Other research has already shown two of the matrix angles to have non-zero values. T2K's work confirms that the third angle - referred to as theta-one-three - also has to have a non-zero value.

This is critical because it allows for the oscillations of normal neutrinos and their anti-particles, anti-neutrinos, to be different - that they can have enough degrees of freedom to display an asymmetrical behaviour called charge parity (CP) violation.

CP-violation has already been observed in quarks, the elementary building blocks of the protons and neutrons that make up atoms, but it is a very small effect - too small to have driven the preference for matter over anti-matter after the Big Bang.

However, if neutrinos can also display the asymmetry - and especially if it was evident in the very massive neutrinos thought to have existed in the early Universe - this might help explain the matter-antimatter conundrum. The scientists must now go and look for it.

It is likely, though, that much more powerful neutrino laboratories than even T2K will be needed to investigate the issue. "We have the idea for a Hyper-Kamiokande which will require an upgrade of the accelerator complex," Prof Weber told BBC News. "And in America there's something called the LBNE, which again would have bigger detectors, more sensitive detectors and more intense beams, as well as a longer baseline to allow the neutrinos to travel further."

<http://bit.ly/12PKIR3>

### Genomes of Giant Viruses Hint at "4th Domain" of Life

*Just 7 percent of the viruses' genes match those in existing databases, a finding that confirms that viral diversity is still largely underexplored*

By Ed Yong and Nature magazine | Friday, July 19, 2013 | 5

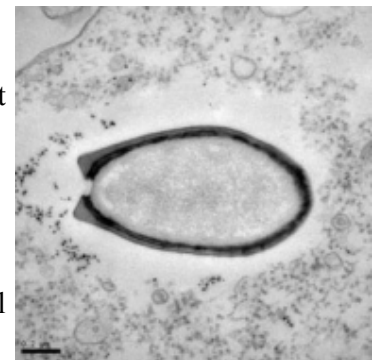
The organism was initially called NLF, for "new life form". Jean-Michel Claverie and Chantal Abergel, evolutionary biologists at Aix-Marseille University in France, found it in a water sample collected off the coast of Chile, where it seemed to be infecting and killing amoebae. Under a microscope, it appeared as a large, dark spot, about the size of a small bacterial cell.

Later, after the researchers discovered a similar organism in a pond in Australia, they realized that both are viruses — the largest yet found. Each is around 1 micrometer long and 0.5 micrometers across, and their respective genomes top out at 1.9 million and 2.5 million bases — making the viruses larger than many bacteria and even some eukaryotic cells. But these viruses, described today in *Science*, are more than mere record-breakers — they also hint at unknown parts of the tree of life. Just 7% of their genes match those in existing databases.

"What the hell is going on with the other genes?" asks Claverie. "This opens a Pandora's box. What kinds of discoveries are going to come from studying the contents?" The researchers call these giants Pandoraviruses. "This is a major discovery that substantially expands the complexity of the giant viruses and confirms that viral diversity is still largely underexplored," says Christelle Desnues, a virologist at the French National Center for Scientific Research in Marseilles, who was not involved in the study.

Claverie and Abergel have helped to discover other giant viruses — including the first, called Mimivirus, in 2003, and Megavirus chilensis, until now the largest virus known, in 2011. Pandoravirus salinus came from the same Chilean water sample as *M. chilensis*. Claverie picked up the second Pandoravirus, *P. dulcis*, from a pond near Melbourne, where he was attending a conference.

The viruses' presence on separate continents helped to establish that they were not artifacts of known cells. It also suggests that the Pandoraviruses are widespread, Claverie says. Indeed, other scientists had previously mistaken them for parasitic or symbiotic bacteria. Rolf Michel, a parasitologist from the Central Institute of the Bundeswehr Medical Service in Koblenz, Germany, found one in 2008, in an amoeba living in the contact lens of a woman with keratitis. "Reading this stunning article, I recognized that both *P. salinus* and *P. dulcis* are almost identical to what we described a few years ago," he says. "We had no idea that those giant organisms could be viruses at all!"



