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## **New study reveals bitter taste receptors regulate the upper respiratory defense system** ***Findings could help uncover novel diagnostic tools and treatments for patients with chronic sinus conditions***

PHILADELPHIA – A new study from a team of researchers at the Perelman School of Medicine at the University of Pennsylvania, the Monell Chemical Senses Center, and the Philadelphia VA Medical Center, reveals that a person's ability to taste certain bitter flavors is directly related to their ability to fight off upper respiratory tract infections, specifically chronic sinus infections. The new research is published in the latest edition of the *Journal of Clinical Investigation*.

Most humans experience five types of tastes: sweet, salty, sour, bitter, and savory. The sense of taste is mediated by taste receptor cells which are bundled in our taste buds. "Sour" and "bitter" taste sensations alert the body to harmful foods that have spoiled or are toxic. But based on genetics, up to 25 percent of the population cannot detect certain bitter flavors (non-tasters), 25 percent can detect exceedingly small quantities (super-tasters), and the rest of us fall somewhere between these two extremes.

So what exactly does drinking a cup of bitter coffee have to do with chronic sinus infections, which account for approximately 18-22 million physician visits in the U.S. each year? Recent investigations have shown that these taste receptors (known as T2Rs) are also found in both upper and lower human respiratory tissue, likely signaling a connection between activation of bitter tastes and the need to launch an immune response in these areas when they are exposed to potentially harmful bacteria and viruses.

"With this information in mind, we wanted to better understand the exact role that bitter taste receptors play in the upper airway, especially between these super and non-tasters," says Noam Cohen, MD, PhD, assistant professor of Otorhinolaryngology: Head and Neck Surgery, staff physician at the Philadelphia VAMC, and senior author of the new study.

Cohen and his colleagues formulated the following hypotheses around the connection: (1) bitter taste receptors are functional in the nose (upper respiratory tract), and each receptor detects a specific type of bacteria; (2) upon activation by a specific bacterial product, the bitter taste receptor initiates a local defensive response to combat the attacking bacteria; and (3) genetic variability of the bitter taste receptors alters the vigorosity of the response, thus leaving certain individuals with very strong defenses and others with weak defenses against a specific bacteria.

To test these hypotheses, the team grew cell cultures from sinus and nasal tissue samples collected during sinus surgical procedures. These cultures develop cilia, produce mucus, and reflect many of the defensive workings found inside the nose and sinuses.

They found that one of the bitter taste receptors that functions in upper airway cells, known as T2R38, acts as a type of "security guard" for the upper airway by detecting molecules that a certain class of bacteria secretes.

"These molecules instruct other bacteria to form a biofilm, which helps harbor the bacteria. From previous work, we know that these biofilms spur the immune system to mount an over-exuberant inflammatory response that can lead to sinusitis symptoms. When the T2R38 receptor detects these molecules, it activates local defensive maneuvers to increase mucus clearance and kill the invading bacteria. It's really like modern warfare – intercept the enemies' early communications to thwart their plans and win the battle," Cohen said.

Through the cultures, the research team demonstrated that super-tasters detect very small concentrations of the offending molecules, while non-tasters and the middle-ground individuals require 100 times more of the molecule for detection. The research team also examined the patients that the original sinus tissue samples were collected from. They found that none of the super tasters were infected with the specific type of bacteria that are detected by the T2R38 receptor, known as a gram-negative bacteria.

"Based on these findings, we believe that other bitter taste receptors in the airway perform the same "guard duty" function for early detection of attack by different types of bacteria, and we hope to translate these findings into personalized diagnostics for patients with chronic rhinosinusitis," Cohen says.

The research team is also using the results of the current study to develop a simple "taste-test" protocol to be conducted during clinic visits. "We're optimistic that a test of this nature will help us predict who is at risk to develop biofilms based on their ability to taste various bitter compounds. Additionally, we are looking at therapeutic outcomes, both surgical and medical, based on the taster/non-taster genetic status to determine whether knowing this status will stratify patients to either surgical or medical interventions."

*Other study authors from Penn include Robert J. Lee (first author), Jennifer M. Kofonow, Bei Chen, Laurel Doghramji, Nithin D. Adappa, James N. Palmer, David W. Kennedy, Paschalis-Thomas Doulias, and Harry Ischiropoulos.*

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**Fast walking and jogging halve development of heart disease and stroke risk factors  
But an hour's walk every day makes no difference: Intensity rather than duration is what counts**

The findings indicate that it is the intensity, rather than the duration, of exercise that counts in combating the impact of metabolic syndrome - a combination of factors, including midriff bulge, high blood pressure, insulin resistance, higher than normal levels of blood glucose and abnormal blood fat levels - say the authors. Genes, diet, and lack of exercise are thought to be implicated in the development of the syndrome, which is conducive to inflammation and blood thickening.

The authors base their findings on more than 10,000 Danish adults, between the ages of 21 and 98, who were initially assessed in 1991-94 and then monitored for up to 10 years. All the participants were quizzed on the amount of physical activity they did, which was categorised according to intensity and duration.

At the initial assessment, around one in five (20.7%) women and just over one in four (27.3%) men had metabolic syndrome. Prevalence was closely linked to physical activity level.

Among the women, almost one in three of those who had a sedentary lifestyle had the syndrome whereas only one in 10 of those who were very physically active had it. Among men, the equivalent proportions were just under 37% and just under 14%

Of the remaining 6,088 participants without metabolic syndrome, just under two thirds (3,992) completed the fourth and final survey and assessment, by which point one in seven (15.4%; 585) had developed it.

Again, the prevalence was higher among those leading a sedentary lifestyle, with almost one in five (19.4%) affected compared with around one in nine (11.8%) of those who were very physically active.

It was not only the amount of exercise, but also the intensity which helped curb the likelihood of developing the syndrome.

After taking account of factors likely to influence the results, fast walking speed halved the risk, while jogging cut the risk by 40 per cent. But going for an hour's walk every day made no difference.

"Our results confirm the role of physical activity in reducing [metabolic syndrome] risk and suggest that intensity rather than volume of physical activity is important," conclude the authors.

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**Can eating tomatoes lower the risk of stroke?**

***Eating tomatoes and tomato-based foods is associated with a lower risk of stroke***

MINNEAPOLIS – Eating tomatoes and tomato-based foods is associated with a lower risk of stroke, according to new research published in the October 9, 2012, print issue of *Neurology*®, the medical journal of the American Academy of Neurology. Tomatoes are high in the antioxidant lycopene.

The study found that people with the highest amounts of lycopene in their blood were 55 percent less likely to have a stroke than people with the lowest amounts of lycopene in their blood.

The study involved 1,031 men in Finland between the ages of 46 and 65. The level of lycopene in their blood was tested at the start of the study and they were followed for an average of 12 years. During that time, 67 men had a stroke.

Among the men with the lowest levels of lycopene, 25 of 258 men had a stroke. Among those with the highest levels of lycopene, 11 of 259 men had a stroke. When researchers looked at just strokes due to blood clots, the results were even stronger. Those with the highest levels of lycopene were 59 percent less likely to have a stroke than those with the lowest levels.

"This study adds to the evidence that a diet high in fruits and vegetables is associated with a lower risk of stroke," said study author Jouni Karppi, PhD, of the University of Eastern Finland in Kuopio. "The results support the recommendation that people get more than five servings of fruits and vegetables a day, which would likely lead to a major reduction in the number of strokes worldwide, according to previous research."

The study also looked at blood levels of the antioxidants alpha-carotene, beta-carotene, alpha-tocopherol and retinol, but found no association between the blood levels and risk of stroke.

*The study was supported by Lapland Central Hospital.*

<http://www.bbc.co.uk/news/health-19873171>

## **Typhoid vaccine failure warning**

***More than 700,000 people recently immunised against typhoid may not have full protection because of a dud vaccine that has now been recalled, say experts.***

**By Michelle Roberts Health editor, BBC News online**

Manufacturer Sanofi Pasteur MSD has recalled 88% of its stock - 16 batches - of Typhim Vi vaccine because tests found some samples were too weak. Anyone immunised with the vaccine since January 2011 could be affected. Officials stress that the vaccine was safe and posed no health threat.

But it could mean as many as 729,606 people who potentially received the affected vaccine are not fully immunised against typhoid, according to the body that regulates drugs in the UK, the Medicines and Healthcare products Regulatory Agency (MHRA).

Experts say people should not get revaccinated but should take precautions against typhoid when abroad. If you received this vaccine and have recently returned from abroad, and are unwell, you should contact your doctor.

### **Precautions**

Typhoid fever is uncommon in the UK, but people visiting South Asia and South East Asia, where the life-threatening bacterial disease is most common, are at greater risk.

Typhoid is very contagious. An infected person can pass the bacteria in their faeces.

If someone else eats food or drinks water that has been contaminated, they can catch typhoid fever.

It can be treated with antibiotics if diagnosed early enough.

The MHRA said: "There are no concerns over the safety of this vaccine, but the recall has taken place because the vaccine may not be as effective as it should be. "Anyone who has been to a typhoid region of the world and has a fever, abdominal pain and vomiting should contact a healthcare professional. They can also give them information and advice about minimising the risk of getting typhoid."

Supplies of another injectable typhoid vaccine called Typherix, made by GlaxoSmithKline, are unaffected, as are those of an oral typhoid vaccine called Vivotif.

A spokesman for Sanofi Pasteur MSD said: "We are working hard to resolve the issue, but we cannot confirm an exact date when normal supplies will resume, although we hope this will be by the beginning of 2013.

"While 16 batches of vaccine are being recalled - 88% of the available stock in the UK - there are two batches in the supply chain that are unaffected and these will be distributed shortly."

A statement from the company said: "We understand the difficulties this recall may cause for our customers and people relying upon our vaccines. We would like to offer our most sincere apologies for the inconveniences incurred. "The company is using all possible means at its disposal to address the matter and working to resume normal supplies of Typhim Vi® as quickly as possible."

A Department of Health spokeswoman said: "Vaccine is still available and we are working with vaccine manufacturers to help ensure that current supply problems are resolved as soon as possible.

"People who have recently been immunised, should seek medical advice about precautions to take whilst abroad to minimise the risk of infection, in case the vaccine has not provided full protection."

<http://bit.ly/TIGK9n>

## **Organism without a brain creates external memories for navigation**

***The slime mold stores a record of where it's been using, well, slime.***

**by John Timmer - Oct 9 2012, 6:30am TST**

Is it possible to know where you've been when you don't have a brain? Depending on your definition of "know," the answer may be yes. Researchers have shown that the slime mold, an organism without anything that resembles a nervous system (or, for that matter, individual cells), is capable of impressive feats of navigation. It can even link food sources in optimally spaced networks. Now, researchers have shown it's capable of filling its environment with indications of where it has already searched for food, allowing it to "remember" its past efforts and focus its attention on routes it hasn't explored.

And it does this all using, as the authors put it, "a thick mat of nonliving, translucent, extracellular slime." As you might expect, given the name.

Slime molds are odd creatures: organisms that have a nucleus and complex cells, but are evolutionarily distant from the multicellular animals and plants. When food is plentiful, they exist as single-celled, amoeba-like creatures that forage on the food. But once starvation sets in, the cells send out a signal that causes them to aggregate and fuse. This creates an organism that's visible to the naked eye and all a single cell, but filled with nuclei containing the genomes of many formerly individual cells. That turns out to be advantageous, because

this collective can move more efficiently, and go about foraging for food. In the course of this foraging, the organism leaves behind a trail of slime.

