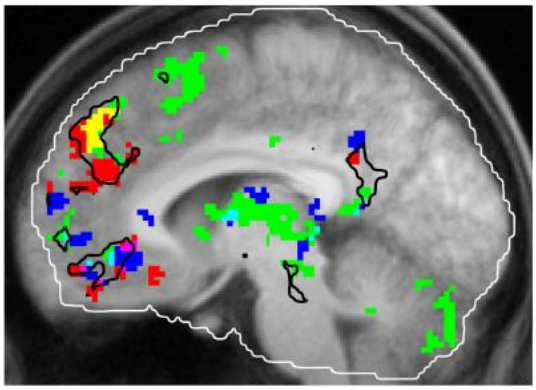
Study finds brain hub that links music, memory and emotion

We all know the feeling: a golden oldie comes blaring over the radio and suddenly we're transported back - to a memorable high-school dance, or to that perfect afternoon on the beach with friends. But what is it about music that can evoke such vivid memories?

By mapping the brain activity of a group of subjects while they listened to music, a researcher at the University of California, Davis, now thinks he has the answer: The region of the brain where memories of our past are supported and retrieved also serves as a hub that links familiar music, memories and emotion.



The discovery may help to explain why music can elicit strong responses from people with Alzheimer's disease, said the study's author, Petr Janata, associate professor of psychology at UC Davis' Center for Mind and Brain. The hub is located in the medial prefrontal cortex region - right behind the forehead - and one of the last areas of the brain to atrophy over the course of the disease.

When people are familiar with a tune, their brains show increased activity in the regions shaded in green in this fMRI image. Red areas respond to salient autobiographical memories, and blue areas respond to tunes that a person enjoys. The brain region known as the dorsal medial prefrontal cortex responds both to familiarity and autobiographical associations (yellow). **Petr Janata/UC Davis**

"What seems to happen is that a piece of familiar music serves as a soundtrack for a mental movie that starts playing in our head. It calls back memories of a particular person or place, and you might all of a sudden see that person's face in your mind's eye," Janata said. "Now we can see the association between those two things – the music and the memories."

His study, "The Neural Architecture of Music-Evoked Autobiographical Memories," will be published online on Feb. 24 in the journal Cerebral Cortex and will appear in the journal's print version later this year. Earlier work of Janata's had documented that music serves as a potent trigger for retrieving memories. In order to learn more about the mechanism behind this phenomenon, he enrolled 13 UC Davis students into a new study.

While his subjects listened to excerpts of 30 different tunes through headphones, Janata recorded their brain activity using functional magnetic resonance imaging, or fMRI. To assure the best chance that students would associate at least some of the tunes with memories from their past, he chose songs randomly from "top 100" charts from years when each subject would have been 8 to 18 years old.

After each excerpt, the student responded to questions about the tune, including whether it was familiar or not, how enjoyable it was, and whether it was associated with any particular incident, episode or memory.

Immediately following the MRI session, students completed a survey about the content and vividness of the memories that each familiar tune had elicited.

The surveys revealed that, on average, a student recognized about 17 of the 30 excerpts, and of these, about 13 were moderately or strongly associated with an autobiographical memory. Moreover, tunes that were linked to the strongest, most salient memories were the ones that evoked the most vivid and emotion-laden responses.

When he took a look at his fMRI images and compared them to these self-reported reactions, Janata discovered that the degree of salience of the memory corresponded to the amount of activity in the upper (dorsal) part of the medial pre-frontal cortex.

While this correlation confirmed Janata's hypothesis that this brain region links music and memory, it was another discovery that sealed his conclusion.

A lifelong music buff, Janata had earlier created a model for "mapping" the tones of a piece of music as it moves from chord to chord and into and out of major and minor keys. By making tonal maps of each musical excerpt and comparing them to their corresponding brain scans, he discovered that the brain was tracking these tonal progressions in the same region as it was experiencing the memories: in the dorsal part of the medial pre-frontal cortex, as well as in regions immediately adjacent to it. And in this case, too, the stronger the autobiographical memory, the greater the "tracking" activity.

"What's cool about this is that one of the main parts of the brain that's tracking the music is the same part of the brain that's responding overall to how autobiographically salient the music is," Janata said.

Because memory for autobiographically important music seems to be spared in people with Alzheimer's disease, Janata said, one of his long-term goals is to use this research to help develop music-based therapy for people with the disease.

"Providing patients with MP3 players and customized playlists," he speculated, "could prove to be a quality-of-life improvement strategy that would be both effective and economical."

The work was supported by a Templeton Advanced Research Program grant from the Metanexus Institute.

Janata's paper is freely accessible on the journal's Web site. It can be found under the "Advance Access" link at [*http://cercor.oxfordjournals.org/*](http://cercor.oxfordjournals.org/)

Re-shaping the family: What happens when parents seek siblings of their donor-conceived children

Findings of new study have wider implications for policy in this area

Parents who have conceived children with the help of sperm or egg donors and then try to find the donors and also other children conceived with the donors' help, often end up creating new forms of extended families, according to research published today (Tuesday 24 February).

The study in Europe's leading reproductive medicine journal Human Reproduction [1], found that parents set out to find their children's donor and other donor siblings through feelings of curiosity and a desire to enhance their children's sense of identity, and without expecting any very close contact. However, once they had identified the donor and their children's donor siblings, they not only found the experiences of contacting and meeting the donor siblings very positive, but in many cases formed close and continuing bonds.

Dr Tabitha Freeman, a research associate at the Centre for Family Research, University of Cambridge (UK), said: "Our most important finding is that the practice of donor conception is creating new family forms. These family forms are based on genetic links between families with children conceived by the same donor, as well as between donor-conceived children's families and their donors' families. Contrary to what might be expected, this research has found that contact between these new family forms can be a very positive experience for those involved. For example, one very striking finding is that family members in this sample formed close links based on notions of family and kinship; for example the mothers experienced maternal feelings towards their children's donor siblings.

"In addition, it is very interesting that this process is being driven by parents of donor conceived children who, whilst having conceived using anonymously donated sperm, regard it as important for their children to have access to information about their genetic relations."

Dr Freeman and colleagues recruited 791 parents via the Donor Sibling Registry, a US-based international registry that facilitates contact between donor conception families who share the same donor. The parents completed an online questionnaire and data were collected on their reasons for searching for their child's donor siblings and/or the donor, the outcome of these searches and the parents' and children's experiences of any resulting contact.

The parents consisted of 39% lone mothers, 35% lesbian couples and 21% heterosexual couples. In this study, 91% (717) of parents lived in the United States, 5% (37) in Canada and 1% (8) in the UK; other countries of residence included Austria, Germany, Ireland, Spain, Sweden, Australia, New Zealand and Israel. Some parents had discovered large numbers of donor siblings; 11% (55) of parents who had found their child's donor siblings had found 10 or more, with one parent finding as many as 55. An overwhelming majority of parents reported positive experiences of contacting and meeting their child's donor siblings and donor. They frequently described feeling excited and happy on their child's behalf when they found donor siblings, and viewed the addition of such relationships to their children's lives as "enriching", "wonderful" and "fun".

Dr Freeman said the findings have wider implications for research and policy, particularly as an increasing number of countries have removed the right to donor anonymity.

In the paper, the authors write: "The finding that parents placed more importance on tracing and establishing contact with their child's donor siblings than their child's donor has important implications for research and policy in this field. In particular, it is crucial that donor siblings are incorporated into discussions about the regulation of gamete donation, with a key consideration being the number of donor offspring to be conceived using any one donor. The potential for parents and children to form relationships with members of families who share the same donor is a significant consequence of the removal of donor anonymity that has yet to receive adequate attention. This study shows that, while the donor sibling relationship lies at the centre of this phenomenon, a series of wider kinship networks are created, described by those involved as an 'extended family'. These kinship relationships are based on both direct and indirect genetic connections and shared understandings and experiences, out of which new concepts of the family are being defined and negotiated."