***Pandoraviruses infect amoebae and are larger than some bacteria.*** Image: Chantal Abergel/Jean-Michel Claverie

The researchers showed that Pandoraviruses lack many of the hallmarks of cellular organisms such as bacteria. They do not make their own proteins, produce energy via ATP or reproduce by dividing.

They do, however, contain some of the core genes that are common to giant viruses, and they have a viral life cycle. Under an electron microscope, the researchers saw the viruses being taken up by amoeba hosts, emptying their proteins and DNA into the host cells, commandeering the host-cell nuclei, producing hundreds of new viral particles and, finally, splitting the host cells open.

The researchers are now trying to determine the viruses' origins by characterizing the unknown genes and the proteins they encode. They have long suspected that giant viruses evolved from cells; if they are right, the ancestors of Pandoraviruses must have been very different from the bacteria, archaea and eukaryotes we have today. "We think that at some point, the dynasty on Earth was much bigger than those three domains," says Abergel. Some cells gave rise to modern life, and others survived by parasitizing them and evolving into viruses.

The discovery suggests that scientists' may revise their concept of what a virus looks like. "After reading the article, many people may wonder if they have something on their shelves that might be a giant virus," says Abergel. "We still have more crazy things in store that we expect to be able to publish next year."

[http://www.eurekalert.org/pub\\_releases/2013-07/smh-rdp071913.php](http://www.eurekalert.org/pub_releases/2013-07/smh-rdp071913.php)

## **Researchers describe potential for MERS coronavirus to spread internationally**

### ***Researchers encouraged health-care providers to learn from the experience of SARS***

TORONTO - The life-threatening MERS coronavirus that has emerged in the Middle East could spread faster and wider during two international mass gatherings involving millions of people in the next few months, according to researchers who describe the most likely pathways of international spread based upon worldwide patterns of air travel.

Researchers led by Dr. Kamran Khan of St. Michael's Hospital encouraged health care providers to learn from the experience of SARS by anticipating rather than reacting to the introduction of MERS in travelers returning from the Middle East. SARS, which was also caused by a previously unknown coronavirus, killed 800 people worldwide a decade ago, including 44 in Toronto, and cost the Canadian economy an estimated \$2 billion. The MERS coronavirus, which appears to have emerged in the Middle East in early 2012, has spread to several countries in Western Europe and North Africa where there have been localized clusters of cases. Worldwide about 80 cases have been confirmed, with a mortality rate of more than 50 per cent.

Dr. Khan said there is potential for the virus to spread faster and wider during two annual events that draw millions of domestic and foreign Muslims to Saudi Arabia. The first is umrah, a pilgrimage that can be performed at any time of year but is considered particularly auspicious during the month of Ramadan, which this year began on July 9 and ends on Aug. 7. The second is the hajj, a five-day pilgrimage required of all physically and financially able Muslims at least once in their life. It takes place Oct. 13-18 this year and is expected to draw more than 3 million people.

Dr. Khan's team analyzed 2012 worldwide airline traffic and historic hajj data to predict population movements in and out of Saudi Arabia and the broader Middle East during these two mass gatherings to help countries assess their potential for MERS introduction via returning travelers and pilgrims. He also used World Bank economic and per capita health care expenditure data to help gauge individual countries' abilities to detect imported MERS in a timely manner and mount an effective public health response.

Results of the study were published in the online journal PLOS Currents: Outbreaks.

Dr. Khan, an infectious disease physician, is the founder of BioDiaspora, a web-based technology that uses global air traffic patterns to predict the international spread of infectious disease. The BioDiaspora platform has been used by numerous international agencies, including the U.S. Centers for Disease Control and Prevention, the European Centre for Disease Prevention and Control and the World Health Organization to evaluate emerging infectious disease threats, including those during global mass gatherings such as the Olympics and the hajj.

"With millions of foreign pilgrims set to congregate in Mecca and Medina between Ramadan and the hajj, pilgrims could acquire and subsequently return to their home countries with MERS, either through direct exposure to the as-of-yet unidentified source or through contact with domestic pilgrims who may be infected," he said.