In the course of studying the slime mold, some researchers noticed that the slime mold would avoid any areas covered in slime. So they decided to quantify that. They set up two equal food sources at both ends of a Y-shaped container, and put some slime mold at the base. One of the arms had plain media for the organism to crawl across; the other coated the surface of the media with slime. The results were dramatic: in 39 of the 40 tests they ran, the slime mold avoided the arm that was pre-slimed.

Based on this finding, the authors hypothesized that the mold "uses its [the slime's] presence as an externalized spatial memory system to recognize and avoid areas it has already explored." So, they came up with a test that, in their words, "challenged our slime mold."

They created a three-sided box, and placed it with the open end facing a slime mold. Behind the box, the authors placed a tasty treat of glucose, which could slowly diffuse through the box. But the slime mold was unable to pass through the walls of the box, and thus couldn't take a straight path towards the food source. To find it, it would have to explore the interior of the box, give up, and start looking for a way around it.

Within a few days, 96 percent of them had. But, when the authors covered the entire setup in slime so the mold had no way of telling what areas it had already visited, only about a third of the organisms succeeded in making their way to the food. So, the authors conclude, the slime isn't just the mold's calling card. Instead, it's a way of marking the environment so that the organism can sense where it's been, and not expend effort on searches that won't pay off.

Although the situation isn't an exact parallel, the authors make a comparison to the pheromone trails used by ants. (This comparison may have come about because two of the authors work in the Behaviour and Genetics of Social Insects Laboratory at the University of Sydney.) No individual ants have to remember where a food source is. Instead, by laying down a trail of scent molecules, workers that find food leave a trail in the environment the ants can collectively use. In effect, the colony has a memory that's stored in the environment. In this case, the slime mold does the opposite, in that it avoids the areas of its environment that are chemically marked. The other big difference, of course—the slime mold doesn't have a brain at all. Still, the general principles of placing a memory in the environment are the same.

*PNAS, 2012. DOI: 10.1073/pnas.1215037109 (About DOIs).*

[http://www.eurekalert.org/pub\\_releases/2012-10/uoc--ubs100812.php](http://www.eurekalert.org/pub_releases/2012-10/uoc--ubs100812.php)

### **UC Berkeley study finds flirting can pay off for women** **Haas School of Business research on effective negotiation**

University Of California - When Madeleine Albright became the first female U.S. Secretary of State, she led high-level negotiations between mostly male foreign government leaders. In 2009, comedian Bill Maher asked Albright if she ever flirted on the job and she replied, "I did, I did." Flirtatiousness, female friendliness, or the more diplomatic description "feminine charm" is an effective way for women to gain negotiating mileage, according to a new study by Haas School of Business Professor Laura Kray.

"Women are uniquely confronted with a tradeoff in terms of being perceived as strong versus warm. Using feminine charm in negotiation is a technique that combines both," says Kray, who holds the Warren E. and Carol Spieker Chair in Leadership at the Haas School.

The study, "Feminine Charm: An Experimental Analysis of its Costs and Benefits in Negotiations," was published in October in the journal *Personality and Social Psychology Bulletin* and co-authored by Haas PhD alumna Connson C. Locke of the London School of Economics and Haas PhD candidate Alex B. Van Zant. Flirtation that generates positive results, says Kray, is not overt sexual advances but authentic, engaging behavior without serious intent. In fact, the study found female flirtation signals attractive qualities such as confidence, which is considered essential to successful negotiators.

To determine whether women who flirt are more effective in negotiating than men who flirt, the researchers asked 100 participants to evaluate to what extent they use social charm in negotiation on a one-to-seven scale. Earlier that week, the participants evaluated their partners' negotiating effectiveness. Women who said they used more social charm were rated more effective by their partners. However, men who said they used more social charm were not regarded as more effective.

In the second experiment, the researchers asked subjects to imagine they were selling a car worth \$1,200 and asked for how much would they sell the car. Next, the subjects read one of two scenarios about a potential buyer named Sue. The first group meets Sue, who shakes hands when she meets the seller, smiles, and says, "It's a pleasure to meet you,." and then "What's your best price?" in a serious tone. The second group reads an alternate scenario in which Sue greets the seller by smiling warmly, looking the seller up and down, touching



the seller's arm, and saying, "You're even more charming than over email," followed by a playful wink and asking, "What's your best price?"

The result? Male sellers were willing to give the "playful Sue" more than \$100 off the selling price whereas they weren't as willing to negotiate with the "serious Sue." Playful Sue's behavior did not affect female car sellers.

Kray says many of her students who are senior women executives admit they love to flirt and describe themselves as "big flirts." Kray maintains flirting is not unprofessional if it remains playful and friendly.

"The key is to flirt with your own natural personality in mind. Be authentic. Have fun. That will translate into confidence, which is a strong predictor of negotiation performance."

<http://bit.ly/Oii9DU>

## **Can Wall Street Financial "Wizardry" Foster Drug Innovation?**

***Biotech has always been as much about showing the money as it has been about quantitative secretome analysis.***

**By Gary Stix | October 9, 2012**

Most articles in the journal Nature Biotechnology have titles like "Selective Enrichment of Newly Synthesized Proteins for Quantitative Secretome Analysis."

They don't usually contain sentences like this:

"The special-purpose vehicle's capital structure, priority of payments and various coverage tests and credit enhancements are collectively known as the 'cash flow waterfall'—a reference to the manner in which cash flow from the special purpose vehicle's assets spills over from senior to junior tranches..."

Nothing to be found in that sentence or the rest of the article about the minutiae of monoclonal antibodies, RNA interference or the Nobel-winning biology of induced pluripotent stem cells.

The article in the October issue of Nature Biotech arrives replete with esoterica about cash flow waterfalls and junior tranches, and includes that sentence penned by Andrew Lo, a prominent MIT professor of finance, and colleagues, Jose-Maria Fernandez and Roger M. Stein, also from MIT's Sloan School of Management. In fact, in reading the article I came away with the impression that maybe Nature Biotech needs more articles like this one. (Scientific American is part of Nature Publishing Group, but it might also be worthwhile for Science Translational Medicine to also follow suit with more coverage.)

Biotech has always been as much about showing the money as it has been about quantitative secretome analysis. The article "Commercializing Biomedical Research Through Securitization Techniques" by Lo and colleagues makes the point that cash waterfalls these days aren't flowing to the right places.

The doubling of pharmaceutical R&D from 2002 to 2010, from \$68 billion to \$127 billion, has had scant impact on the number of new drugs approved. The venture capitalists who are putting up the funding for biotech startups have come away with a negative one percent return over the 10-year period from 2001 through 2010. Yet the shortfall in drug therapies comes at a time of fecund research that points toward prospects for gene therapies, cancer drugs aimed at molecular targets, new methods of medical imaging, diagnostic markers for cancers and heart disease, among others.

The authors offer explanations for the disparity between innovation and an absence of new medicines and technologies. The increasing complexity of the science has created a multitude of molecular markers that can be investigated for possible drugs. The cost of undertaking research on so many targets—combined with less tolerance for risk because of declining R&D, increased regulatory uncertainty, patent expirations and the like—has meant that the industry lacks the wherewithal to pursue all of these leads. Health-care finance professionals sometimes refer to the gap between research and latter stages of clinical development as the "valley of death."

Into the breach, Lo and company propose using financial engineering—yes, some of the same techniques that provoked the financial crisis about five years ago—to cope with this disconnect between invention and product. Specifically, they suggest setting up a megafund, issuing stocks and bonds worth as much as \$30 billion, to support dozens or hundreds of drug and other biomedical programs—the diversification here intended to decrease the risk of the overall portfolio and thereby enhance the ability to raise money. Also, relying on bonds more than stock would enable the raising of the huge sums cited, as the debt markets dwarf stock sales.

The money would be raised through securitization: an investor in a stock or bond in the megafund would be buying a little piece of all of the multitude of projects in which the fund is invested, in the way that mortgage securities gave the owner a partial stake in a package of mortgages. The way the fund is structured, the authors contend, would allow unparalleled investment flexibility for projects at all stages of the development cycle. Big drug companies, by contrast, avoid early-stage development and biotech companies are restricted by financing constraints to only a few projects.

Many of the projects would fail but the diversification would mean that, in a few cases, the fund would likely hit the jackpot. A simulation carried out by the authors showed that a cancer megafund with assets of \$5 to \$15 billion could reap returns of 8.9 to 11.4 percent for equity holders and 5 to 8 percent for bond, or “research-backed obligation,” holders, insufficient for venture investors but enough to attract more patient capital from pension funds and insurance companies.

I asked Lo whether he had met with any skepticism from colleagues in academia or on Wall Street. Here is what he said in an e-mail:

“Yes, at first we received a great deal of skepticism from all quarters: pharma companies, biotech VCs, and academics. Much of this skepticism came from the ridiculously large numbers we were quoting (\$30 billion??), but that’s what the problem calls for given the cost of developing a single compound into a drug. But once they saw what our arguments were, and then looked at our historical simulations, and considered all that seems to be wrong with the existing business models of the biopharma industry, they usually become much more receptive.” The article itself addresses the question of whether it’s crazy to use a form of financing that was responsible, in part, for the greatest financial crisis since the Great Depression. The authors emphasize that securitization was developed originally as a means to diminish risk and got hijacked during the Great Recession because of poor corporate governance, inadequate disclosure and shoddy sales practices. Structured properly, the authors contend, a megafund might be viewed as another example of the type of venture philanthropy practiced by, say, the Gates Foundation. Lo said that he and his colleagues now want to assemble a collection of leaders from Wall Street, biotech, pharma, the NIH, the FDA and non-profits to explore further the feasibility of the concept. Will it work? Hard to say.

But the industry needs some new thinking about ways to traverse the precipitous chasm of the Valley of Death.

<http://www.sciencedaily.com/releases/2012/10/121009092531.htm>

**Coffee Speeds Up Return of Bowel Function After Colon Surgery, Study Finds**  
***Patients who drank coffee, rather than water, after bowel surgery to remove a part of their colon experienced a quicker return to bowel movements and tolerance of solid food.***

ScienceDaily - Those are two of the key findings of a comparative study of 80 patients, carried out at University Hospital Heidelberg, Germany, and published in the surgical journal BJS.

"Post-operative bowel obstruction is a common problem after abdominal surgery and the aim of this study was to test our theory that coffee would help to alleviate this" says lead author Dr Sascha Müller, who is now based at Kantonsspital St Gallen, Switzerland.

The 80 patients were randomised into coffee and water groups before their operation, with one patient in the water arm subsequently excluded due to a change in their surgical procedure.

Patient characteristics were similar in both groups. Their average age was 61 years and 56 per cent were male. Just over half (56 per cent) had colonic cancer, 28 per cent had diverticular disease (a structural problem with the wall of their colon), 13 per cent had inflammatory bowel disease and four per cent had other conditions. The majority had open surgery (61 per cent) and the remainder had laparoscopic surgery.

The patients were given 100mls of coffee or water three times a day.

Key findings were:

***Time to first bowel movement after surgery was just over 60 hours in the coffee group and 74 hours in the water group.***

***The coffee group were able to tolerate solid food in just over 49 hours, compared to just under 56 hours in the water group.***

***The coffee drinkers were also able to pass wind just under 41 hours after surgery, compared with over 46 hours for the water group.***

***Length of hospital stay and ill health were similar in both groups.***

"This randomised trial showed that the time to first bowel movement after surgery was much shorter in the coffee drinkers than the water drinkers" says Dr Müller.