Dr Freeman added: "Donor siblings have rarely been mentioned in policy discussions about the regulation of gamete donation, beyond concerns about the possibility of unwitting 'incestual' relationships between people conceived with the same donor.

"A recent example is the proposal made in a report from the British Fertility Society's (BFS) Working Party on Sperm Donation Services in the UK that the maximum number of families created by a single donor should be raised from the current limit of 10. This was proposed as a means of tackling concerns about falling numbers of donors following the removal of donor anonymity. Despite widespread media attention, the potential psychological effects on donor conceived offspring of discovering large numbers of genetic siblings in different families was not considered in this debate.

"Part of the reason that there has been limited discussion of donor siblings is that there has been a lack of research in this area. Whilst this current study provides valuable empirical information, it must be highlighted that further research is required into the experiences of those donor offspring who have found, contacted and met large numbers of donor siblings in order to assess the long-term impact on their psychological well-being."

The study also found differences between types of families had a significant impact on parents' motivations in searching for donor relations. Parents in households without fathers were much more curious about their child's donor and donor siblings.

Dr Freeman said: "Greater differences were found between one- and two-parent families than between father-present (i.e. heterosexual couple families) and father-absent families (lone mother and lesbian couple families). This is important because, in media and policy discussions, lone mothers and lesbian couples are often grouped together and compared to heterosexual-couple families."

She continued: "It is also important to bear in mind that the age and manner in which individuals are told about their donor conception has been found to have a significant impact on how they deal with this information, with those who find out younger in life experiencing more positive outcomes. This may have a knock-on effect in terms of the experience of contacting donor siblings. In this light, it is important to note that the large majority (97%) of the parents in this study had told, or planned to tell, their offspring about their donor conception, with most having done so at an early age."

The study is the first large-scale investigation into the experiences of parents of donor-conceived children searching for and contacting their child's donor relations, and it was conducted by one of the world's leading research groups studying embryo, sperm and egg donation and surrogacy. It is one of three papers in the current issue of Human Reproduction (a journal of the European Society of Human Reproduction and Embryology) that look at parents' attitudes and experiences towards donors [2].

One of these papers is an editorial commentary by Dr Pim Janssens, an associate editor of Human Reproduction. Writing about Dr Freeman's study, he says: "Overall, these findings suggest that knowledge of donor sibling families is a good thing, and that disclosure of the donor identity makes sense, and need not be a problem. They also suggest that for many parents and children, having only information about donors is not satisfactory – real encounters are the ultimate desire. Unexpectedly these findings might also lead us to question the importance of a common family history for the creation of 'family feeling'. After all, none of the donor families calling their donor sibling relatives shared anything but genes. Nonetheless, many said they felt intuitively bonded."

[1] Gamete donation: parents' experiences of searching for their child's donor siblings and donor. Human Reproduction, volume 24, issue 3, pages 505-516; doi:10.1093/humrep/den469.

[2] The other two papers are: "Embryo donation parents' attitudes towards donors: comparison with adoption," (volume 24, issue 3, pages 517-523; doi:10.1093/humrep/den386) by Fiona MacCallum and "Colouring the different phases in gamete and embryo donation," (volume 24, issue 3, pages 502-504;doi:10.1093/humrep/den431) by Pim M.W. Janssens.

Get personal to improve heart health

Scare tactics may not be necessary when trying to get patients at risk of heart disease to change their diet or behaviour, a new study has found. Instead, doctors and nurses should be aware of the stage of life their patients are at, and offer them very specific and targeted advice.

"The goal is to produce interventions which are sensitive to the lives and social position of those who find themselves at 'high risk' of coronary heart disease (CHD) in later-middle age, and which inspire change rather than inhibit it," say researchers, from Egenis, the ESRC Centre for Genomics in Society at the University of Exeter.

High-risk patients will often downgrade their risk in their own minds, yet could still be receptive to the behavioural change which is the purpose of CHD screening, explained Dr Hannah Farrimond, who studied the reaction of patients to being told they were at high risk. Boosting patients' sense of vulnerability does not help, and may even hinder, their efforts to change, the study found.

"Once patients have got over the shock of being at high risk of heart disease, they then tend to underplay their risk," says Dr Farrimond. "They compare themselves favourably with, say, others of the same age. In the past, researchers have thought we need to scare people into feeling at risk to make them change. This study

suggests that even those who downplayed their risk still made changes, such as taking statins or exercising more. In other words, we don't need to scare people to get results. Clinical staff need to find other ways of encouraging patients to make the necessary lifestyle changes, such as offering personalised advice."

The findings of Dr Farrimond's paper 'Making sense of being at 'high risk' of coronary heart disease', are published in the current issue of the journal Psychology and Health.

Current NHS policy advocates screening in primary care to identify 'high risk' individuals for coronary heart disease (CHD), particularly targeting those with family histories of the disease, through schemes such as the new, free 'health MOT' campaign. Until now, there has been little research looking at how people respond to such heart disease screening, particularly in relation to their age and stage of life. This study investigated the impact of the screening on the patients involved by interviewing 38 of them immediately after their intervention, looking particularly at how the age and stage of life of the participants affected their reactions.

"We found that patients struggled to maintain their sense of being 'healthy' in the face of their new 'high risk' status," said Dr Farrimond. "The older they were, the more patients treated the risk of CHD as a normal part of getting older. They would downplay their sense of vulnerability by, for example, comparing their own weight and diet favourably with that of their friends."

The study suggests that CHD intervention programmes need to be more sensitive to the social environment and age of the target group. It adds that most patients believe their diet is already 'balanced' or 'healthy', so clinicians should move away from simply repeating the formulaic set of well-known dietary rules and offering 'added-value' information about a specific CHD preventative diet.

"There's no point in just telling patients to 'be healthy'," said Dr Farrimond. "They need specific advice on how to protect their heart. GPs and nurses are well-placed to give the type of personalised information patients deserve."

Notes for editors

'Making sense of being at 'high risk' of heart disease' is published in the journal Psychology and Health. The article is currently available online at: www.informaworld.com/DOI=10.1080/08870440802499382

'Making sense of being at 'high risk' of coronary heart disease' was part of the larger ADDFAM study, 'Realising the potential of family history in risk assessment and primary prevention of coronary heart disease (CHD) in primary care', led by Dr Nadeem Qureshi from the Primary Care Team at the University of Nottingham and carried out by Dr Hannah Farrimond and Dr Paula Saukko of Egenis and affiliated staff Philip Evans (Peninsula Medical School), Nottingham: Jo Middlemass (Researcher), Joe Kai, Sarah Armstrong, Tracey Sachs, Professor Steve Humphries, Cardiovascular Genetics, UCL, Dr Paula Yoon, Centers for Disease Control, USA. It was funded by the Department of Health.

No longer a gray area: Our hair bleaches itself as we grow older

New research report in the FASEB Journal gets to the roots of gray hair

Wash away your gray? Maybe. A team of European scientists have finally solved a mystery that has perplexed humans throughout the ages: why we turn gray. Despite the notion that gray hair is a sign of wisdom, these researchers show in a research report published online in The FASEB Journal (http://www.fasebj.org) that wisdom has nothing to do with it. Going gray is caused by a massive build up of hydrogen peroxide due to wear and tear of our hair follicles. The peroxide winds up blocking the normal synthesis of melanin, our hair's natural pigment.