Dr. Khan's team found that of the 16.8 million travelers who flew on commercial flights out of Saudi Arabia, Jordan, Qatar and the United Arab Emirates between June and November 2012 (the period starting one month before Ramadan and ending one month after the hajj) 51.6 per cent had destinations in just eight countries: India (16.3 per cent), Egypt (10.4 per cent), Pakistan (7.8 per cent), Britain (4.3 per cent), Kuwait (3.6 per cent), Bangladesh (3.1 per cent), Iran (3.1 per cent) and Bahrain (2.9 per cent).

Twelve cities--Cairo, Kuwait City, London, Bahrain, Beirut, Mumbai, Dhaka, Karachi, Manila, Kozhikode (India), Istanbul and Jakarta--each received more than 350,000 commercial air travelers between June and November 2012 from the four countries where MERS cases have been traced back to.

In contrast to SARS, where the disease was introduced into predominantly high-income countries through air travel, more than half of all air travelers departing Saudi Arabia, Jordan, Qatar and UAE have final destinations in low or lower-middle income countries. Two-thirds of all hajj pilgrims originate from low or lower-middle income countries.

Of particular note is the degree of connectivity between the Middle East and South Asia. Collectively, India, Pakistan, Bangladesh, Afghanistan and Nepal represent the final destinations of nearly one-third of all international air travelers departing Saudi Arabia, Jordan, Qatar and the UAE, and the origins of roughly one in four foreign hajj pilgrims worldwide.

"Given that these countries have limited resources, they may have difficulty quickly identifying imported MERS cases, implementing rigorous infection control precautions and responding effectively to newly introduced cases," Dr. Khan said.

Dr. Khan's previous research suggests that if screening of air travelers for MERS is considered, it would be far more efficient and less disruptive to the world's air traffic to screen travelers as they leave source areas in the Middle East rather than screen the same travelers as they arrive at other airports around the world. However, all countries receiving pilgrims and other travelers from known MERS areas should mobilize their infectious disease surveillance and public health resources in ways that are commensurate with their potential for MERS introduction, he said.

Educating and preparing front-line health care providers to consider the possibility of MERS in patients is also critical, he said, since that is a necessary first step to implement effective infection control practices that could minimize the risk of spread to others. In the SARS epidemic, delays in considering the diagnosis led to delays in implementing appropriate infection control measures, which in turn enabled SARS to spread within health care institutions.

*Funding for this study was provided by the Canadian Institutes of Health Research and the U.S. Centers for Disease Control and Prevention.*

<http://www.sciencedaily.com/releases/2013/07/130719083940.htm>

## **Cheaper Anti-Cancer Drug as Effective as Expensive Drug in Treating Most Common Cause of Blindness in Older Adults**

*An anti-cancer drug has been proven to be equally as effective in treating the most common cause of blindness in older adults as a more expensive drug specifically formulated for this purpose.*

The results of a two-year trial, led by Queen's scientist Professor Usha Chakravarthy, and published in *The Lancet* today (Friday 19 July), show that two drug treatments Lucentis and Avastin are equally effective in treating neovascular or wet age-related macular degeneration (wet AMD).

Wet AMD is a common cause of sight loss in older people with at least 23,000 older people diagnosed with the condition in the UK each year. Without treatment two thirds of people with this condition will experience severe loss of sight within two years of being diagnosed.

Lucentis, the drug most commonly used in the UK at present to treat wet AMD, costs about £700 per injection and Avastin costs about £60 per injection. The NHS could save £84.5 million annually based on injecting 17,295 eyes each year by switching from Lucentis to Avastin. Avastin is already used to treat wet AMD in some parts of the UK and extensively elsewhere in the world and also for other eye conditions.

Over the past five years, a team of scientists and eye specialists from 23 hospitals and UK universities, including Queen's University Belfast, University of Bristol, University of Liverpool, University of Southampton and University of Oxford, have investigated whether Lucentis and Avastin and the way they are given are equally effective and safe.