"Although 10 per cent of the patients did not want to drink strong coffee at this time, it was well accepted by the group and no coffee-related complications were noted.

"It is not clear how coffee stimulates the intestine and caffeine appears to have been ruled out by previous studies, which found that decaffeinated coffee, which was not used in this study, also has beneficial effects.

"Whatever the mechanism, it is clear that postoperative coffee consumption is a cheap and safe way to activate bowel motility after elective colonic surgery."

S. A. Müller, N. N. Rahbari, F. Schneider, R. Warschkow, T. Simon, M. von Frankenberg, U. Bork, J. Weitz, B. M. Schmied, M. W. Büchler. Randomized clinical trial on the effect of coffee on postoperative ileus following elective colectomy. *British Journal of Surgery*, 2012; 99 (11): 1530 DOI: 10.1002/bjs.8885

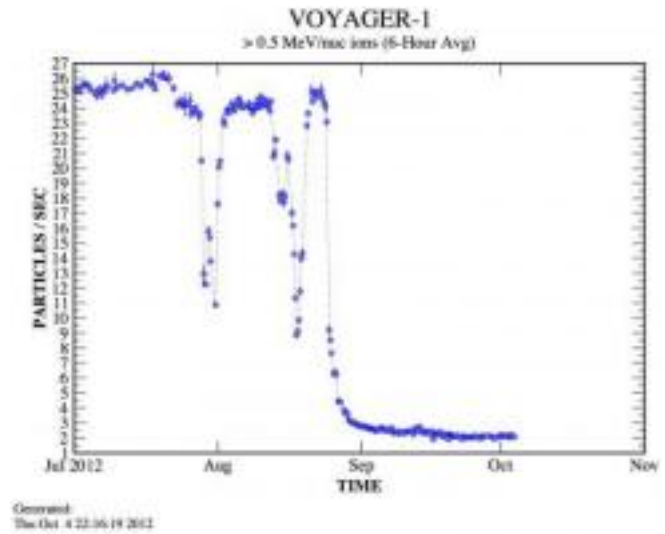
<http://www.universetoday.com/97763/voyage-1-may-have-left-the-solar-system/>

## **Voyager 1 may have left the solar system**

***While there's no official word from NASA on this, the buzz around the blogosphere is that Voyager 1 has left the Solar System.***

The evidence comes from this graph, above, which shows the number of particles, mainly protons, from the Sun hitting Voyager 1 across time. A huge drop at the end of August hints that Voyager 1 may now be in interstellar space. The last we heard from the Voyager team was early August, and they indicated that on July 28, the level of lower-energy particles originating from inside our Solar System dropped by half. However, in three days, the levels had recovered to near their previous levels. But then the bottom dropped out at the end of August.

The Voyager team has said they have been seeing two of three key signs of changes expected to occur at the boundary of interstellar space. In addition to the drop in particles from the Sun, they've also seen a jump in the level of high-energy cosmic rays originating from outside our Solar System.



*Number of particles from the Sun hitting Voyager 1. Credit: NASA*

The third key sign would be the direction of the magnetic field. No word on that yet, but scientists are eagerly analyzing the data to see whether that has, indeed, changed direction. Scientists expect that all three of these signs will have changed when Voyager 1 has crossed into interstellar space.

"These are thrilling times for the Voyager team as we try to understand the quickening pace of changes as Voyager 1 approaches the edge of interstellar space," said Edward Stone, the Voyager project scientist for the entire mission, who was quoted in early August. "We are certainly in a new region at the edge of the solar system where things are changing rapidly. But we are not yet able to say that Voyager 1 has entered interstellar space." Stone added that the data are changing in ways that the team didn't expect, "but Voyager has always surprised us with new discoveries."

Voyager 1 launched on Sept. 5, 1977, is approximately 18 billion kilometers (11 billion miles) from the Sun. Voyager 2, which launched on Aug. 20, 1977, is close behind, at 15 billion km (9.3 billion miles) from the Sun.

<http://phys.org/news/2012-10-predominance-right-handed-uniquely-human-trait.html>

## **A predominance to be right-handed is not a uniquely human trait, but one shared by great apes, study finds**

***Three separate studies support a theory that human right-handedness is a trait that was inherited from an ancestor common to both humans and great apes.***

Phys.org - Dr Gillian Forrester, a visiting fellow in psychology at the University of Sussex and a senior lecturer in psychology at the University of Westminster, analysed hand actions directed towards either objects or individuals in chimpanzees, gorillas and children, and found that all three species are right-handed for actions to objects, but not for actions directed to individuals.

The results of her three separate studies support a theory that human right-handedness, a feature of 90 per cent of the population, is a trait developed through tool use that was inherited from an ancestor common to both humans and great apes.

The most recent findings, published in *Behavioural Brain Research*, challenge a widely held view that right-handed dominance in humans was a species-unique trait linked to the emergence of language. Scientists have long been aware of the association between the left hemisphere specialization for language in the human brain and human right-handedness. For example, 95% of those who are right-handed typically have language function supported by the left hemisphere.

Dr Forrester says: "Humans have been tool users for 2.5 million years, while the current view is that language only emerged one hundred thousand years ago. Our findings provide the first non-invasive results from naturalistic behaviour, suggesting that language emerged as a consequence of left hemisphere brain regions that were already evolved to process regular sequences of actions. The structure found in language may have developed from pre-existing brain processes adapted from experience with tool-use."

Her studies, carried out over the past five years, involved video sampling and coding of activities in individual groups of gorillas, chimpanzees and four-year-old children within their everyday environments. The simple and non-invasive methodology revealed aspects of brain function and organization without the need for a laboratory setting with expensive and invasive equipment or testing.

Each observed hand action was coded as being directed towards either an 'inanimate' object, such as sticks for apes and toys for children, or 'animate', such as touching others or self-grooming. Dr Forrester and her team found that in all groups there was a right-handed dominance only in actions towards inanimate objects. She points out: "Human right-handedness is not species-specific as traditionally thought, but rather is context-dependent – a pattern that has been previously masked by less sensitive experimental measures. Our findings support the idea that both human and ape brains have this left hemisphere specialisation directing the right side of the body for ordered sequences of behaviours, but that humans have been able to extend upon this neural architecture to develop language."

The study may help to further the understanding of language development in children. Dr Forrester is working with Professor Alina Rodriguez from Mid Sweden University in applying the same methodology to study a large cohort of Swedish children from birth through to five years of age.

"We want to see if the children who are more bilateral with their object manipulation skills have a different pattern of language development than children who demonstrate more typically lateralized hand behaviours," says Dr Forrester. "If that turns out to be the pattern, then it could be a great diagnostic measure for clinicians seeking to identify children at risk of delayed or disrupted language development."

*More information: 'Human Handedness: An inherited evolutionary trait', by Gillian S Forrester, Caterina Quaresmini, David A Leavens, Denis Mareschal, Michael S C Thomas, is published in Behavioural Brain Research, October 2012. Provided by University of Sussex*

<http://www.sciencedaily.com/releases/2012/10/121009111942.htm>

### **Flirting Can Pay Off for Women, Study Finds**

#### ***Female flirtation signals attractive qualities such as confidence, which is considered essential to successful negotiators***

ScienceDaily - When Madeleine Albright became the first female U.S. Secretary of State, she led high-level negotiations between mostly male foreign government leaders. In 2009, comedian Bill Maher asked Albright if she ever flirted on the job and she replied, "I did, I did." Flirtatiousness, female friendliness, or the more diplomatic description "feminine charm" is an effective way for women to gain negotiating mileage, according to a new study by Haas School of Business Professor Laura Kray.

"Women are uniquely confronted with a tradeoff in terms of being perceived as strong versus warm. Using feminine charm in negotiation is a technique that combines both," says Kray, who holds the Warren E. and Carol Spieker Chair in Leadership at the Haas School.

The study, "Feminine Charm: An Experimental Analysis of its Costs and Benefits in Negotiations," was published in October in the journal *Personality and Social Psychology Bulletin* and co-authored by Haas PhD alumna Connson C. Locke of the London School of Economics and Haas PhD candidate Alex B. Van Zant. Flirtation that generates positive results, says Kray, is not overt sexual advances but authentic, engaging behavior without serious intent. In fact, the study found female flirtation signals attractive qualities such as confidence, which is considered essential to successful negotiators.

To determine whether women who flirt are more effective in negotiating than men who flirt, the researchers asked 100 participants to evaluate to what extent they use social charm in negotiation on a one-to-seven scale. Earlier that week, the participants evaluated their partners' negotiating effectiveness. Women who said they used more social charm were rated more effective by their partners. However, men who said they used more social charm were not regarded as more effective.

In the second experiment, the researchers asked subjects to imagine they were selling a car worth \$1,200 and asked for how much would they sell the car. Next, the subjects read one of two scenarios about a potential buyer named Sue. The first group meets Sue, who shakes hands when she meets the seller, smiles, and says, "It's a pleasure to meet you,." and then "What's your best price?" in a serious tone. The second group reads an alternate scenario in which Sue greets the seller by smiling warmly, looking the seller up and down, touching the seller's arm, and saying, "You're even more charming than over email," followed by a playful wink and asking, "What's your best price?"

The result? Male sellers were willing to give the "playful Sue" more than \$100 off the selling price whereas they weren't as willing to negotiate with the "serious Sue." Playful Sue's behavior did not affect female car sellers.



Kray says many of her students who are senior women executives admit they love to flirt and describe themselves as "big flirts." Kray maintains flirting is not unprofessional if it remains playful and friendly. "The key is to flirt with your own natural personality in mind. Be authentic. Have fun. That will translate into confidence, which is a strong predictor of negotiation performance."

*L. J. Kray, C. C. Locke, A. B. Van Zant. Feminine Charm: An Experimental Analysis of its Costs and Benefits in Negotiations. Personality and Social Psychology Bulletin, 2012; 38 (10): 1343 DOI: 10.1177/0146167212453074*

<http://www.bbc.co.uk/news/world-asia-19887497>

### **Karachi: Brain-eating amoeba kills 10**

***A rare brain-eating amoeba is responsible for at least 10 deaths in the Pakistani city of Karachi in recent months, health officials believe.***

The source of the parasite is not yet known, but it is thought victims may have been exposed to it when using water to rinse their nasal passages. The amoeba, *Naegleria Fowleri*, lives in warm water and kills its victims by destroying brain tissue.

Officials are now increasing the amount of chlorine in the public water supply. The deaths are in various locations across Karachi, Pakistan's biggest city. Dr Shakeel Mallick, who works for the provincial health department, said nine of those killed were men, while one victim was a child of four.

Officials suspect other cases may have gone undetected. Dr Mallick said hospitals were now being "vigilant". The ministry was "very concerned" about the amoeba, he said.

#### **Cities on alert**

Although the amoeba is usually picked up in contaminated pools or lakes, only one of those killed had been swimming. Officials are therefore concentrating their attention on the possibility that people picked it up when cleaning out their nostrils - a practice which is common in South Asia, BBC regional analyst Jill McGivering says. The amoeba travels to the brain through the nasal passages. Those infected have symptoms including fever, nausea and vomiting, as well as a stiff neck and headaches. Most die within a week.