"Not only blondes change their hair color with hydrogen peroxide," said Gerald Weissmann, MD, Editor-in-Chief of The FASEB Journal. "All of our hair cells make a tiny bit of hydrogen peroxide, but as we get older, this little bit becomes a lot. We bleach our hair pigment from within, and our hair turns gray and then white. This research, however, is an important first step to get at the root of the problem, so to speak."

The researchers made this discovery by examining cell cultures of human hair follicles. They found that the build up of hydrogen peroxide was caused by a reduction of an enzyme that breaks up hydrogen peroxide into water and oxygen (catalase). They also discovered that hair follicles could not repair the damage caused by the hydrogen peroxide because of low levels of enzymes that normally serve this function (MSR A and B). Further complicating matters, the high levels of hydrogen peroxide and low levels of MSR A and B, disrupt the formation of an enzyme (tyrosinase) that leads to the production of melanin in hair follicles. Melanin is the pigment responsible for hair color, skin color, and eye color. The researchers speculate that a similar breakdown in the skin could be the root cause of vitiligo.

"As any blue-haired lady will attest, sometimes hair dyes don't quite work as anticipated," Weissmann added. "This study is a prime example of how basic research in biology can benefit us in ways never imagined."

Research study details: J. M. Wood, H. Decker, H. Hartmann, B. Chavan, H. Rokos, J. D. Spencer, S. Hasse, M. J. Thornton, M. Shalbaf, R. Paus, and K. U. Schallreuter. Senile hair graying: H2O2-mediated oxidative stress affects human hair color by blunting methionine sulfoxide repair. FASEB J. doi:10.1096/fj.08-125435. http://www.fasebj.org/cgi/content/abstract/fj.08-125435v1

Cholesterol-reducing drugs may lessen brain function, says ISU researcher

AMES, Iowa -- Research by an Iowa State University scientist suggests that cholesterol-reducing drugs known as statins may lessen brain function.

Yeon-Kyun Shin, a biophysics professor in the department of biochemistry, biophysics and molecular biology, says the results of his study show that drugs that inhibit the liver from making cholesterol may also keep the brain from making cholesterol, which is vital to efficient brain function.

"If you deprive cholesterol from the brain, then you directly affect the machinery that triggers the release of neurotransmitters," said Shin. "Neurotransmitters affect the data-processing and memory functions. In other words -- how smart you are and how well you remember things."

Shin's findings will be published in this month's edition of the journal Proceedings of the National Academy of Sciences of the United States of America.

Cholesterol is one of the building blocks of cells and is made in the liver. Low-density lipoprotein (LDL) - often referred to as bad cholesterol - is cholesterol in the bloodstream from the liver on the way to cells in the body. High-density lipoprotein (HDL) - so-called good cholesterol - is cholesterol being removed from cells. Too much LDL going to cells and not enough being removed can lead to cholesterol deposits and hardening of the cells.

"If you have too much cholesterol, your internal machinery is not going to be able to take away enough cholesterol from the cells," said Shin. "Then cells harden and you can get these deposits."

Cholesterol-reducing statin drugs are helpful because they keep the liver from synthesizing cholesterol so less of the substance is carried to the cells. This lowers LDL cholesterol.

It is the function of reducing the synthesis of cholesterol that Shin's study shows may also harm brain function.

"If you try to lower the cholesterol by taking medicine that is attacking the machinery of cholesterol synthesis in the liver, that medicine goes to the brain too. And then it reduces the synthesis of cholesterol which is necessary in the brain," said Shin.

In his experiments, Shin tested the activity of the neurotransmitter-release machinery from brain cells without cholesterol present and measured how well the machinery functioned. He then included cholesterol in the system and again measured the protein function. Cholesterol increased protein function by five times.

"Our study shows there is a direct link between cholesterol and the neurotransmitter release," said Shin. "And we know exactly the molecular mechanics of what happens in the cells. Cholesterol changes the shape of the protein to stimulate thinking and memory."

While reducing the cholesterol in the brain may make you have less memory and cognitive skills, more cholesterol in the blood does not make people smarter. Because cholesterol in the blood cannot get across the blood brain barrier, there is no connection to the amount of cholesterol a person eats and brain function.

Shin says that for many people taking cholesterol-lower statins can be very healthful and they should listen to their doctor when taking medication.

Beware the left-digit effect: Price gimmicks may affect choice

When shopping, we often find ourselves choosing between lower- and higher-cost items. But most people make a choice based on the first digit they see, according to a new study in the Journal of Consumer Research.

"Shoppers pay a disproportionate amount of attention to the leftmost digits in prices and these leftmost digits impact whether a product's price is perceived to be relatively affordable or expensive," write authors Kenneth C. Manning (Colorado State University) and David E. Sprott (Washington State University).

In one experiment, Manning and Sprott asked participants to consider two pens, one priced at $2.00 and the other at $4.00. A penny decrease in the price of either pen lowered the price's leftmost digit. The researcher manipulated the prices and found that when the pens were priced at $2.00 and $3.99, 44 percent of the participants selected the higher-priced pen. But when the pens were priced at $1.99 and $4.00, only 18 percent of the participants chose the higher-priced pen.

"The larger perceived price difference between the pens when they are priced at $1.99 and $4.00 led people to focus on how much they were spending and ultimately resulted in a strong tendency to select the cheaper alternative."

The researchers went on to study the impact of two "round prices" (such as $30.00 and $40.00) and two "just-below prices" ($29.99 and $39.99). "When we showed people these sets of prices, most perceived the two round prices to be more similar to one another than the two just-below prices. Based on the perceived price differences, we predicted that people would focus less on how much they were spending when presented with round prices, and as a result, a relatively large percentage of people would opt for the $40.00 option." The experiment supported their expectation. However, when buying a gift for a very close friend or when a

purchase only involves a few dollars, the authors found that rounding or just-below pricing had no impact on choice.

"Consumers should be aware of the subconscious tendency to focus on the leftmost digits of prices and how this tendency might bias their decision-making," write the authors."

Kenneth C. Manning and David E. Sprott. "Price Endings, Left-Digit Effects, and Choice." Journal of Consumer Research: August 2009.

Mole rats may hold secret to long life

THEY may not be the prettiest creatures, but naked mole rats may hold the secret to longevity. They can live for nearly 30 years longer than any other rodent.

Naked mole rats sometimes live almost 30 years longer than other rodents - now scientists think they know why **(Image: Roman Klementschitz / Wikimedia Commons)**

Ageing is often blamed on the oxidising compounds we produce in our bodies, which gradually wear down DNA and proteins. These damaged molecules then go on to wreak havoc in cells.

Yet ageing naked mole rats have similar levels of oxidants to mice that live to be just 3½. To investigate, Rochelle Buffenstein of the University of Texas Health Science Center in San Antonio and colleagues extracted liver tissue from both species and treated it with chemicals that "unravel" proteins to reveal damage. They found twice as many undamaged proteins in naked mole rats as in mice. What's more, the rats' protein recycling machinery was exceptionally active *(Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0809620106).*

The team suspects that naked mole rats manufacture extra quantities of molecules that are responsible for labelling damaged proteins that need to be recycled quickly to minimise their effect on cells. The researchers hope to identify these molecules and test if it is possible to use them to treat age-related disease in humans.

Map-reading skills change how we view beauty

* 22:00 23 February 2009 **by Bob Holmes**

A beautiful scene evokes a different response in men's brains than in women's. The difference may result from different evolutionary pressures on the two sexes in our hunter-gatherer ancestors.

A team led by Camilo Cela-Conde of the Balearic University in Palma de Mallorca, Spain, showed photographs of natural and urban scenes to 10 male and 10 female volunteers, and asked them to classify each scene as beautiful or not beautiful.

As each volunteer did so, the researchers measured the electrical activity of their brains using a technique known as magnetoencephalography. Then they looked to see which parts of the brain were active only for scenes rated as beautiful - in other words, what "beauty" looks like in the brain.