610 people with wet AMD entered a two-year trial known as IVAN which is one of the largest ever carried out in the field of eye disease in the UK. Patients received injections of the drug into the affected eye every month for the first three months. Patients were then subdivided to receive the injections at every visit (monthly group) or only if the specialist decided there was persistent disease activity (as needed group).

The IVAN study's two year results show that sight was equally well preserved with either of the two drugs. Giving the treatment regularly every month, resulted in slightly better levels of sight which was detected through testing of near visual acuity and contrast sensitivity. The 'as needed' group received on average 13 injections over the two year period compared to 23 for the monthly treatment group. However, continuous treatment caused a higher proportion of eyes to develop a condition known as geographic atrophy which is a thinning of the retina and its blood supply.



Professor Usha Chakravarthy of Queen's University Belfast's Centre for Vision and Vascular Science, who led the research study team said: "The IVAN results at the end of year two show that Lucentis and Avastin have similar functional effectiveness regardless of the drug received. With respect to monthly versus as needed treatment, while there was marginally better eyesight in the former, the development of atrophy is a matter of concern in the longer term."

The IVAN study was funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme. The Belfast Health and Social Care Trust sponsored the clinical trial. Professor Ian Young, Director of Research and Development at the Trust said: "The findings of the IVAN study will be of great importance for the management of patients with wet AMD throughout the world. Research to improve patient care is a key aspect of the work of Belfast Trust, and we are committed to sponsoring and leading important clinical trials of this kind which allow our patients early access to new treatments."

Dr Janice Bailie, Assistant Director, Health and Social Care Research and Development Division of the Public Health Agency, which supported the trial said: "With increasing life expectancy and a growing proportion of older people in the population, slowing the progress of conditions like AMD is key to maintaining their independence. The IVAN trial is an example of research led from Northern Ireland with international significance -- the findings have the potential to influence how AMD is managed in the future."

The IVAN study also monitored the drugs for serious adverse events which included death, heart attacks, strokes, and any other event that was life threatening, disabling or resulted in hospitalisation. These were similar for the two drugs. However, deaths occurred less frequently in the group that received monthly treatment, although there were fewer deaths overall among people taking part in the trial than were expected based on their age and gender and national death rates. When these safety results were combined with those of a similar study called the CATT trial which was performed in the USA, the resultant findings continued to indicate fewer deaths when treatment was given monthly.

The researchers state that their findings will be of relevance to the next round of technology appraisals by the National Institute for Health and Care Excellence and could lead to important changes to the way wet AMD is treated. In the meantime, for an older person starting a course of Lucentis or Avastin, it will be important to explain the trade-off between the number of injections, and the chances of developing geographic atrophy and risk of mortality in two years.

*Usha Chakravarthy, Simon P Harding, Chris A Rogers, Susan M Downes, Andrew J Lotery, Lucy A Culliford, Barnaby C Reeves. Alternative treatments to inhibit VEGF in age-related choroidal neovascularisation: 2-year findings of the IVAN randomised controlled trial. The Lancet, 2013; DOI: 10.1016/S0140-6736(13)61501-9*

<http://www.bbc.co.uk/news/health-23374920>

### **HPV virus 'linked to third of throat cancer cases'**

***One third of people diagnosed with throat cancer are infected with a form of the HPV virus, a study suggests.*** HPV (human papillomavirus) is the major cause of cervical cancer, and the virus is known to spread through genital or oral contact.

Actor Michael Douglas is reported to have spoken about the link after his own diagnosis with throat cancer. Experts said this study in the Journal of Clinical Oncology, which quantifies the link, showed "striking" results. There are more than 100 types of HPV. Most people will be infected with HPV at some point, but in most the immune system will offer protection.

There are two HPV strains which are most likely to cause cancer - HPV-16 and HPV-18. HPV-16 is thought to be responsible for around 60% of cervical cancers, 80% of cancers in the anus and 60% of oral cancers. Around 1,500 people are diagnosed with throat cancers each year in the UK, with around 470 people dying from the disease.