The World Health Authority's Musa Khan says other cities across Pakistan have been put on alert. An awareness campaign has also been launched among health workers and the public. "People should avoid getting water too deep into their nostrils," Mr Khan said. "Those with symptoms should seek help immediately." People are being advised to use boiled or chlorinated water to rinse their noses, and to clean out domestic water tanks where amoeba may flourish. The amoeba cannot be passed from person to person.

<http://www.sciencedaily.com/releases/2012/10/121009121805.htm>

### **Caffeine May Block Inflammation Linked to Mild Cognitive Impairment**

***Studies have linked caffeine consumption to a reduced risk of Alzheimer's disease***

ScienceDaily - Recent studies have linked caffeine consumption to a reduced risk of Alzheimer's disease, and a new University of Illinois study may be able to explain how this happens.

"We have discovered a novel signal that activates the brain-based inflammation associated with neurodegenerative diseases, and caffeine appears to block its activity. This discovery may eventually lead to drugs that could reverse or inhibit mild cognitive impairment," said Gregory Freund, a professor in the U of I's College of Medicine and a member of the U of I's Division of Nutritional Sciences.

Freund's team examined the effects of caffeine on memory formation in two groups of mice -- one group given caffeine, the other receiving none. The two groups were then exposed to hypoxia, simulating what happens in the brain during an interruption of breathing or blood flow, and then allowed to recover.

The caffeine-treated mice recovered their ability to form a new memory 33 percent faster than the non-caffeine-treated mice. In fact, caffeine had the same anti-inflammatory effect as blocking IL-1 signaling. IL-1 is a critical player in the inflammation associated with many neurodegenerative diseases, he said.

"It's not surprising that the insult to the brain that the mice experienced would cause learning memory to be impaired. But how does that occur?" he wondered.

The scientists noted that the hypoxic episode triggered the release of adenosine by brain cells.

"Your cells are little powerhouses, and they run on a fuel called ATP that's made up of molecules of adenosine. When there's damage to a cell, adenosine is released," he said.

Just as gasoline leaking out of a tank poses a danger to everything around it, adenosine leaking out of a cell poses a danger to its environment, he noted. The extracellular adenosine activates the enzyme caspase-1, which triggers production of the cytokine IL-1 $\beta$ , a critical player in inflammation, he said.

"But caffeine blocks all the activity of adenosine and inhibits caspase-1 and the inflammation that comes with it, limiting damage to the brain and protecting it from further injury," he added.

Caffeine's ability to block adenosine receptors has been linked to cognitive improvement in certain neurodegenerative diseases and as a protectant against Alzheimer's disease, he said.

"We feel that our foot is in the door now, and this research may lead to a way to reverse early cognitive impairment in the brain. We already have drugs that target certain adenosine receptors. Our work now is to determine which receptor is the most important and use a specific antagonist to that receptor," he said.

*The study appears in the Journal of Neuroscience. Co-authors are Gabriel Chiu, Diptaman Chatterjee, Patrick Darmody, John Walsh, Daryl Meling, and Rodney Johnson, all of the U of I. Funding for the study was provided by the National Institutes of Health. The above story is reprinted from materials provided by University of Illinois College of Agricultural, Consumer and Environmental Sciences. The original article was written by Phyllis Picklesimer.*

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

*G. S. Chiu, D. Chatterjee, P. T. Darmody, J. P. Walsh, D. D. Meling, R. W. Johnson, G. G. Freund. Hypoxia/Reoxygenation Impairs Memory Formation via Adenosine-Dependent Activation of Caspase 1. Journal of Neuroscience, 2012; 32 (40): 13945 DOI: 10.1523/JNEUROSCI.0704-12.2012*

<http://phys.org/news/2012-10-intestinal-bacteria-phages-weapons.html>

## Researchers find intestinal bacteria create phages for use as weapons

**Researchers at the University of Texas have found that a certain type of bacteria that lives in the mammalian gut creates a virus to kill off competitors.**

Phys.org - In their paper published in the Proceedings of the National Academy of Sciences, the team says their discovery came about purely by accident.

Phages, short for bacteriophages, are viruses created by bacteria that target and destroy other bacteria. They are of great interest to scientists because if they could be controlled, they could provide perhaps the ultimate anti-bacterial agent. Unfortunately, despite a lot of research since their discovery nearly century ago, very little is known about how they function, particularly, in the human gut. In this new research, the team discovered something that had never been seen before, a strain of bacteria that create a phage for the express purpose of killing off other bacteria that are competing for the same resources.



**Enterococcus faecalis.** Credit: United States Department of Agriculture

The gut, as most know, is home to trillions of bacteria; some provide benefits to the host, such as helping to digest certain foods, while others are not so good, causing digestive problems. One in particular, the plentiful *Enterococcus faecalis*, appears to live without creating problems in the gut, but causes a lot of problems when it gets in the bloodstream, accounting for many hospital acquired infections. In looking at a particular strain of *E. faecalis* known as V583, the researchers found that when it was introduced alone into a germ-free mouse gut, it began churning out phages, which seemed counter-productive as it takes a lot of energy to do so.

In looking closer, the team discovered that V583 did have a purpose, and that was to kill any other strains of *E. faecalis* that might show up, gobbling resources. Thus, the gut bacteria were creating phages to use as a weapon against closely related bacteria that might consume shared resources. The researchers call it a form of bacterial warfare, but also suggest that the discovery might offer some insight into how bacteria in general might be used to create phages in ways that can be controlled, allowing for the development of targeted anti-bacterial agents that kill offending bacteria without harming those that are beneficial.

*More information: A composite bacteriophage alters colonization by an intestinal commensal bacterium, PNAS, Published online before print October 8, 2012, doi: 10.1073/pnas.1206136109*

### Abstract

*The mammalian intestine is home to a dense community of bacteria and its associated bacteriophage (phage). Virtually nothing is known about how phages impact the establishment and maintenance of resident bacterial communities in the intestine. Here, we examine the phages harbored by *Enterococcus faecalis*, a commensal of the human intestine. We show that *E. faecalis* strain V583 produces a composite phage ( $\phi$ V1/7) derived from two distinct chromosomally encoded prophage elements. One prophage, prophage 1 ( $\phi$ V1), encodes the structural genes necessary for phage particle production. Another prophage, prophage 7 ( $\phi$ V7), is required for phage infection of susceptible host bacteria. Production of  $\phi$ V1/7 is controlled, in part, by nutrient availability, because  $\phi$ V1/7 particle numbers are elevated by free amino acids in culture and during growth in the mouse intestine.  $\phi$ V1/7 confers an advantage to *E. faecalis* V583 during competition with other *E. faecalis* strains in vitro and in vivo. Thus, we propose that *E. faecalis* V583 uses phage particles to establish and maintain dominance of its intestinal niche in the presence of closely related competing strains. Our findings indicate that bacteriophages can impact the dynamics of bacterial colonization in the mammalian intestinal ecosystem.*

<http://phys.org/news/2012-10-hormones-unravel-ancient-urges-social.html>

## **Swimming with hormones: Researchers unravel ancient urges that drive social decisions of fish**

### ***Oxytocin - the hormone responsible for making humans fall in love - has a similar effect on fish***

Researchers have discovered that a form of oxytocin—the hormone responsible for making humans fall in love - has a similar effect on fish, suggesting it is a key regulator of social behaviour that has evolved and endured since ancient times.

The findings, published in the latest edition of the journal *Animal Behaviour*, help answer an important evolutionary question: why do some species develop complex social behaviours while others spend much of their lives alone?

"We know how this hormone affects humans," explains Adam Reddon, lead researcher and a graduate student in the Department of Psychology, Neuroscience & Behaviour at McMaster University. "It is related to love, monogamy, even risky behaviour, but much less is known about its effects on fish."

Specifically, researchers examined the cichlid fish *Neolamprologus pulcher*, a highly social species found in Lake Tanganyika in Africa.

These cichlids are unusual because they form permanent hierarchical social groups made up of a dominant breeding pair and many helpers that look after the young and defend their territory.

For the experiments, researchers injected the cichlids with either isotocin—a "fish version" of oxytocin—or a control saline solution.

When placed in a simulated territorial competition with a single perceived rival, the isotocin-treated fish were more aggressive towards large opponents, regardless of their own size.

When placed in a larger group situation, isotocin-treated fish became more submissive when faced with aggression from more dominant group members. Such signals are important in this species because they placate the dominant members of the group, say researchers.

"The hormone increases responsiveness to social information and may act as an important social glue," says Reddon. "It ensures the fish handle conflict well and remain a cohesive group because they will have shorter, less costly fights."

"We already knew that this class of neuropeptides are ancient and are found in nearly all vertebrate groups," says Sigal Balshine, a professor in the Department of Psychology, Neuroscience & Behaviour. "What is especially exciting about these findings, is that they bolster the idea that function of these hormones, as modulators of social behaviour, has also been conserved."

<http://bit.ly/Q9XaRs>

### **DNA's half-life identified using fossil bones**

#### ***We are used to radioactive substances having a half-life, but DNA?***

**00:00 10 October 2012 by Colin Barras**

Now a study of bones from extinct birds suggests the double helix too has a measurable half-life – and that we have underestimated its ability to survive in the fossil record.

"DNA degrades at a certain rate, and it therefore makes sense to talk about a half-life," says Morten Allentoft at Copenhagen University, Denmark, who together with Mike Bunce at Murdoch University in Perth, Australia, and colleagues, extracted DNA from the leg bones of 158 extinct flightless birds called moas.

Part of the reason a DNA half-life has been so elusive is that it is hard to find a large enough cache of samples that have been exposed to similar conditions. The moa bones were all between 600 and 8000 years old, and came from a 5-kilometre-wide area of New Zealand's South Island, key factors for helping identify a regular pattern of decay.

With an estimated burial temperature of 13 °C, the DNA's half-life was 521 years – almost 400 times longer than expected from lab experiments at similar temperatures, says Allentoft.

#### **Half-life of 158,000 years**

The oldest DNA to date belongs to insects and plants and was found in 450,000 to 800,000-year-old ice. Under subzero conditions, Allentoft and Bunce estimate that DNA's half-life can be up to 158,000 years, meaning the last remnants would disappear around the 6.8-million-year mark. Allentoft does say that is an optimistic assessment, and doesn't imply that samples of DNA large enough to measure could be extracted from such old bones.

Eva-Maria Geigl at the Jacques Monod institute in Paris, France, is still to be convinced by the half-life claims, which she says rest on statistically weak evidence. She points out, for example, that the correlation relies heavily on the moa bones older than 6000 years – when fewer than 10 of the 158 bones are this ancient.

"Old fossils are rare and hence there will be less data in this part of the analysis," says Bunce. "There is nothing we can do about it other than present what we have at hand – and clearly, the signal is present. The correlation is highly significant."

If DNA decays in a predictable way, can we calculate the chances of finding it at key sites? Ever since the Indonesian island of Flores yielded remains of the "hobbit", *Homo floresiensis* in 2004, speculation has been rife that some specimens might contain DNA that would help pin down its position in the human family tree. This notion has been spurred by evidence that the hobbits may have survived until as recently as 18,000 years ago.

Unfortunately, Bunce thinks the new calculations will be difficult to apply to specific sites. "A host of other factors come into play," he says, including the season the organism died. In fact, although the moa bones in the analysis had been buried in a similar environment, the age of the specimens could account for only about 40 per cent of the variation in DNA preservation – in other words, the half-life signal is noisy.