Both men and women showed increased activity in the parietal region, near the top of the brain, in response to beautiful scenes. In women, this increased activity occurred in both hemispheres of the brain, while in men it was restricted mainly to the right hemisphere.

Mental maps

The researchers suggest that this distinction may reflect differences between the sexes in the way they process landscape imagery.

In early humans, men tended to be hunters and thus developed mental maps based on distance and direction, while women tended to gather plant foods and thus oriented themselves by means of landmarks, they argue.

This fits with existing evidence that the left hemisphere handles "categorical" spatial relations such as landmarks, while the right handles "coordinate" spatial relations like distance and direction.

The researchers hope to go on to study whether these brain differences affect men's and women's decisions about whether a scene is beautiful.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0900304106 (in press)

Million women study shows even moderate alcohol consumption associated with increased cancer risk

Low to moderate alcohol consumption among women is associated with a statistically significant increase in cancer risk and may account for nearly 13 percent of the cancers of the breast, liver, rectum, and upper aero-digestive tract combined, according to a report in the February 24 online issue of the Journal of the National Cancer Institute.

With the exception of breast cancer, little has been known about the impact of low to moderate alcohol consumption on cancer risk in women.

To determine the impact of alcohol on overall and site-specific cancer risk, Naomi Allen, D.Phil., of the University of Oxford, U.K., and colleagues examined the association of alcohol consumption and cancer

incidence in the Million Women Study, which included 1,280,296 middle-aged women in the United Kingdom. Participants were recruited to the study between 1996 and 2001. Researchers identified cancer cases through the National Health Service Central Registries.

Women in the study who drank alcohol consumed, on average, one drink per day, which is typical in most high-income countries such as the U.K. and the U.S. Very few drank three or more drinks per day. With an average follow-up time of more than 7 years, 68,775 women were diagnosed with cancer.

The risk of any type of cancer increased with increasing alcohol consumption, as did the risk of some specific types of cancer, including cancer of the breast, rectum, and liver. Women who also smoked had an increased risk of cancers of the oral cavity and pharynx, esophagus, and larynx. The type of alcohol consumed--wine versus spirits or other types--did not alter the association between alcohol consumption and cancer risk.

Each additional alcoholic drink regularly consumed per day was associated with 11 additional breast cancers per 1000 women up to age 75; one additional cancer of the oral cavity and pharynx; one additional cancer of the rectum; and an increase of 0.7 each for esophageal, laryngeal, and liver cancers. For these cancers combined, there was an excess of about 15 cancers per 1000 women per drink per day. (The background incidence for these cancers was estimated to be 118 per 1000 women in developed countries.)

"Although the magnitude of the excess absolute risk associated with one additional drink per day may appear small for some cancer sites, the high prevalence of moderate alcohol drinking among women in many populations means that the proportion of cancers attributable to alcohol is an important public health issue," the authors write.

In an accompanying editorial, Michael Lauer M.D., and Paul Sorlie, Ph.D., of the National Heart, Lung, and Blood Institute, in Bethesda, M.D., emphasize that these new results derived from such a large study population should give readers pause. Although previous epidemiological studies have suggested that there is a cardiovascular benefit associated with moderate alcohol consumption, the excess cancer risk identified in the current study may outweigh that benefit. "From a standpoint of cancer risk, the message of this report could not be clearer. There is no level of alcohol consumption that can be considered safe," the editorialists write.

Contacts:

** Article: Sally Staples, Cancer Research UK Press Office, sally.staples@cancer.org.uk, + 020 7061 8313*

** Editorial: NHLBI Office of Communications, nhlbi_news@nhlbi.nih.gov, 301-496-4236*

Citations:

** Article: Allen N et al. Moderate Alcohol Intake and Cancer Incidence in Women. J Natl Cancer Inst 2009;101: 296-305*

** Editorial: Alcohol, Cardiovascular Disease, and Cancer: Treat With Caution. J Natl Cancer Inst 2009;101: 282-283*

Goserelin improves long-term survival in premenopausal women with early breast cancer

Goserelin, a lutenizing hormone-releasing hormone agonist, reduces the long-term risk of disease recurrence and deaths in premenopausal women with early breast cancer who did not take tamoxifen, according to trial data reported in the February 24 online issue of the Journal of the National Cancer Institute.

Systematic reviews have shown that lutenizing hormone-releasing hormone agonists, including goserelin, reduce the risk of disease recurrence and death due to breast cancer in premenopausal women. However the long-term impact of goserelin was not known, particularly in comparison to women who did or did not take tamoxifen.

Women with breast cancer were randomly assigned to take goserelin (Zoladex), tamoxifen, both agents, or neither drug for two years in the Zoladex in Premenopausal Patients study. In this analysis, which included 2,706 women, Allan Hackshaw, of the Cancer Research UK Trials Centre at University College London, and colleagues examined the long-term impact of the agents on various outcomes, including the risk of the cancer returning and the risk of dying from breast cancer or any cause.

The effect of two years of goserelin treatment was comparable to that conferred by two years of tamoxifen. Among patients who took goserelin alone, there were 13.9 fewer events per 100 women 15 years after starting treatment, compared with those who did not take either drug. Among women who took both drugs, the benefit of adding goserelin to tamoxifen was smaller (2.8 fewer events per 100 patients) and did not reach statistical significance.

The number of breast cancer deaths was lower by 8.5 per 100 women in those who took goserelin alone, compared to those who took neither drug. The difference was statistically significant. Among those who added goserelin to tamoxifen, there was an additional reduction of 2.6 deaths per 100 women. But again, the additional reduction was not statistically significant.

"In summary, long-term follow-up of our large trial showed that goserelin had a demonstrable effect on survival and recurrence 15 years after starting treatment and is as effective as tamoxifen when each are given

for 2 years," the authors write. "It may be that women who are unlikely to complete 5 years of tamoxifen tablets may prefer 2 years of goserelin injections."

Citation: Hackshaw A et al. Moderate Long-term effectiveness of adjuvant goserelin in pre-menopausal women with early breast cancer. J Natl Cancer Inst 2009;101:341-349

Contact: Ruth Metcalfe, r.metcalfe@ucl.ac.uk, +44 (0)20 7679 9739

Researchers identify molecule that helps the sleep-deprived to mentally rebound

DALLAS - Sleep experts know that the mental clarity lost because of a few sleepless nights can often be restored with a good night's rest. Now, UT Southwestern Medical Center researchers have identified a key molecular mechanism that regulates the brain's ability to mentally compensate for sleep deprivation.

Working with mice, they found that a molecule called an adenosine receptor is necessary for sleep-restricted animals to attain adequate levels of slow-wave activity in the brain once normal sleep resumes. It is this increase in slow-wave activity, or SWA, during rebound sleep that helps restore normal working memory and attention skills to the sleep-deprived, the scientists report in the Feb. 4 issue of the Journal of Neuroscience.

"Normal society pushes people to burn candles at both ends - going to bed late, getting up early, and somehow performing mentally with lack of adequate sleep," said senior author Dr. Robert Greene, professor of psychiatry at UT Southwestern. "We need to have our adenosine receptors intact to do that."

Adenosine receptors on nerve cells, including brain cells, are akin to docking points for the molecule adenosine. Adenosine levels increase in the brain with each hour of waking activity, and "docking" of the molecule with its receptor is shown in this study to help promote the slow-wave activity of sleep. Scientists have known that recovery from sleep deprivation involves not only an increase in sleep time, or rebound sleep, but also an elevation in this slow-wave activity.

To investigate how adenosine receptors and SWA might be linked, Dr. Greene and his team engineered mice that lacked a receptor to pair up with adenosine.