#### **Survival benefit**

This study looked at HPV's link with cancer of the back of the throat - oropharyngeal cancer. It looked at blood test results collected from people who took part in a huge prospective study into lifestyle and cancer, who were all healthy at the start. Everyone gives a blood sample when they join the study, and in this case the researchers were able to check for the presence of antibodies to one of HPV's key proteins - E6.

E6 knocks out part of cells' protection system, which should prevent cancer developing. Having the antibodies means HPV has already overcome that defence and caused cancerous changes in cells.

The researchers compared blood test results - some more than 10 years old - for 135 people who went on to develop throat cancer and for 1,599 cancer-free people. The University of Oxford team found 35% of those with throat cancer had the antibodies, compared with fewer than 1% of those who were cancer-free.

However, these patients were more likely to survive throat cancer than people whose disease had other causes, such as alcohol or tobacco use.

The study found 84% of people with the antibodies were still alive five years after diagnosis, compared with 58% of those without.

### **Broader effect?**

Dr Ruth Travis, a Cancer Research UK scientist at Oxford who worked on the study, said: "These striking results provide some evidence that HPV-16 infection may be a significant cause of oropharyngeal cancer."

Sara Hiom, Cancer Research UK's director of health information, said: "HPV is an extremely common virus. "Practising safer sex may reduce the risk of getting or passing on HPV, but condoms won't stop infections completely."

She added: "If the HPV vaccine can also protect against oral HPV infections and cancers, then it could have a broader potential protective effect, but we don't have enough research yet to tell us. "

[http://www.eurekalert.org/pub\\_releases/2013-07/w-at071913.php](http://www.eurekalert.org/pub_releases/2013-07/w-at071913.php)

### **Antioxidants -- too much of a good thing?**

#### *A compound in red grapes, including red wine, counteracts exercise benefits in older men*

In older men, a natural antioxidant compound found in red grapes and other plants -- called resveratrol -- blocks many of the cardiovascular benefits of exercise, according to research published today [22 July 2013] in The Journal of Physiology.

Resveratrol has received widespread attention as a possible anti-aging compound and is now widely available as a dietary supplement; much has been made of its role in explaining the cardiovascular health benefits of red wine, and other foods.

But now, new research at The University of Copenhagen surprisingly suggests that eating a diet rich in antioxidants may actually counteract many of the health benefits of exercise, including reduced blood pressure and cholesterol.

In contrast to earlier studies in animals in which resveratrol improved the cardiovascular benefits of exercise, this study in humans has provided surprising and strong evidence that in older men, resveratrol has the opposite effect.

What is emerging is a new view that antioxidants are not a fix for everything, and that some degree of oxidant stress may be necessary for the body to work correctly. This pivotal study suggests that reactive oxygen species, generally thought of as causing aging and disease, may be a necessary signal that causes healthy adaptations in response to stresses like exercise. So too much of a good thing (like antioxidants in the diet) may actually be detrimental to our health.

Lasse Gliemann, a PhD student who worked on the study at The University of Copenhagen, explains how they conducted the research, and the results they found: "We studied 27 healthy, physically inactive men around 65 years old for 8 weeks.

During the 8 weeks all of the men performed high-intensity exercise training and half of the group received 250 mg of resveratrol daily, whereas the other group received a placebo pill (a pill containing no active ingredient). The study design was double-blinded, thus neither the subjects nor the investigators knew which participant that received either resveratrol or placebo.

"We found that exercise training was highly effective in improving cardiovascular health parameters, but resveratrol supplementation attenuated the positive effects of training on several parameters including blood pressure, plasma lipid concentrations and maximal oxygen uptake."

Ylva Hellsten, the leader of the project, says: "We were surprised to find that resveratrol supplementation in aged men blunts the positive effects of exercise training on cardiovascular health parameters, in part because our results contradict findings in animal studies.

"It should be noted that the quantities of resveratrol given in our research study are much higher than what could be obtained by intake of natural foods."

This research adds to the growing body of evidence questioning the positive effects of antioxidant supplementation in humans.