Alan Cooper, director of the Australian Centre for Ancient DNA at the University of Adelaide, South Australia, agrees. "The rotting process after death is very seasonal and context dependent, and has a major impact on DNA survival."

Cooper has attempted to extract DNA from *Homo floresiensis* remains, but is beginning to think that none will ever be found. He says that recent unpublished dating estimates indicate that "the hobbit material may be considerably older than currently suggested".

*Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2012.1745*

[http://www.eurekalert.org/pub\\_releases/2012-10/aaon-ssb100212.php](http://www.eurekalert.org/pub_releases/2012-10/aaon-ssb100212.php)

### **Study: Stroke becoming more common in young people**

#### ***New research reveals that stroke may be affecting people at a younger age.***

MINNEAPOLIS - The study is published in the October 10, 2012, online issue of *Neurology*®, the medical journal of the American Academy of Neurology.

"The reasons for this trend could be a rise in risk factors such as diabetes, obesity and high cholesterol," said study author Brett Kissela, MD, MS, with the University of Cincinnati College of Medicine in Ohio and a Fellow of the American Academy of Neurology. "Other factors, such as improved diagnosis through the increased use of MRI imaging may also be contributing. Regardless, the rising trend found in our study is of great concern for public health because strokes in younger people translate to greater lifetime disability."

For the study, researchers looked at occurrences of strokes in people between the ages 20 and 54 in the Greater Cincinnati/Northern Kentucky area during three separate, one year-long periods between July of 1993 and June of 1994, and the calendar years of 1999 and 2005. Only first ever strokes were included in the analysis.

The study found that the average age of people who experienced stroke fell from 71 years in 1993 and 1994 to 69 years in 2005. In addition, the study found that strokes among people under 55 made up a greater percentage of all strokes over time, growing from about 13 percent in 1993-94 to 19 percent in 2005. The stroke rate in young people increased in both African-Americans and Caucasians, from 83 strokes per 100,000 people in 1993-94 in African-Americans to 128 per 100,000 in 2005 and in Caucasians from 26 strokes per 100,000 people in 1993-94 to 48 per 100,000 in 2005.

"The good news is that some of the possible contributing factors to these strokes can be modified with lifestyle changes, such as diet and exercise," said Kissela. "However, given the increase in stroke among those younger than 55, younger adults should see a doctor regularly to monitor their overall health and risk for stroke and heart disease." *The study was supported by the National Institutes of Health.*

[http://www.eurekalert.org/pub\\_releases/2012-10/tmsh-msr101012.php](http://www.eurekalert.org/pub_releases/2012-10/tmsh-msr101012.php)

### **Mount Sinai researchers discover gene signature that predicts prostate cancer survival**

#### ***This is the first study to demonstrate how prognostic markers may be useful in a clinical setting.***

Researchers from Mount Sinai School of Medicine have identified a six-gene signature that can be used in a test to predict survival in men with aggressive prostate cancer, according to new research published in the October issue of *The Lancet Oncology*.

Using blood from 202 men with treatment-resistant prostate cancer, researchers found six genes characteristic of treatment-resistant prostate cancer. Men with the six-gene signature were high-risk, with a survival time of 7.8 months, and men without it were low-risk, with a survival time of approximately 34.9 months. A replication study of 140 additional patients validated these findings. William K. Oh, MD, Chief of the Division of Hematology and Medical Oncology of The Tisch Cancer Institute at The Mount Sinai Medical Center, led the research team.



"There is an urgent need for predictive models that help assess how aggressive the disease is in prostate cancer patients, as survival can vary greatly," said Dr. Oh. "Our six-gene model, delivered in a simple blood test, will allow clinicians to better determine the course of action for their patients, determine clinical trial eligibility, and lead to more targeted studies in late-stage disease."

Until now, disease prognosis in advanced prostate cancer could only be determined through clinical predictors or, occasionally, tumor biopsies with only moderately predictive results. This study shows the efficacy of the six-gene model blood test in determining length of survival.

"The genes noted in the model suggest possible changes in the immune system related to late-stage disease that warrant further study as a target for immune-based therapies," said Dr. Oh.

Dr. Oh's team is conducting additional studies exploring the feasibility of the six-gene signature in other types of prostate cancer, the stability of the signature during the course of a patient's illness, and the predictive ability of this signature in patients with prostate cancer treated with immune-based therapies.

*This work was done in collaboration with colleagues at Dana-Farber Cancer Institute in Boston and Memorial Sloan-Kettering Cancer Center in New York City.*

<http://www.sciencedaily.com/releases/2012/10/121010084158.htm>

### **Astrocytes as a Novel Target in Alzheimer's Disease**

#### ***Have identified astrocytes as a novel target for the development of future treatment strategies***

ScienceDaily - Alzheimer's disease is a severe neurodegenerative disease that affects 45% of people over 85 years of age. The research teams of Prof. Jin-Moo Lee at Washington University in Saint Louis, USA, and Prof. Milos Pekny at Sahlgrenska Academy in Gothenburg, Sweden, The results have just been published in the FASEB Journal.

Astrocytes are known as cells that control many functions of the healthy as well as diseased brain, including the control of regenerative responses. In patients suffering from Alzheimer's disease, astrocytes in the vicinity of amyloid plaques and degenerating neurons become hyperactive.

Until now, many researchers considered this astrocyte hyperactivity in the brains of Alzheimer's disease patients as negative and contributing to the progression of this devastating disease.

The current study generated groundbreaking data with important implications. The US and Swedish research teams used a mouse model of Alzheimer's disease in which they genetically reduced astrocyte hyperactivity. They found that such mice developed more amyloid deposits and showed more pronounced signs of neurodegeneration than mice with normal response of astrocytes.

This suggests that astrocyte response to the disease process slows down the disease progression.

- We are truly excited about these findings. Now we need to understand the mechanism underlying the beneficial role of hyperactive astrocytes in Alzheimer's disease progression. Understanding this process on a molecular level should help us to design strategies for optimization of the astrocyte response, says Prof. Milos Pekny.

- We see that astrocyte hyperactivity in Alzheimer's disease brains is tightly connected to activation of microglia, the brain's own immune cells. This implies that the two cell types communicate to mediate a coordinated response to disease states, says Prof. Jin-Moo Lee.

This international collaborative team of neuroscientists is pursuing further studies to understand molecular mechanisms by which astrocytes prevent the deposition of amyloid plaques in Alzheimer's disease.

*The above story is reprinted from materials provided by Expertsvar, via AlphaGalileo. Note: Materials may be edited for content and length. For further information, please contact the source cited above.*

*Journal Reference: A. W. Kraft, X. Hu, H. Yoon, P. Yan, Q. Xiao, Y. Wang, S. C. Gil, J. Brown, U. Wilhelmsson, J. L. Restivo, J. R. Cirrito, D. M. Holtzman, J. Kim, M. Pekny, J.-M. Lee. Attenuating astrocyte activation accelerates plaque pathogenesis in APP/PS1 mice. The FASEB Journal, 2012; DOI: 10.1096/fj.12-208660*

[http://www.eurekalert.org/pub\\_releases/2012-10/nymc-dbp101112.php](http://www.eurekalert.org/pub_releases/2012-10/nymc-dbp101112.php)

### **Developmental biologist proposes new theory of early animal evolution**

#### ***Alternative model challenges a basic assumption of evolution***

VALHALLA - A New York Medical College developmental biologist whose life's work has supported the theory of evolution has developed a concept that dramatically alters one of its basic assumptions—that survival is based on a change's functional advantage if it is to persist. Stuart A. Newman, Ph.D., professor of cell biology and anatomy, offers an alternative model in proposing that the origination of the structural motifs of animal form were actually predictable and relatively sudden, with abrupt morphological transformations favored during the early period of animal evolution.

Newman's long view of evolution is fully explained in his perspective article, "Physico-Genetic Determinants in the Evolution of Development," which is to be published in the October 12 issue of the journal Science, in a

special section called Forces in Development. The paper has been selected for early online publication and a podcast interview with the scientist\*.

Evolution is commonly thought to take place opportunistically, by small steps, with each change persisting, or not, based on its functional advantage. Newman's alternative model is based on recent inferences about the genetics of the single-celled ancestors of the animals and, more surprisingly, the physics of "middle-scale" materials.

Animal bodies and the embryos that generate them exhibit an assortment of recurrent "morphological motifs" which, on the evidence of the fossil record, first appeared more than a half billion years ago. During embryonic development of present-day animals, cells arrange themselves into tissues having non-mixing layers and interior cavities. Embryos contain patterned arrangements of cell types with which they may form segments, exoskeletons and blood vessels. Developing bodies go on to fold, elongate, and extend appendages, and in some species, generate endoskeletons with repeating elements (e.g., the human hand).

These developmental motifs are strikingly similar to the forms assumed by nonliving condensed, chemically active, viscoelastic materials when they are organized by relevant physical forces and effects, although the mechanisms that generate the motifs in living embryos are typically much more complex. Newman proposes that the ancestors of the present-day animals acquired these forms when ancient single-celled organisms came to reside in multicellular clusters and physical processes relevant to matter at this new (for cellular life) spatial scale were immediately mobilized.

The unicellular progenitors are believed to have contained genes of the "developmental-genetic toolkit" with which all present-day animals orchestrate embryonic development, though they used the genes for single-cell functions. It was precisely these genes whose products enabled the ancestral clusters to harness the middle-scale physical effects that produced the characteristic motifs. And since not every ancestral cluster contained the same selection of toolkit genes, different body forms arose in parallel, giving rise to the modern morphologically distinct animal phyla.

Natural selection, acting over the hundreds of millions of years since the occurrence of these origination events led, according to Newman's hypothesis, to more complex developmental processes which have made embryogenesis much less dependent on potentially inconsistent physical determinants, although the "physical" motifs were retained. As Newman describes in his article, this new perspective provides natural interpretations for puzzling aspects of the early evolution of the animals, including the "explosive" rise of complex body forms between 540 and 640 million years ago and the failure to add new motifs since that time. The model also helps us to understand the conserved use of the same set of genes to orchestrate development in all of the morphologically diverse phyla, and the "embryonic hourglass" of comparative developmental biology: the observation that the species of a phylum can have drastically different trajectories of early embryogenesis (e.g., frogs and mice), but still wind up with very similar "body plans."

*This link will take you to the podcast segment featuring the interview with Dr. Newman:*

*<http://www.sciencemag.org/content/338/6104/217/suppl/DC1>*

[http://www.eurekalert.org/pub\\_releases/2012-10/ynu-nsl100912.php](http://www.eurekalert.org/pub_releases/2012-10/ynu-nsl100912.php)

### **Nearby super-Earth likely a diamond planet**

***New research led by Yale University scientists suggests that a rocky planet twice Earth's size orbiting a nearby star is a diamond planet.***

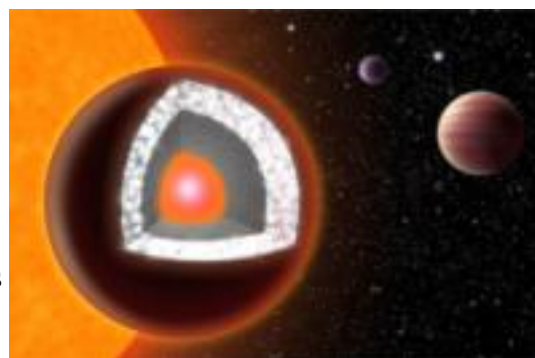
New Haven, Conn. - "This is our first glimpse of a rocky world with a fundamentally different chemistry from Earth," said lead researcher Nikku Madhusudhan, a Yale postdoctoral researcher in physics and astronomy. "The surface of this planet is likely covered in graphite and diamond rather than water and granite."