Sleep-restricted mice were kept awake by being placed on a moving treadmill. Researchers then electronically monitored sleep and waking activity of both normal and genetically engineered mice, including monitoring electronically the brain waves of the animals. The mice also traveled a maze with eight paths, each with a piece of chocolate at the end of it.

Electronic measurements showed that, unlike normal mice, the mice lacking the adenosine receptor could not increase the intensity of their slow-wave activity in response to the sleep deprivation. Under normal sleep conditions both the normal and mutant mice were almost error-free on the maze test. However, when sleep-deprived, the engineered mice made significantly more errors on the maze test than their normal counterparts. This type of skills test represents the human equivalent of the attention and working memory needed to multitask or build on tasks already done, such as being given a phone number, reaching for a pen to write it down and recalling the number, said Dr. Greene.

Linking the lack of functioning adenosine receptors to depressed normal SWA rebound response might aid in developing treatments for people with sleep-related cognitive deficits, he said.

The research also further explains the effects of caffeine, which also "docks" to adenosine receptors, preventing the docking of adenosine and keeping the caffeine-drinker awake. Dr. Greene compared the study mice's behavior response on the maze test to how a person drinking a "permanent cup of coffee" might behave.

"They probably won't get the regular amount of slow-wave activity or deep sleep as they normally would," Dr. Greene said. "This is not to say that coffee is bad, but drinking it all the time or in the evening could affect your mental performance the next day."

The researchers next will investigate the relationship between sleep, adenosine and energy metabolism, a biological process in which adenosine plays a key role.

Other researchers from UT Southwestern involved in the study were lead author Dr. Theresa Bjorness, postdoctoral research fellow in psychiatry, and Virginia Poffenberger, research technician in psychiatry.

The study was funded by the U.S. Department of Veterans Affairs and the National Institutes of Health.

Visit http://www.utsouthwestern.org/neurosciences to learn more about UT Southwestern's clinical services in the neurosciences, including psychiatry.

Bizarre bird behavior predicted by game theory

A team of scientists, led by the University of Exeter, has used game theory to explain the bizarre behaviour of a group of ravens. Juvenile birds from a roost in North Wales have been observed adopting the unusual strategy of foraging for food in 'gangs'. New research, published in the journal PLoS One (on Wednesday 25 February 2009), explains how this curious behaviour can be predicted by adapting models more commonly used by economists to analyse cdd financial trends.

This is the first time game theory has been used to successfully predict novel animal behaviour in the real world. The researchers believe this analysis could also shed light on the variation in feeding strategies in different populations in other species.

Ravens feed on the carcasses of large animals. Most populations live in temperate forests, where individuals search for carcasses and finds are then defended by a pair of territorial adults. Unpaired younger birds, on the other hand, gather at communal roosts from which they search individually for carcasses on adult territories and recruit each other to overwhelm adult protectionism. However, at one raven roost on Anglesey, things work differently: juveniles forage in gangs. This level of coordination had not been seen before in a raven population.

The researchers built a mathematical model to understand how this behaviour evolved and why it might occur in some roosts and not others. The model designed for this study was based on techniques used in other game theory models, which identify the most profitable behaviours of individuals in different situations to predict what would be favoured by evolution.

The study revealed two strategies as being most profitable for ravens to find food. One is for birds to search independently for food and recruit each other. The other is for the birds to forage in gangs.
The findings showed that gang foraging should occur when searching for food individually is no more efficient than foraging in groups. This is likely to be the case if the roost covers landscape that can be thoroughly explored by a gang over the course of a day. The deforested Welsh countryside offers just such conditions.

The study also identifies the availability of food as a key factor. The roost in Anglesey is situated in an agricultural area, which means that the carcasses of farm animals are often available so food is more plentiful than in wild locations. When food is abundant, the opportunity for social advancement becomes more important. These ravens seem to be using foraging behaviour, not only to find food, but also to gain social status, which could help in other aspects of their lives, including finding a mate.

Lead author Dr Sasha Dall of the University of Exeter said: "This is a rare example of how game theory has been used to predict behaviour in animals in the real world. Our study shows the potential for game theory to help biologists understand how different social structures and behaviours evolve in different environments and in response to human activities."

This study, entitled Rich pickings near large communal roosts favour 'gang' foraging by juvenile common ravens, Corvus corax, was carried out by a team from the University of Exeter's Cornwall Campus and the Institute of Biology, NTNU, Trondheim, Norway.

Physical fitness improves spatial memory, increases size of brain structure

Illinois psychology professor Art Kramer and his colleagues found that fitness increases hippocampus size and improves spatial memory in human subjects.

Click here for more information.

When it comes to the hippocampus, a brain structure vital to certain types of memory, size matters. Numerous studies have shown that bigger is usually better. Now researchers have found that elderly adults who are more physically fit tend to have bigger hippocampi and better spatial memory than those who are less fit.

The study, in the journal Hippocampus, shows that hippocampus size in physically fit adults accounts for about 40 percent of their advantage in spatial memory.

The hippocampus, a curved structure deep inside the medial temporal lobe of the brain, is essential to memory formation. Remove it – as was done in the well-known case of surgical patient Henry Gustav Molaison – and a person's ability to store most new experiences in memory is destroyed.

The hippocampus also is a key player in spatial navigation and other types of relational memory.

Certain activities are believed to modify hippocampus size in humans. For example, a study of London taxi drivers found that the posterior portion of the hippocampus was larger in experienced taxi drivers than in other subjects. And a study of German medical students found that the same region of the hippocampus increased in size as they studied for their final exams.

Studies also have found that the hippocampus shrinks with age, a process that coincides with small but significant cognitive declines. The rate at which this occurs, however, differs among individuals.

Earlier studies found that exercise increases hippocampus size and spatial memory in rodents, but the new study is the first to demonstrate that exercise can affect hippocampus size and memory in humans.

The researchers, from the University of Illinois and the University of Pittsburgh, measured the cardiorespiratory fitness of 165 adults (109 of them female) between 59 and 81 years of age. Using magnetic resonance imaging, the researchers conducted a volumetric analysis of the subjects' left and right hippocampi. They also tested the participants' spatial reasoning.

They found a significant association between an individual's fitness and his or her performance on certain spatial memory tests. There was also a strong correlation between fitness and hippocampus size.

"The higher fit people have a bigger hippocampus, and the people that have more tissue in the hippocampus have a better spatial memory," said U. of I. psychology professor Art Kramer, who led the study with Pittsburgh psychology professor Kirk Erickson.

"Even ignoring the hippocampus data, we see there is this significant and substantial relationship between how fit you are and how good your memory is, or at least a certain kind of memory, a certain kind of memory that we need all the time," Kramer said.

"This is really a clinically significant finding because it supports the notion that your lifestyle choices and behaviors may influence brain shrinkage in old age," Erickson said. "Basically, if you stay fit, you retain key regions of your brain involved in learning and memory."

An impairment of spatial memory "is one of a number of reasons why older people end up losing their independence," Kramer said. "Here is yet more evidence that becoming fit has implications for how well you're going to live your life."

Kramer is a full-time faculty member of the Beckman Institute for Advanced Science and Technology at Illinois.

Researchers Generate Functional Neurons From Somatic Cells

Los Angeles, Calif. - In a new study, researchers were able to generate functionally mature motor neurons from induced pluripotent stem (iPS) cells, which are engineered from adult somatic cells and can differentiate into most other cell types. A potential new source of motor neurons that does not require human eggs or embryos could be an enormous boon to research into conditions such as amyotrophic lateral sclerosis (ALS) and spinal cord injury and could open the door to eventual treatments. The study is published in Stem Cells.