Michael Joyner, from The Mayo Clinic USA, says how the study has wider implications for research: "In addition to the surprising findings on exercise and resveratrol, this study shows the continuing need for mechanistic studies in humans. Too often human studies focus on large scale outcomes and clinical trials and not on understanding the basic biology of how we adapt."

[http://www.eurekalert.org/pub\\_releases/2013-07/gi-ftd071913.php](http://www.eurekalert.org/pub_releases/2013-07/gi-ftd071913.php)

## **Failure to destroy toxic protein -- not buildup of protein itself -- contributes to Huntington's disease**

### ***Gladstone-led study also finds target that boosts protein clearance, prolongs cell life***

SAN FRANCISCO, CA - Alzheimer's, Huntington's, Parkinson's. Names forever linked to what they represent: diseases that ravage the brain's neurons and leave entire regions to wither and die. These and other so-called neurodegenerative diseases are often associated with the buildup of toxic proteins that lead to the death of neurons. But now, scientists at the Gladstone Institutes have discovered that the progression of disease is not due to the buildup of toxins itself, but rather in the individual neurons' ability to flush these toxins out. Further, they have identified a therapeutic target that could boost this ability, thereby protecting the brain from the diseases' deadly effects.

In the latest issue of *Nature Chemical Biology*, researchers in the laboratory of Gladstone Investigator Steve Finkbeiner, MD, PhD, describe how a newly developed technology allowed them to see—for the first time—how individual neurons fight back against the buildup of toxic proteins over time. Focusing their efforts on a model of Huntington's disease, the team observed how different types of neurons in the brain each responded to this toxic buildup with different degrees of success, offering clues as to why the disease causes neurons in one region to die, while neurons in another are spared.

"Huntington's—an inherited and fatal disorder that leads to problems with muscle coordination, cognition and personality—is characterized by the toxic buildup of a mutant form of the huntingtin protein in the brain," explained Dr. Finkbeiner, who directs the Taube-Koret Center for Neurodegenerative Disease Research at Gladstone. Dr. Finkbeiner is also a professor of neurology and physiology at the University of California, San Francisco, with which Gladstone is affiliated. "A long-standing mystery among researchers was how the buildup of the mutant huntingtin protein caused cells to degrade and die, but previous technology made it virtually impossible to see and monitor this process at the cellular level. In this study, we employed a method called optical pulse-labeling, or OPL, which allowed us to see how the mutant huntingtin ravaged the brain over time—neuron by neuron."

Using neurons extracted from rodent models of Huntington's, the team employed the OPL method, which monitored the speed and efficiency with which different types of neurons were able to flush out the mutant huntingtin. The faster a cell could clear out the toxins, the longer the neuron survived, and vice versa. Surprisingly, the research team noticed clear differences in the ability of different types of neurons to clear mutant huntingtin. Neurons located in the striatum—the region of the brain primarily affected by Huntington's disease that is involved in muscle movement—were particularly susceptible. Neurons found in other regions, such as the cortex and cerebellum, were less so. And when they tracked the striatal neurons carrying the mutant huntingtin, they found them much more likely to die than those from other brain regions.

All cells depend on two main processes to clear excess proteins: the ubiquitin-proteasome system (UPS) and autophagy. Although their mechanisms are distinct, their goal is the same: to literally gobble up excess proteins, ensuring they are efficiently flushed out so as to not interfere with normal cellular activity.

The research team found that striatal neurons were particularly sensitive to disruptions to the autophagy process. But the team found a way around this problem. They artificially accelerated autophagy by boosting the activity of a protein called Nrf2 in these neurons, which prolonged cell survival.

"If we could develop drugs that boost Nrf2 production in the neurons most susceptible to Huntington's, we might extend their survival, thereby staving off the worst effects of the disease," said former Gladstone Postdoctoral Fellow Andrey Tsvetkov, PhD, the study's lead author. "Importantly, our results also demonstrate that the brain itself has evolved powerful coping mechanisms against diseases such as Huntington's. For example, the fact that people don't start experiencing symptoms of Huntington's until the fourth or fifth decade of their lives—even though the mutant huntingtin is present at birth—is further evidence of the brain's ability to stave off the effects of the disease."