The paper reporting the findings has been accepted for publication in the journal *Astrophysical Journal Letters*.

The planet - called 55 Cancri e - has a radius twice Earth's, and a mass eight times greater, making it a "super-Earth." It is one of five planets orbiting a sun-like star, 55 Cancri, that is located 40 light years from Earth yet visible to the naked eye in the constellation of Cancer.

The planet orbits at hyper speed - its year lasts just 18 hours, in contrast to Earth's 365 days. It is also blazingly hot, with a temperature of about 3,900 degrees Fahrenheit, researchers said, a far cry from a habitable world.

The planet was first observed transiting its star last year, allowing astronomers to measure its radius for the first time. This new information, combined with the most recent estimate of its mass, allowed Madhusudhan and



colleagues to infer its chemical composition using models of its interior and computing all possible combinations of elements and compounds that would yield those specific characteristics.

Astronomers had previously reported that the host star has more carbon than oxygen, and Madhusudhan and colleagues confirmed that substantial amounts of carbon and silicon carbide, and a negligible amount of water ice, were available during the planet's formation.

Astronomers also thought 55 Cancri e contained a substantial amount of super-heated water, based on the assumption that its chemical makeup was similar to Earth's, Madhusudhan said. But the new research suggests the planet has no water at all, and appears to be composed primarily of carbon (as graphite and diamond), iron, silicon carbide, and, possibly, some silicates. The study estimates that at least a third of the planet's mass — the equivalent of about three Earth masses - could be diamond.

"By contrast, Earth's interior is rich in oxygen, but extremely poor in carbon - less than a part in thousand by mass," says co-author and Yale geophysicist Kanani Lee.

The identification of a carbon-rich super-Earth means that distant rocky planets can no longer be assumed to have chemical constituents, interiors, atmospheres, or biologies similar to those of Earth, Madhusudhan said. The discovery also opens new avenues for the study of geochemistry and geophysical processes in Earth-sized alien planets. A carbon-rich composition could influence the planet's thermal evolution and plate tectonics, for example, with implications for volcanism, seismic activity, and mountain formation.

"Stars are simple — given a star's mass and age, you know its basic structure and history," said David Spergel, professor of astronomy and chair of astrophysical sciences at Princeton University, who is not a co-author of the study. "Planets are much more complex. This 'diamond-rich super-Earth' is likely just one example of the rich sets of discoveries that await us as we begin to explore planets around nearby stars."

In 2011, Madhusudhan led the first discovery of a carbon-rich atmosphere in a distant gas giant planet, opening the possibility of long-theorized carbon-rich rocky planets (or "diamond planets"). The new research represents the first time that astronomers have identified a likely diamond planet around a sun-like star and specified its chemical make-up. Follow-up observations of the planet's atmosphere and additional estimates of the stellar composition would strengthen the findings about the planet's chemical composition.

*The authors of the paper are Madhusudhan, Lee, and Olivier Mousis, a planetary scientist at the Institut de Recherche en Astrophysique et Planetologie in Toulouse, France.*

*The paper is titled "A Possible Carbon-rich Interior in Super-Earth 55 Cancri e."*

*The research was supported by the Yale Center for Astronomy and Astrophysics (YCAA) in the Yale Department of Physics through Madhusudhan's YCAA postdoctoral prize fellowship.*

[http://www.eurekalert.org/pub\\_releases/2012-10/tcob-stu100912.php](http://www.eurekalert.org/pub_releases/2012-10/tcob-stu100912.php)

### **Soft-shelled turtles urinate through mouth**

#### ***Discovery that turtles effectively urinate through the mouth***

Chinese soft-shelled turtles are exquisitely adapted to their aquatic lifestyle, sitting contentedly on the bottom of brackish muddy swamps or snorkelling at the surface to breathe. According to Y. K. Ip from the National University of Singapore, they even immerse their heads in puddles when their swampy homes dry up: which intrigued Ip and his colleagues. Why do these air-breathing turtles submerge their heads when they mainly depend on their lungs to breathe and are unlikely to breathe in water? Given that some fish excrete waste nitrogen as urea – in addition to ammonia – and expel the urea through their gills, the team wondered whether the turtles were plunging their heads into water to excrete waste urea through their mouths, where they have strange gill-like projections. Ip and his colleagues publish their discovery that turtles effectively urinate through the mouth in *The Journal of Experimental Biology* at <http://jeb.biologists.org>.

Purchasing turtles from the local China Town wet market and immersing them in water for 6 days, the team measured the amount of urea that passed into the turtles' urine and found that only 6% of the total urea that the animals produced was excreted through the kidneys. Removing the turtles from the water and providing them with a puddle to dip their heads into, the team noticed that the turtles submerged their heads occasionally and could remain underwater for periods lasting up to 100 minutes. They also calculated the excretion rate of urea through the mouth by measuring the amount of urea that accumulated in the water and found that it was as much as 50 times higher than the excretion rate through the cloaca. And when the team injected urea into the turtles and measured their blood- and saliva-urea levels, they realised that the saliva-urea levels were 250 times greater than in the blood. The turtles were dipping their heads into water to excrete urea through their mouths. Knowing this, the team reasoned that the animals must produce a specialised class of protein transporters in their mouths to expel the waste and, as these transporters can be deactivated by phloretin, the team decided to test the effect of phloretin on the turtle's ability to excrete urea. When the turtles were supplied with phloretin in



their puddle of water, they were unable to excrete urea from their mouths when they submerged their head. And when the team analysed the turtles' cDNA, they found that the animals carried a gene that was very similar to urea transporters found in other animals. Finally, they checked to see if the turtles express this gene in their mouths and found evidence of the mRNA that is necessary to produce the essential urea transporter, allowing the reptiles to excrete urea waste through the mouth.

So, why do Chinese soft-shelled turtles go to such great lengths to excrete urea through their mouths when most other creatures do it through their kidneys? Ip and his colleagues suspect that it has something to do with their salty environment. Explaining that animals that excrete urea have to drink a lot, they point out that this is a problem when the only water available is salty – especially for reptiles that cannot excrete the salts. The team says, 'Since the buccopharyngeal [mouth and throat] urea excretion route involves only rinsing the mouth with ambient water, the problems associated with drinking brackish water... can be avoided'.

REFERENCE: Ip, Y. K., Loong, A. M., Lee, S. M. L., Ong, J. L. Y., Wong, W.P. and Chew, S. F. (2012). *The Chinese soft-shelled turtle, Pelodiscus sinensis, excretes urea mainly through the mouth instead of the kidney.* *J. Exp. Biol.* 215, 3723-3733. <http://jeb.biologists.org/content/215/21/3723.abstract>

<http://bit.ly/Rt3t7h>

### **Black glass holds first Mars soil sample on Earth**

***Veins of black glass in a meteorite that recently crashed in Morocco contain the first chemical traces of Martian soil brought to Earth.***

**19:00 11 October 2012 by Joanna Carver**

The find represents a rare chance to look closely at ancient surface conditions on Mars.

Robots sent to Mars, such as NASA's Curiosity rover, only have limited capabilities to analyse the soil samples that they take.

Until the launch of a sample-return mission, the most thorough way to study Martian rock is via meteorites that originated on Mars, says Hasnaa Chennaoui Aoudjehane of Hassan II University in Casablanca.

In July 2011 people saw a fireball streak across the sky and smash into the Moroccan desert. The 7-kilogram meteorite, dubbed Tissint, broke apart as it fell, and both scientists and private collectors quickly retrieved the fragments.



*The Martian sample we always wanted (Image: Natural History Museum, London)*

Initial analysis showed that the rock's chemical composition matches that of a type of Martian basalt. The meteorite was most likely thrown up from the planet about 700,000 years ago as the result of an asteroid impact.

#### **Pristine sample**

Tissint is only the fifth Martian meteorite collected promptly after falling to Earth. Most of the 90 or so known Mars rocks that have been found on Earth had been lying around for years.

By contrast, the Tissint fragments should provide an unadulterated look at Mars's geology. "It's so fresh, such pristine material," says Aoudjehane.

Her team found that the meteorite is laced with a large amount of bubbly black glass. It contains carbon and nitrogen isotopes that are characteristic of those found in Mars's atmosphere, something that has been seen in other Martian meteorites.

More surprisingly, the glass contains relatively high amounts of light rare-earth elements not found in the rest of the meteorite, including an unusual ratio of cerium isotopes that indicates some of the cerium got oxidised. Conditions that would oxidise cerium are most likely to exist close to Mars's surface.

The team says weakly acidic water may have leached rare-earth elements from Martian soil and deposited them in fractures in surface rocks.

Heat from the asteroid impact that ejected Tissint melted the material in the fractures, which crystallised as it cooled to form the black glass.

Further analysis of Tissint should reveal more details of such geochemical processes on Mars, rounding out our picture of the planet's past.

"The history of Mars is interesting for us because it's related to the history of the Earth, and it's important to know how Mars was in the past and how it evolved with the times," says Aoudjehane.

Journal reference: *Science*, DOI: 10.1126/science.1224514



<http://www.sciencedaily.com/releases/2012/10/121011123740.htm>

## **New Model Explains Role of Dopamine in Immune Regulation**

### ***Role of dopamine in modulating the immune system and new possibilities for treating diseases such as Parkinson's and Alzheimer's disease***

ScienceDaily - Dopamine is a neurotransmitter that is associated with emotions, movement, and the brain's pleasure and reward system. In the current issue of *Advances in Neuroimmune Biology*, investigators provide a broad overview of the direct and indirect role of dopamine in modulating the immune system and discuss how recent research has opened up new possibilities for treating diseases such as Parkinson's and Alzheimer's disease, schizophrenia, multiple sclerosis or even the autoimmune disorders.

Dopamine can be synthesized not only in neurons, but also in immune cells which orchestrate the body's response to infection or malignancy. "Data strongly supports the theory that an autocrine/paracrine regulatory loop exists in lymphocytes, where dopamine produced and released by the cells then acts on its own receptors, and can have an influence on its own function," explains lead investigator György M. Nagy, PhD, DSc, of the Department of Human Morphology, Cellular and Molecular Neuroendocrine Research Laboratory, Hungarian Academy of Sciences, and Semmelweis University, Budapest, Hungary.

Elements of dopamine signaling and metabolites can also serve as a communication interface between the central nervous system and immune system, and that communication can work in both directions. Lymphocytes that can pass the blood brain barrier can be "educated" by locally secreted neurotransmitters, including dopamine. Then they transmit brain-driven messages to other cells of the immune system via direct or indirect pathways.

Permanent dysfunctions of either the central (CNS) or the peripheral (immune) dopaminergic system are frequently associated with immune malfunctions. Current dopamine replacement or receptor blocking therapies are based on the supposed action of these drugs at the target site, and they often only relieve disease symptoms. The mainstream in design of new therapies is to find drugs having more-and-more specific action and minimal or no potential side effects, however, there is always a risk/benefits consideration in the drug development processes. These approaches may need to be revisited with the concepts of neuroimmunomodulatory influence, and focus on the cross-talk between the immune and nervous systems," Dr. Nagy says.