This study is the first to use human iPS cells to generate electrically active motor neurons, a key hallmark of functional maturation that is essential for any future application of iPS cells. “To our knowledge, our results present the first demonstration of the electrical activity of iPS-derived neurons and further suggest the feasibility of using these cells to explore how changes in motor neuron activity contributes to the degeneration of these cells underlying these disorders,” the authors state.

Led by William Lowry, and in collaboration with Bennett Novitch, Harley Kornblum, and Martina Wiedau-Pazos of the University of California Los Angeles, researchers compared the ability of different human cell lines to generate motor neuron progenitors and fully differentiated motor neurons. “These findings support the possibility that reprogrammed somatic cells might prove to be a viable alternative to embryo-derived cells in regenerative medicine,” the authors note.

When measuring the electrophysical properties of the iPS-derived neurons, the researchers found that the iPS cells followed a normal developmental progression to mature, electrically active neurons.

“It seems possible that disease-specific somatic cells may be reprogrammed and utilized to model, and ultimately to treat a variety of human neurological disorders,” says Miodrag Stojković, co-editor of the journal.

This study is published in Stem Cells. Media wishing to receive a PDF of this article may contact journalnews@bos.blackwellpublishing.net.

Fear of heights linked to vertical perception

* 00:01 25 February 2009 **by Ewen Callaway**

People who shudder atop skyscrapers or feel their knees buckle going over bridges have troubling perceiving vertical dimensions, two new studies suggest.

Those with an extreme fear of heights - a condition called acrophobia and often mislabelled "vertigo" - significantly overestimate vertical distances. The stronger their fear, the bigger the error, say researchers.

This runs counter to traditional theories of acrophobia, says Russell Jackson, a cognitive psychologist at California State University in San Marcos, who led one of the studies. Psychologists generally hold that "acrophobia is an excessive fear in response to something that's perceived normally," he says.

But Jackson's new results indicate otherwise. "An important component of acrophobia appears to be that they are perceiving something different in the first place" and reacting normally, he says.

Jackson tested 43 students who had previously filled out a psychological survey that included questions to gauge acrophobia. The survey asked subjects to rate their anxiety over situations such as crossing a bridge or riding a Ferris wheel.

Universal fear

To test perception, Jackson's team asked each volunteer to approximate the height of a five-storey, 14.4-metre parking garage. With test subjects at the top or bottom of the building, a research assistant marched away slowly. When subjects felt the assistant had paced a distance equal to the height of the building, researchers took note.

All but one volunteer overestimated height – whether from the top or bottom of the building. However, volunteers proved better judges from the bottom of the building than the top, and a person's score on the acrophobia test did a decent job of predicting how far off he or she was.

Those most scared of heights judged the building 3 metres higher from the bottom and 12 metres higher from the top, compared with those who scored lowest on the acrophobia test.

Because subjects erred both on top of the building – where being scared is more rational – and when safe on the ground, their fear seems to be driven primarily by misperception, Jackson says.

Acrophobiacs who see a 14-metre building like it's 50 metres react like normal people would to a 50-metre building. "There's no-one that's fearless when it comes to heights," he says.

Reversed relationship

Jeanine Stefanucci, a psychologist at the College of William and Mary in Williamsburg, Virginia, who led the second study agrees that misperception is key to acrophobia. However, she thinks fear drives misperception, not the other way around.

Her team asked volunteers to judge vertical distance above a two-storey balcony. When they showed volunteers provocative images – guns or snakes, for instance – volunteers tended to misjudge vertical, but not horizontal distances. But when volunteers suppressed their gut reactions to the images, they judged vertical distance more accurately. When people reacted strongly to the photos, their misjudgements increased.

This suggests that fear is driving misperception, though the relationship could more complex than one causing the other, Stefanucci says.

Either way, both team's findings offer a new approach to treating acrophobia. Traditionally, psychologists provide cognitive therapy to help them overcome their fears, and then expose them to higher and higher heights, Jackson says.

Psychologists could equate decreases in patients' vertical misperceptions to clinical improvements, only challenging them to conquer higher heights when they see the world normally, Stefanucci says.

Journal reference: Jackson's study – Proceedings of the Royal Society B (DOI: 10.1098/rspb.2009.0004)
Journal reference: Stefanucci's study – Journal of Experimental Psychology (DOI: 10.1037a0014797)

Gestures lend a hand in learning mathematics

Hand movements help create new ideas

Gesturing helps students develop new ways of understanding mathematics, according to research at the University of Chicago.

Scholars have known for a long time that movements help retrieve information about an event or physical activity associated with action. A report published in the current issue of the journal Psychological Science, however, is the first to show that gestures not only help recover old ideas, they also help create new ones. The information could be helpful to teachers, scholars said.

"This study highlights the importance of motor learning even in nonmotor tasks, and suggests that we may be able to lay the foundation for new knowledge just by telling learners how to move their hands," writes lead author and psychologist Susan Goldin-Meadow in the article "Gesturing Gives Children New Ideas About Math".

Goldin, Meadow, the Beardsley Ruml Distinguished Service Professor in Psychology, was joined by Susan Wagner Cook, now Assistant Professor of Psychology a the University of Iowa and University of Chicago research assistant Zachary Mitchell, in writing the article and doing the research.

For the study, 128 fourth-grade students were given problems of the type 3+2+8=__+8. None of the students had been successful in solving that type of problem in a pre-test. The students were randomly divided into three instruction groups.

One group was taught the words, "I want to make one side equal to the other side." Another group was taught the same words along with gestures instantiating a grouping problem-solving strategy--a V-shaped hand indicating 3+2, followed by a point at the blank (group and add 3 and 2 and put the sum in the blank). A third group was taught the words along with gestures instantiating the grouping strategy but focusing attention on the wrong numbers--a V-shaped hand indicating 2+8, followed by a point at blank. The experimenter demonstrating the gesture did not explain the movement or comment about it.

All of the students were then given the same mathematics lesson. On each problem during the lesson, they were told to repeat the words or words/gestures they had been taught.

After the lesson, students were given a test in which they solved new problems of this type and explained how they reached their answers. Students who repeated the correct gesture during the lesson solved more problems correctly than students who repeated the partially correct gesture, who, in turn, solved more problems correctly than students who repeated only the words.

The number of problems children solved correctly could be explained by whether they added the grouping strategy to their spoken repertoires after the lesson, Goldin-Meadow said. Because the experimenter never expressed the grouping strategy in speech during the lesson, and students picked it up on their own as a new idea, the study demonstrates that gesture can help create new concepts in learning.

"The grouping information students incorporated into their post-lesson speech must have come from their own gestures," Goldin-Meadow said.

"Children were thus able to extract information from their own hand movements. This process may be the mechanism by which gesturing influences learning," she said.

Physical fitness improves spatial memory, increases size of brain structure

When it comes to the hippocampus, a brain structure vital to certain types of memory, size matters. Numerous studies have shown that bigger is usually better. Now researchers have found that elderly adults who are more physically fit tend to have bigger hippocampi and better spatial memory than those who are less fit.

The study, in the journal Hippocampus, shows that hippocampus size in physically fit adults accounts for about 40 percent of their advantage in spatial memory.

The hippocampus, a curved structure deep inside the medial temporal lobe of the brain, is essential to memory formation. Remove it – as was done in the well-known case of surgical patient Henry Gustav Molaison – and a person's ability to store most new experiences in memory is destroyed.

The hippocampus also is a key player in spatial navigation and other types of relational memory.

Certain activities are believed to modify hippocampus size in humans. For example, a study of London taxi drivers found that the posterior portion of the hippocampus was larger in experienced taxi drivers than in other subjects. And a study of German medical students found that the same region of the hippocampus increased in size as they studied for their final exams.

Studies also have found that the hippocampus shrinks with age, a process that coincides with small but significant cognitive declines. The rate at which this occurs, however, differs among individuals.