"Our findings are critical not only for informing us as to the underlying mechanisms behind diseases such as Huntington's, but also to remind researchers that focusing only on the disease-causing protein—and not how individual cells respond to it—is only one side of the coin," said Dr. Finkbeiner. "To truly understand a complex disease like Huntington's, we must also look to the brain's naturally evolved defense mechanisms, which as we've shown here could represent an entirely new therapeutic strategy."

*Montserrat Arrasate, PhD, Sami Barmada, MD, PhD, and Punita Sharma, PhD, also participated in this research at Gladstone, which received support from the National Institute of Neurological Disease and Stroke, the National Institute on Aging, the Huntington's Disease Society of America, the Taube-Koret Center for Neurodegenerative Disease, the Hereditary Disease*

[http://www.eurekalert.org/pub\\_releases/2013-07/uoe-mrc071913.php](http://www.eurekalert.org/pub_releases/2013-07/uoe-mrc071913.php)

## MS research could help repair damage affecting nerves

*Multiple sclerosis treatments that repair damage to the brain could be developed thanks to new research.*

A study has shed light on how cells are able to regenerate protective sheaths around nerve fibres in the brain. These sheaths, made up of a substance called myelin, are critical for the quick transmission of nerve signals, enabling vision, sensation and movement, but break down in patients with multiple sclerosis (MS). The study, by the Universities of Edinburgh and Cambridge, found that immune cells, known as macrophages, help trigger the regeneration of myelin.

Researchers found that following loss of or damage to myelin, macrophages can release a compound called activin-A, which activates production of more myelin. Dr Veronique Miron, of the Medical Research Council Centre for Regenerative Medicine at the University of Edinburgh, said: "In multiple sclerosis patients, the protective layer surrounding nerve fibres is stripped away and the nerves are exposed and damaged.

"Approved therapies for multiple sclerosis work by reducing the initial myelin injury – they do not promote myelin regeneration. This study could help find new drug targets to enhance myelin regeneration and help to restore lost function in patients with multiple sclerosis."

The study, which looked at myelin regeneration in human tissue samples and in mice, is published in Nature Neuroscience and was funded by the MS Society, the Wellcome Trust and the Multiple Sclerosis Society of Canada.

Scientists now plan to start further research to look at how activin-A works and whether its effects can be enhanced. Dr Susan Kohlhaas, Head of Biomedical Research at the MS Society, said: "We urgently need therapies that can help slow the progression of MS and so we're delighted researchers have identified a new, potential way to repair damage to myelin. We look forward to seeing this research develop further."

Dr Karen Lee, Vice-President, Research at the MS Society of Canada, said: "We are pleased to fund MS research that may lead to treatment benefits for people living with MS. We look forward to advances in treatments that address repair specifically, so that people with MS may be able to manage the unpredictable symptoms of the disease."

<http://www.bbc.co.uk/news/health-23374623>

## 'Big leap' towards curing blindness in stem cell study

*The prospect of reversing blindness has made a significant leap, according to scientists in the UK.*

An animal study in the journal Nature Biotechnology showed the part of the eye which actually detects light can be repaired using stem cells. The team at Moorfields Eye Hospital and University College London say human trials are now, for the first time, a realistic prospect. Experts described it as a "significant breakthrough" and "huge leap" forward.

Photoreceptors are the cells in the retina which react to light and convert it into an electrical signal which can be sent to the brain. However, these cells can die off in some causes of blindness such as Stargardt's disease and age-related macular degeneration. There are already trials in people to use stem cells to replace the "support" cells in the eye which keep the photoreceptors alive.

### Blind mice

Now the London-based team have shown it is possible to replace the light-sensing cells themselves, raising the prospect of reversing blindness.

They have used a new technique for building retinas in the laboratory.

It was used to collect thousands of stem cells, which were primed to transform into photoreceptors, and injected them into the eyes of blind mice.