Various immune mechanisms may contribute to the pathogenesis of neurological disorders. The pharmacological design of targeted drug delivery systems could carry a desired compound right to the sites of cellular pathologies, Dr. Nagy observes. "Well designed clinical trials are needed for the critical evaluation of the new theories in human therapy, either by the use of available drugs with extended immunomodulatory functions, or newly designed compounds, or the combination of both. Evaluation of clinical efficacy and data on safety of patients should provide an answer to these questions," he concludes.

In a commentary accompanying the article, Istvan Berczi and Toshihiko Katafuchi, Editors-in-Chief of *Advances in Neuroimmune Biology*, ask why a central nervous system mediator such as dopamine would be produced locally, when dopamine made centrally could be deployed when necessary. "We suggest that the function of paracrine/autocrine (P/A) circuits is to maintain tissue viability in emergency situations, when no other regulators are available. Local P/A circuits are the key to healing and recovery," they say.

Dr. Berczi and Prof. Katafuchi note that the science of cryobiology, which deals with the medical application of hypothermia and freezing and tissue culture techniques, which grow cells and tissues in vitro from animals and man, owe their existence to P/A circuits to preserve tissue viability and reactivity beyond clinical death or under proper culture conditions. "Clearly, P/A circuits hold the possibility of resurrection after clinical death," they conclude.

*B.E. Tóth, M. Vecsernyés, T. Zelles, K. Kádár, G.M. Nagy. Role of Peripheral and Brain-Derived Dopamine (DA) in Immune Regulation. Advances in Neuroimmune Biology, 2012 DOI: 10.3233/NIB-2012-012044*

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<http://www.sciencedaily.com/releases/2012/10/121011123713.htm>

## **HIV and Breast Cancer May Share a Common Enemy: Nelfinavir**

### ***Nelfinavir slows the progress of HER2-positive tumor cells***

ScienceDaily - After screening more than 2,300 drugs for their ability to halt the growth of breast cancer cells, Johns Hopkins researchers have discovered that the anti-HIV drug nelfinavir slows the progress of HER2-positive tumor cells, even if they are resistant to other breast cancer drugs.

In a report on the discovery published online Oct. 5 in the *Journal of the National Cancer Institute*, the investigators also say nelfinavir worked at concentrations already approved by the U.S. Food and Drug

Administration. So-called HER2-positive breast cancers, which contain the protein HER2 and comprise 25 to 30 percent of cases, are more aggressive and less responsive to hormone treatments than HER2-negative cancers, a status that has fueled the search for better drug therapies and especially for ways to speed up the search by "repurposing" drugs already on the market.

"New drug development, beginning from scratch, is extremely expensive and time-consuming, taking an estimated \$1 billion and more than 10 years to get each new compound to market," says Jun O. Liu, Ph.D., professor of pharmacology and molecular sciences at the Johns Hopkins University School of Medicine. "An existing drug has already passed most of the costly safety and regulatory hurdles," says Liu, who has worked on "repurposing" them for almost a decade.

To speed up drug discovery, Liu and his colleagues created the Johns Hopkins Drug Library, which currently includes nearly 2,900 drugs, most of which are FDA-approved. All have passed through phase I clinical trials to test their dosing safety. In the new study, Liu and his team began with breast cancer cells from two patients, then tested all of the drugs in the library for their ability to stop cells from multiplying. Seventy of the best performers were selected for round two, in which they tested cells from seven patients, each genetically different, to see which drugs worked best.

Five of these drugs were selected for their ability to stop or slow the growth of HER2-positive cells. One of the five, nelfinavir, was selected for further testing because it appeared to work better than the others on HER2-positive cells and, says Liu, seemed to interfere with the protein HER2 itself. Nelfinavir was also already known to have a broad anti-cancer effect against melanoma, non-small-cell lung cancer and pancreatic cancer. To see if nelfinavir worked in mice implanted with HER2-positive or HER2-negative human breast cancer cells, the team gave mice a fake drug or a human-dose equivalent of nelfinavir, then measured tumor size for a month. Nelfinavir slowed the growth of HER2-positive tumors, but had no effect on HER2-negative tumors in mice. To see if nelfinavir could slow the growth of tumors that had become resistant to the commonly used breast cancer drugs trastuzumab and lapatinib, the researchers treated drug-resistant and non-drug-resistant cells growing in the lab with nelfinavir, trastuzumab or lapatinib. Only nelfinavir was able to prevent both drug-resistant and non-drug-resistant cells from growing.

When combating HIV, nelfinavir inhibits enzymes called proteases that break down proteins, and Liu's team wanted to know if nelfinavir uses that same mechanism to slow the growth of breast cancer cells. To test this, they gave nelfinavir to a wide variety of yeast cells, which are commonly used to study drug effects on genes because of the similarity between their cells and ours. Each type of yeast was genetically engineered to make less of a particular protein, making them more vulnerable to environmental stresses. They found that when yeast making less of the HSP90 protein were given the drug, the cells died, suggesting that nelfinavir interacts with HSP90, which is not a protease.

"This was interesting because we know that HSP90 also binds to HER2, and we now think that nelfinavir may be interfering with this interaction," says Liu. "This is a good starting point for clinical trials," he adds.

*Other authors of the paper include Joong Sup Shim, Rajini Rao and Inkyu Han from The Johns Hopkins University; Kristin Beebe and Len Neckers from the National Cancer Institute; and Rita Nahta from Emory University School of Medicine.*

*This work was supported by grants from the National Cancer Institute (R01CA122814), the National Center for Research Resources (UL1 RR025005), Flight Attendant Medical Research Institute, the Commonwealth Foundation and the National Institute of Allergy and Infectious Diseases (R01AI065983).*

*J. S. Shim, R. Rao, K. Beebe, L. Neckers, I. Han, R. Nahta, J. O. Liu. Selective Inhibition of HER2-Positive Breast Cancer Cells by the HIV Protease Inhibitor Nelfinavir. JNCI Journal of the National Cancer Institute, 2012; DOI: 10.1093/jnci/djs396*

<http://www.bbc.co.uk/news/education-19895531>

### **Pre-exam anxiety 'can boost grades'**

***Sitting exams and tests is often a nerve-racking experience, but being anxious beforehand may boost a candidate's grades, researchers say.***

A study published in the British Journal of Psychology finds being anxious only has a negative impact on results if a child's memory is poor. But if a young person has a good memory, a tendency to feel anxious is linked with getting better marks. The research assessed 96 children aged 12 to 14 in memory and anxiety tests. A questionnaire established how anxious the children usually felt, and the results were measured against their ability to perform computerised tests involving "complex" or working-memory skills.

"We found that for individuals with low working-memory capacity, increases in [a tendency towards] anxiety were related to decreases in cognitive test performance," the study says. "For those with high working-memory capacity, however, the pattern of results was reversed. An increase in [a tendency towards] anxiety was linearly associated with higher test scores. "These effects were not better accounted for by gender, age, or time of testing."

**Poor memory**

The researchers say the results of the study should encourage education professionals to target help at anxious children with poor complex memory skills.

"Given that the relationship between anxiety and cognitive performance was only a negative one in the low working-memory capacity group, young people with poor working-memory skills are likely to benefit the most from any intervention that aims to reduce symptoms of anxiety," the report says.

Lead researcher Dr Matthew Owens, who carried out the study at the University of Southampton, said: "The research is exciting because it enhances our knowledge of when, specifically, anxiety can have a negative impact on taking tests. "The findings also suggest that there are times when a little bit of anxiety can actually motivate you to succeed."

*The study was funded by the Economic and Social Research Council and Action Medical Research.*

[http://www.eurekalert.org/pub\\_releases/2012-10/lm-pcc101212.php](http://www.eurekalert.org/pub_releases/2012-10/lm-pcc101212.php)

**Prostate cancer: Curcumin curbs metastases*****Curcumin inhibits inflammatory reactions, it can also inhibit formation of metastases***

Powdered turmeric has been used for centuries to treat osteoarthritis and other illnesses. Its active ingredient, curcumin, inhibits inflammatory reactions. A new study led by a research team at Ludwig-Maximilians-Universität (LMU) in Munich now shows that it can also inhibit formation of metastases.

Prostate cancer is one of the most prevalent malignancies in the Western world, and is often diagnosed only after metastatic tumors have formed in other organs. In three percent of cases, these metastases are lethal.

A research team led by PD Dr. Beatrice Bachmeier at LMU Munich has been studying the mode of action of a natural product that inhibits the formation of metastases. The compound is found in turmeric, a plant that has been used for medicinal purposes for thousands of years, and is a major ingredient of curry.

Bachmeier's research centers on curcumin, the polyphenol responsible for the characteristic color of curry.

Curcumin is well tolerated and is therefore, in principle, suitable both for prophylactic use (primary prevention) and also for the suppression of metastases in cases where an established tumor is already present (secondary prevention). In a previous study Bachmeier and her colleagues had demonstrated that the substance reduces statistically significantly the formation of lung metastases in an animal model of advanced breast cancer.

**Mitigating metastasis**

The new study was designed to investigate the efficacy of curcumin in the prevention of prostate cancer metastases, and to determine the agent's mechanism of action. The researchers first examined the molecular processes that are abnormally regulated in prostate carcinoma cells.

Breast and prostate cancers are often associated with latent or chronic inflammatory reactions, and in both cases, the tumor cells were found to produce pro-inflammatory immunomodulators including the cytokines CXCL1 und CXCL2.

The researchers went on to show that curcumin specifically decreases the expression of these two proteins, and in a mouse model, this effect correlated with a decline in the incidence of metastases.

"Due to the action of curcumin, the tumor cells synthesize smaller amounts of cytokines that promote metastasis," says Bachmeier. "As a consequence, the frequency of metastasis formation in the lungs is significantly reduced, in animals with breast cancer, as we showed previously, or carcinoma of the prostate, as demonstrated in our new study."

**Curcumin and chemoprevention**

Bachmeier therefore believes that curcumin may be useful in the prevention of breast and prostate cancers – which are both linked to inflammation – and in reducing their metastatic potential. "This does not mean that the compound should be seen as a replacement for conventional therapies. However, it could play a positive role in primary prevention – before a full-blown tumor arises – or help to avert formation of metastases. In this context the fact that the substance is well tolerated is very important, because one can safely recommend it to individuals who have an increased tumor risk."

A daily intake of up to 8g of curcumin is regarded as safe, and its anti-inflammatory properties have long been exploited in traditional oriental medicine.

Men with benign hyperplasia of the prostate (BHP) are one possible target group for prophylaxis, as are women who have a family history of breast cancer. The agent might also be valuable as a supplement to certain cancer therapies. At all events, curcumin's beneficial effects must first be confirmed in controlled clinical tests.

Bachmeier is now planning such a trial in patients who suffer from therapy-resistant carcinoma of the prostate.

<http://www.sciencedaily.com/releases/2012/10/121012074655.htm>

## **Reason Discovered for the Toxicity of Indoor Mould**

***A team of researchers at the University of Helsinki has discovered how indoor mould makes people sick.***

ScienceDaily - The only remedy is to heal the living environment.