Earlier studies found that exercise increases hippocampus size and spatial memory in rodents, but the new study is the first to demonstrate that exercise can affect hippocampus size and memory in humans.

The researchers, from the University of Illinois and the University of Pittsburgh, measured the cardiorespiratory fitness of 165 adults (109 of them female) between 59 and 81 years of age. Using magnetic resonance imaging, the researchers conducted a volumetric analysis of the subjects' left and right hippocampi. They also tested the participants' spatial reasoning.

They found a significant association between an individual's fitness and his or her performance on certain spatial memory tests. There was also a strong correlation between fitness and hippocampus size.

"The higher fit people have a bigger hippocampus, and the people that have more tissue in the hippocampus have a better spatial memory," said U. of I. psychology professor Art Kramer, who led the study with Pittsburgh psychology professor Kirk Erickson.

"Even ignoring the hippocampus data, we see there is this significant and substantial relationship between how fit you are and how good your memory is, or at least a certain kind of memory, a certain kind of memory that we need all the time," Kramer said.

"This is really a clinically significant finding because it supports the notion that your lifestyle choices and behaviors may influence brain shrinkage in old age," Erickson said. "Basically, if you stay fit, you retain key regions of your brain involved in learning and memory."

An impairment of spatial memory "is one of a number of reasons why older people end up losing their independence," Kramer said. "Here is yet more evidence that becoming fit has implications for how well you're going to live your life."

UCR scientists identify stem-cell genes that help form plant organs

Discovery can help researchers develop improved crop plants

RIVERSIDE, Calif. – Plant stem-cells are master cells located at the tip of the stem and are part of a structure called the shoot apical meristem (SAM). Here, the stem cells - all clumped together - divide throughout the life of the plant to give rise to other cells, resulting in the formation of above-ground organs such as leaves, flowers, branches and stem. But despite the important role the stem cells play in plant development, their molecular composition has eluded researchers for long.

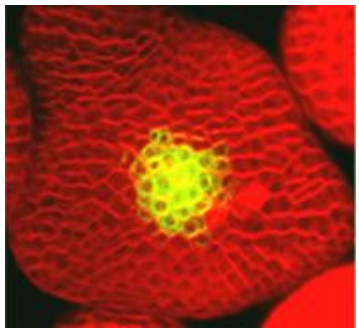
Now, working on Arabidopsis, a mustard-like plant that is a model for studying plant biology, a team of researchers at UC Riverside has identified all the genes expressed in the plant's stem cells.

The researchers also identified all the genes expressed in two other SAM cells: niche cells (which are located just beneath the stem cells and which provide signals that regulate the stem cells), and differentiating cells (which are generated by, and surround, the stem cells).

The final product of the researchers' work is a genome-scale, expression map of SAM - an achievement that paves the way to developing better varieties of crops and plants.

Besides revealing the molecular pathways that stem cells employ, the discovery also can help scientists better understand why stem cells - in both plants and animals - give rise to specialized cells at all. Study results appear online this week in the early edition of the Proceedings of the National Academy of Sciences.

"Our study is the first to reveal the stem-cell signatures for any plant and the first to provide a global view of which genes are expressed, and where, within the SAM," said G. Venugopala Reddy, the lead author of the study and an assistant professor of plant cell biology in the Department of Botany and Plant Sciences. "Since SAM stem-cells are responsible for forming plant organs and determining plant architecture, further analysis of their genes may provide a handle in altering growth rates and growth patterns in economically important crop-species in order to maximize yield."



Arabidopsis stem-cells (greenish-yellow) surrounded by differentiating cells (red). Niche cells (not seen here) are located beneath the stem cells. **Reddy lab, UC Riverside**

Reddy stressed that understanding the function and regulation of stem-cell-specific genes is critical to gaining insights into basic questions such as what constitutes stem-cell identity (the ability of cells to remain unspecialized) and what makes them differentiate into specialized cells.

"A comparative analysis of stem-cell-specific genes between plant and animal systems may also lead to a better understanding of stem-cell identity, a concept common to both the systems," he said.

The study breaks ground also in the way Reddy's research team pinned down the stem-cell genes in Arabidopsis.

His lab initially labeled the three different SAM cell types - stem cells, niche cells and differentiating cells - by using different fluorescent proteins. Next, the researchers isolated the three discrete cell populations by first stripping the cell walls to release the cells as free populations. Then, using an instrument called Fluorescence Activated Cell Sorter, they separated each set of cells from the rest of the cell populations.

"Plant biologists have found it difficult to isolate the approximately 35 stem cells in the Arabidopsis shoot system for two main reasons: this is an extremely low number of stem cells and this clump of cells is tightly packed with a waxy coating covering its outer layer," Reddy said. "To meet this challenge, we used specific mutants of Arabidopsis that make more SAMs per plant. In the lab, we also formulated specific combinations of enzymes that efficiently digest away the cell walls."

Reddy explained that the gene expression map his team generated can help researchers track how genes give rise to complex tissues. It also will allow researchers to determine the expression patterns of SAM genes by a mere click of a button on a computer.

"Development of an organ such as SAM is a complex process in which cells constantly exchange information through regulated gene activities," he said. "What we have done so far is to find out which genes are expressed and where. One of the future challenges is to represent the gene expression on actual templates of plant cells, which would generate a dynamic atlas of stem-cell development. Such an atlas can be used to explore how genes function as a network to bring about stem-cell function."

Reddy acknowledged that developing the atlas is a difficult venture, requiring a synthesis of multiple disciplines such as genomics, live-imaging and informatics sciences. "But our work breaks ground to make this a reality and we have already initiated some work in this direction," he said.

Reddy, who is also a member of UCR's Center for Plant Cell Biology, was joined in the research by Ram Kishor Yadav, Thomas Girke, Sumana Pasala and Mingtang Xie. The 24-month research project was funded by a grant from the National Science Foundation.

Stroke treated significantly faster and just as safely by medical residents

St. Louis - Diagnosing acute stroke is a high-pressure decision. The speed with which treatment is delivered makes all the difference. Early treatment can stop brain damage, but if treatment is given inappropriately, it can dangerously increase the risk of bleeding in the brain.

Because of this risk, the final decision to administer stroke treatment - a clot-busting enzyme known as tissue plasminogen activator (tPA) - is usually reserved for neurologists or, in some cases, other attending physicians. But now a study conducted by researchers at Washington University School of Medicine in St. Louis with neurology residents at Barnes-Jewish Hospital has shown that residents with appropriate training can safely make the call, ensuring that effective treatment is delivered faster.

"Door-to-needle" times, measured as the time between a patient's arrival and the administration of tPA, were reduced by 26%, from an average of 81 minutes to 60 minutes.

"What's critical here is ability to safely reduce 'door-to-needle' time without unnecessarily increasing the risk of a brain hemorrhage," says Jin-Moo Lee, M.D., Ph.D., director of the cerebrovascular section in Neurology at Washington University and Barnes-Jewish Hospital. "What we've shown is that with proper training, feedback and supervision, residents are more than capable of making this complex decision safely." The study appears online in Stroke.

Although they have completed medical school and passed the license exams necessary to practice general medicine, residents are working in hospitals to undertake more advanced postgraduate training. A select group of critical life-and-death treatment decisions traditionally have been reserved only for physicians who have already completed their residencies.

Stroke treatment is one such decision. At academic and community medical centers, it is usually held for specialists in neurology, or, in some cases, emergency medicine. But while residents are almost always immediately available in the emergency room, neurologists may not be, and the time spent waiting for such a physician to be summoned can allow harm from the stroke to intensify and spread.