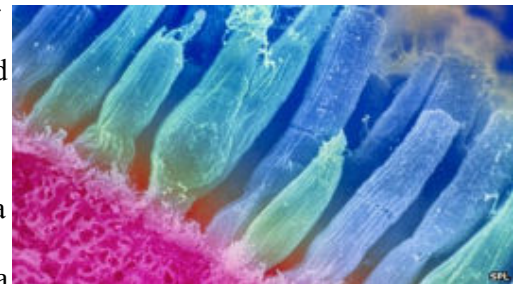
The study showed that these cells could hook up with the existing architecture of the eye and begin to function.

However, the effectiveness is still low. Only about 1,000 cells out of a transplant of 200,000 actually hooked up with the rest of the eye.

Lead researcher Prof Robin Ali told the BBC News website: "This is a real proof of concept that photoreceptors can be transplanted from an embryonic stem cells source and it give us a route map to now do this in humans. "That's why we're so excited, five years is a now a realistic aim for starting a clinical trial."

*Rods, blue, and cones, blue-green, detect light and create electrical signals which are sent to the brain.*

The eye is one of the most advanced fields for stem cell research.



It is relatively simple as the light sensing cells only have to pass their electrical message on to one more cell in order to get their message to the brain, unlike an attempt to reverse dementia which would require cells to hook up with far more cells all across the brain.

The immune system is also very weak in the eye so there is a low chance of the transplant being rejected. A few cells can also make a big difference in the eye. Tens of thousands of stem cells in the eye could improve vision, but that number of stem cells would not regenerate a much larger organ such as a failing liver.

Prof Chris Mason, from University College London, told the BBC: "I think they have made a major step forward here, but the efficiency is still too low for clinical uses.

"At the moment the numbers of tiny and it will take quite a bit of work to get the numbers up and then the next question is 'Can you do it in man?' "But I think it is a significant breakthrough which may lead to cell therapies and will give a much expanded knowledge on how to cure blindness."

Dr Marcelo Rivolta, from the University of Sheffield, said the study was a "huge leap" forward for treating blindness and could have implications across stem cell research.

[http://www.eurekalert.org/pub\\_releases/2013-07/nrr-chm071913.php](http://www.eurekalert.org/pub_releases/2013-07/nrr-chm071913.php)

### **Chinese herbal medicines are safe and effective for vascular dementia**

*Chinese herbal medicine, which has been used for thousands of years in China, has long been considered an effective treatment for vascular dementia.*

There are already meta-analyses of the effects of herbal extracts (ginkgo biloba and huperzine A) on vascular dementia. However, there has been no systematic review of the efficacy and safety of Chinese herbal medicines for vascular dementia, despite its wide use in clinical practice. A recent study published in the Neural Regeneration Research (Vol. 8, No. 18, 2013) evaluated the efficacy and safety of Chinese herbal medicines for vascular dementia, using efficacy, Mini-Mental State Examination score, Hasegawa Dementia Scale score, and adverse reactions as evaluation indices by performing a meta-analysis. The results suggested that Chinese herbal medicine appears to be safer and more effective than control measures in the treatment of vascular dementia. Chinese herbal medicines for vascular dementia exert characteristics of syndrome differentiation of traditional Chinese medicine, and have good potential in the clinic.

*Article: " A meta-analysis of Chinese herbal medicines for vascular dementia " by Xiude Qin<sup>1, 2</sup>, Yu Liu<sup>3</sup>, Yanqing Wu<sup>1</sup>, Shuo Wang<sup>1</sup>, Dandan Wang<sup>1</sup>, Jinqiang Zhu<sup>1</sup>, Qiaofeng Ye<sup>1</sup>, Wei Mou<sup>1</sup>, Liyuan Kang<sup>1</sup> (1 Institute of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China; 2 Department of Encephalopathy, the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300150, China; 3 GCP Center, the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin 300150, China)*

*Qin XD, Liu Y, Wu YQ, Wang S, Wang DD, Zhu JQ, Ye QF, Mou W, Kang LY. A meta-analysis of Chinese herbal medicines for vascular dementia. Neural Regen Res. 2013;8(18):1685-1692.*