For more than a decade, it has been known that the fungus *Trichoderma longibrachiatum* is the most common finding wherever people are suffering from health hazards related to damp building damage. However, it has not been known how this mould -- which is typical of most buildings with indoor air problems -- harms people's health. Published in September, a study by a team of researchers at the Department of Food and Environmental Sciences of the University of Helsinki explains how microbial metabolites in the living environment cause health problems

With their colleagues, Raimo Mikkola, Maria Andersson and Mirja Salkinoja-Salonen have studied indoor mould for a long time. They discovered that the toxic substance produced by the mould fungus *Trichoderma longibrachiatum* consists of small peptides that contain alpha-aminoisobutyric acid and other amino acids not found in proteins. The discovery and purification of the toxin to determine its molecular structure was made possible by a sperm test developed earlier by the same team. This test served as a detector in tracing the toxin molecules produced by the fungus.

### **Nanochannels cause health problems**

The toxic foreign peptides produced by the *Trichoderma longibrachiatum* fungus were named trilongins. Their toxicity is based on their ability to be absorbed in tissues and cells in the body and produce nanochannels that permeate potassium and sodium. A channel formed by trilongins can obstruct vital channels that carry potassium and sodium and control communication systems that regulate heart cells, respiratory cells and nerve cells, for example. Health hazards related to foreign peptides cannot be prevented with antimicrobial drugs. Trilongins are also highly resistant to heat and antimicrobial chemicals. Diseases caused by the mould fungus can only be prevented by healing the living environment.

The team discovered more than ten chemically resistant foreign peptides and determined their molecular structures. Mass produced by the fungus *Trichoderma longibrachiatum* was measured to contain as much as 10 percent trilongins. Of the nanochannels produced by trilongins, 2:1 combinations of long and short trilongins were the most harmful for the cells of humans and other warm-blooded animals. These channels remained active for a longer time than channels consisting of one type of trilongin.

The study was carried out by the Finnish Centre of Excellence in Integrative Photosynthesis and Bioactive Compound Research at Systems Biology Level with support from the Academy of Finland and the Finnish Work Environment Fund.

Raimo Mikkola, Maria A. Andersson, László Kredics, Pavel A. Grigoriev, Nina Sundell, Mirja S. Salkinoja-Salonen. 20-Residue and 11-residue peptaibols from the fungus *Trichoderma longibrachiatum* are synergistic in forming Na<sup>+</sup>/K<sup>+</sup>-permeable channels and adverse action towards mammalian cells. *FEBS Journal*, 2012; DOI: 10.1111/febs.12010

[http://www.eurekalert.org/pub\\_releases/2012-10/osu-csd101012.php](http://www.eurekalert.org/pub_releases/2012-10/osu-csd101012.php)

**Chronic stress during pregnancy prevents brain benefits of motherhood, study shows**  
***A new study in animals shows that chronic stress during pregnancy prevents brain benefits of motherhood, a finding that researchers suggest could increase understanding of postpartum depression.***

COLUMBUS, Ohio – Rat mothers showed an increase in brain cell connections in regions associated with learning, memory and mood. In contrast, the brains of mother rats that were stressed twice a day throughout pregnancy did not show this increase. The researchers were specifically interested in dendritic spines – hair-like growths on brain cells that are used to exchange information with other neurons.

Previous animal studies conducted by lead author Benedetta Leuner of Ohio State University showed that an increase of dendritic spines in new mothers' brains was associated with improved cognitive function on a task that requires behavioral flexibility – in essence, enabling more effective multitasking. The dendritic spines increased by about 20 percent in these brain regions in new mothers, according to her findings.

The stress in this new study negated those brain benefits of motherhood, causing the stressed rats' brains to match brain characteristics of animals that had no reproductive or maternal experience.

The stressed rats also had less physical interaction with their babies than did unstressed rats, a behavior observed in human mothers who experience postpartum depression.

"Animal mothers in our research that are unstressed show an increase in the number of connections between neurons. Stressed mothers don't," said Leuner, assistant professor of psychology and neuroscience at Ohio State.



"We think that makes the stressed mothers more vulnerable. They don't have the capacity for brain plasticity that the unstressed mothers do, and somehow that's contributing to their susceptibility to depression."

Leuner described the research during a talk Saturday (10/13) in New Orleans at Neuroscience 2012, the annual meeting of the Society for Neuroscience.

Previous research has suggested that there are a number of risk factors for postpartum depression, including hormone fluctuations, prior history of mental illness and environmental factors such as smoking or low socioeconomic status. One of the strongest predictors, however, is chronic stress during pregnancy, so Leuner sought to create an animal model that could help explain brain changes linked to postpartum depression.

"It's devastating not only for the mother, because it affects her well-being, but previous research also has shown that children of depressed mothers have impaired cognitive and social development, may have impaired physical development, and are more likely as adults to have depression or anxiety," she said. "A better understanding of postpartum depression is important to help the mother but also to prevent some of the damaging effects that this disorder can have on the child."

The researchers exposed pregnant rats to stress twice a day by limiting their mobility on some days and on other days placing them in water. For three weeks after the rats gave birth, Leuner and colleagues monitored the rats. The animals showed classic signs of the effects of stress, including lower than normal weight gain and enlarged adrenal glands, a sign of high stress-hormone production. The mothers stressed during pregnancy also gave birth to smaller pups.

"And they were not very good mothers," Leuner said. After separation from pups for 30 minutes, unstressed mothers would gather up their babies, put them in the nest and nurse them. Stressed mother rats left the pups scattered around, wandered around the cage and fed the babies less frequently. The stressed mother rats also exhibited more floating than unstressed rats in a water test; animals that float rather than swim are showing depressive-like symptoms. "These findings in rats mimic some of the symptoms that are seen in women with postpartum depression," Leuner said.

An examination of the animals' brains showed that the rats exposed to chronic stress did not grow the additional dendritic spines in the hippocampus and prefrontal cortex that the unstressed mother rats did. The stressed rats' brains more closely resembled the brains of control rats that had never been mothers.

"We don't yet know what the exact trigger is for the increase in spines in motherhood, but we know that the increase goes away with stress," Leuner said. She is continuing the work by investigating whether the beneficial effects of motherhood on cognitive functions are also blocked in mothers who are exposed to pregnancy stress as well as whether hormonal factors play a role.

*This work was supported by the National Institute of Mental Health and a Brain & Behavior Research Foundation Young Investigator Award. Leuner co-authored the presentation with Peter Fredericks of Ohio State's Department of Psychology.*

[http://www.eurekalert.org/pub\\_releases/2012-10/ps-ecm101112.php](http://www.eurekalert.org/pub_releases/2012-10/ps-ecm101112.php)

### **Early-Earth cells modeled to show how first life forms might have packaged RNA A chemical model that mimics a possible step in the formation of cellular life on Earth four-billion years ago**

Researchers at Penn State University have developed a chemical model that mimics a possible step in the formation of cellular life on Earth four-billion years ago. Using large "macromolecules" called polymers, the scientists created primitive cell-like structures that they infused with RNA -- the genetic coding material that is thought to precede the appearance of DNA on Earth -- and demonstrated how the molecules would react chemically under conditions that might have been present on the early Earth. The journal *Nature Chemistry* will post the research as an Advance Online Publication on 14 October 2012.

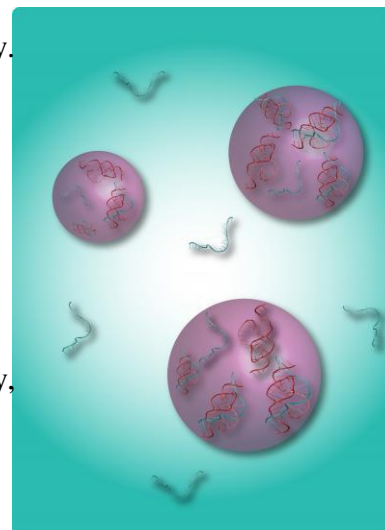
In modern biology, all life, with the exception of some viruses, uses DNA as its genetic storage mechanism. According to the "RNA-world" hypothesis, RNA appeared on Earth first, serving as both the genetic-storage material and the functional molecules for catalyzing chemical reactions, then DNA and proteins evolved much later. Unlike DNA, RNA can adopt many different molecular conformations and so it is functionally interactive on the molecular level. In the soon-to-be-published research paper, two professors of chemistry, Christine Keating and Philip Bevilacqua, and two graduate students, Christopher Strulson and Rosalynn Molden, probe one of the nagging mysteries of the RNA-world hypothesis.

"A missing piece of the RNA-world puzzle is compartmentalization," Bevilacqua said. "It's not enough to have the necessary molecules that make up RNA floating around; they need to be compartmentalized and they need to stay together without diffusing away. This packaging needs to happen in a small-enough space -- something analogous to a modern cell -- because a simple fact of chemistry is that molecules need to find each other for a chemical reaction to occur."

To test how early cell-like structures could have formed and acted to compartmentalize RNA molecules even in the absence of lipid-like molecules that make up modern cellular membranes, Strulson and Molden generated simple, non-living model "cells" in the laboratory.

"Our team prepared compartments using solutions of two polymers called polyethylene glycol (PEG) and dextran," Keating explained. "These solutions form distinct polymer-rich aqueous compartments, into which molecules like RNA can become locally concentrated."

The team members found that, once the RNA was packed into the dextran-rich compartments, the molecules were able to associate physically, resulting in chemical reactions. "Interestingly, the more densely the RNA was packed, the more quickly the reactions occurred," Bevilacqua explained. "We noted an increase in the rate of chemical reactions of up to about 70-fold. Most importantly, we showed that for RNA to 'do something' -- to react chemically -- it has to be compartmentalized tightly into something like a cell. Our experiments with aqueous two-phase systems (ATPS) have shown that some compartmentalization mechanism may have provided catalysis in an early-Earth environment."



*Shown are RNA strands (blue) and RNA enzymes (red) coming together within droplets of dextran. Scientists at Penn State have shown that this compartmentalization helps to catalyze chemical reactions. C. A. Strulson, Penn State University*

Keating added that, although the team members do not suggest that PEG and dextran were the specific polymers present on the early Earth, they provide a clue to a plausible route to compartmentalization -- phase separation. "Phase separation occurs when different types of polymers are present in solution at relatively high concentrations. Instead of mixing, the sample separates to form two distinct liquids, similar to how oil and water separate." Keating explained. "The aqueous-phase compartments we manufactured using dextran and PEG can drive biochemical reactions by increasing local reactant concentrations. So, it's possible that some other sorts of polymers might have been the molecules that drove compartmentalization on the early Earth." Strulson added that, "In addition to the RNA-world hypothesis, these results may be relevant to RNA localization and function in non-membrane compartments in modern biology."

The team members also found that the longer the string of RNA, the more densely it would be packed into the dextran compartment of the ATPS, while the shorter strings tended to be left out. "We hypothesize that this research result might indicate some kind of primitive sorting method," Bevilacqua said. "As RNA gets shorter, it tends to have less enzyme activity. So, in an early-Earth system similar to our dextran-PEG model system, the full-length, functional RNA would have been sorted and concentrated into one phase, while the shorter RNA that is not only less functional, but also threatens to inhibit important chemical reactions, would not have been included."

The scientists hope to continue their investigations by testing their model-cell method with other polymers. Keating added, "We are interested in looking at compartmentalization in polymer systems that are more closely related to those that may have been present on the early Earth, and also those that may be present in contemporary biological cells, where RNA compartmentalization remains important for a wide range of cellular processes." *This research was funded by the National Science Foundation (grant CHE-0750196)*