For the study, which began in 2004, neurology residents at Barnes-Jewish Hospital started taking an annual three- to four-hour mini-course on use of tPA. The course taught them how to appropriately choose candidates for tPA and how to administer it. After residents were given the authority to administer tPA, a committee of medical faculty and staff met monthly to review the case of every patient evaluated for stroke treatment, giving residents feedback on their decision-making.

Researchers assessed the results by comparing the outcomes and complications of stroke patients treated by residents from 2004 to 2007 against the same data for stroke patients treated by attendings and fellows from 1998 to 2002. There was no significant increase in negative outcomes, including bleeding in the brain, and door-to-needle times were notably shorter for patients treated by residents.

"It makes sense - residents are always in house, and if they can make a direct decision on treatment without waiting for an attending or a fellow to respond to a pager, then the treatment time is going to be shorter," says lead author Andria Ford, M.D., a Washington University neurologist at Barnes-Jewish Hospital.

Neurology residents at Barnes-Jewish Hospital continue to regularly train in tPA usage and to have the authority to administer tPA. Given an academic medical center where the resources exist to expand resident training and provide regular feedback, Lee thinks the model can be applied "across the board - not just to neurologists in training but to emergency department physicians in training, for example."

Lee characterizes the study as the culmination of two major branches of the work of senior author Abdullah Nassief, M.D., a stroke expert who died suddenly of coronary artery disease on Feb. 3. "Dr. Nassief was both director of the neurology department's residency program and of the Clinical Stroke Center and acute rehabilitation program at Barnes-Jewish Hospital, so he was very interested in the residents and in stroke treatment," he says. "In this last paper, he let the resident physicians teach the attending physicians a lesson: that with the proper training, they can make these complex decisions as well as the attendings."

Ford AL, Connor LT, Tan DK, Williams JA, Lee J-M, Nassief AM. Resident-based acute stroke protocol is expeditious and safe. Stroke, online publication.

Stunning finding: Compounds protect against cerebral palsy

Two compounds developed by Northwestern University chemists have been shown to be effective in pre-clinical trials in protecting against cerebral palsy, a condition caused by neurodegeneration that affects body movement and muscle coordination.

"The results were just stunning, absolutely amazing," said Richard B. Silverman, John Evans Professor of Chemistry in the Weinberg College of Arts and Sciences at Northwestern, who led the drug development effort. "There was a remarkable difference between animals treated with a small dose of one of our compounds and those that were not."

The findings, which are published online by the journal Annals of Neurology, suggest that a preventive strategy for cerebral palsy may be feasible for humans in the future. (The paper also will appear in the journal's February issue, in print the week of March 2.)

None of the fetuses born to animals treated with the two compounds died; more than half of those born to untreated animals died. Eighty-three percent of animals treated with one of the compounds were born normal, with no cerebral palsy characteristics. Sixty-nine percent of animals treated with the other compound were born normal. There was no sign of toxicity in the treated animals, and their blood pressure was normal.

Cerebral palsy is caused by an injury to the brain before, during or shortly after birth, although it typically is not diagnosed until after the age of one. Approximately 750,000 children and adults in the United States have a form of cerebral palsy, with the majority having been born with the condition.

The new compounds Silverman and his team developed inhibit an enzyme found in brain cells that produces nitric oxide, thus lowering nitric oxide levels. At normal levels, nitric oxide acts as a neurotransmitter and is important to neuronal functioning, but at high levels it has been shown to damage brain tissue. An overabundance of nitric oxide is believed to play a role in cerebral palsy.

After a lengthy drug development process, Silverman went to his collaborator Sidhartha Tan, M.D., a neonatologist from NorthShore University HealthSystem, to test the two best compounds on Tan's cerebral palsy animal model. A diminished supply of oxygen (hypoxia) from mother to fetus causes an increase in nitric oxide levels in the brain, which leads to brain damage and newborns with cerebral palsy characteristics.

Silverman and Tan wanted to see if they could prevent brain damage in the fetuses by administering one of the compounds to the mother before the hypoxic event. They expected some degree of success but were surprised by how effective the treatment was. The researchers attribute the protection from cerebral palsy to the decrease in the brain enzyme and the nitric oxide that is produced.

"We still have to bring the phenomenon to humans, which would be very exciting," said Tan, who has been investigating the impact of nitric oxide on neuronal damage. "There is such a dire need. If we could safely give the drug early to mothers in at-risk situations, we could prevent the fetal brain injury that results in cerebral palsy."

In developing the potential drugs, Silverman and his team were able to produce something that pharmaceutical companies so far have not: highly selective compounds that inhibit the enzyme found in brain cells that produces nitric oxide but that do not affect similar nitric oxide-producing enzymes found in endothelial and macrophage cells.

Endothelial cells regulate blood pressure, and macrophage cells play an important role in the immune system. Reducing their production of nitric oxide would have deleterious effects on an animal, such as increasing blood pressure or compromising the immune system.

"The challenge was to lower only the nitric oxide in the brain and not in the other cells where the nitric oxide is very important," said Silverman, a member of Northwestern's Center for Drug Discovery and Chemical Biology.

"Early compounds developed by drug companies to target the brain enzyme actually bound to all three nitric oxide enzymes," he said. "This made me think that the three enzymes must be very similar in structure. We decided to look for differences away from the normal binding site to get selectivity for only the brain enzyme."

This approach paid off. Silverman and his team started with a molecule that showed good selectivity of the brain enzyme over the macrophage enzyme but with no selectivity over the endothelial enzyme. The researchers then made modifications to the molecule and built a library of 185 different compounds that could be tested for the selectivity they wanted. They found 10 good ones. More modifications were made until they had a few compounds that were very selective and very potent for the brain enzyme.

Silverman then started collaborating with Thomas Poulos, Chancellor's Professor of Molecular Biology and Biochemistry and a crystallographer from University of California, Irvine, who had been working on the structure of the neuronal brain enzyme. Silverman sent him several potent and selective compounds, and Poulos produced crystal structures showing each compound bound to the brain enzyme.

"Thanks to the talents of Tom and his associate Huiying Li we could, for the first time, see visually why these compounds were selective and also see the difference between them," said Silverman.

Haitao Ji, a postdoctoral fellow who is an expert in structure-based design, joined Silverman's team. Ji took the crystal structures of their molecules bound to the enzyme and, using computer modeling, designed new structures with even better properties.

These compounds were more potent and much more selective than earlier ones. Poulos produced crystal structures of the new compounds. These are the compounds that Tan tested on his cerebral palsy animal model with such promising results, as reported by the research team in the Annals of Neurology paper.

"This is a great example of a multi-institutional collaboration that could not have been done without each of the parts - we each contributed something different," said Silverman. "Science is going in that direction these days." The researchers caution that taking the compounds to human clinical trials is a lengthy and complicated process. Silverman says they next plan to make the compounds even more potent, selective and bioavailable and then envision partnering with a company that would want to develop the drugs further.

Silverman, Tan, Poulos, Li and Ji (lead author) are all authors of the paper, titled "Selective Neuronal Nitric Oxide Synthase Inhibitors and the Prevention of Cerebral Palsy." Other authors are Jotaro Igarashi, from the University of California, Irvine; Matthew Derrick, M.D., from NorthShore University HealthSystem (formerly Evanston Northwestern Healthcare); Pavel Martasek, M.D., and Linda J. Roman, from the University of Texas Health Science Center; and Jeannette Vasquez-Vivar, from the Medical College of Wisconsin.

From One Genome, Many Types of Cells. But How?

Secrets of the Cell - A Cell's Many Faces

This is the first in a series of occasional articles on a frontier of biology - the workings of the cell.

By NICHOLAS WADE

One of the enduring mysteries of biology is that a variety of specialized cells collaborate in building a body, yet all have an identical genome. Somehow each of the 200 different kinds of cells in the human body - in the brain, liver, bone, heart and many other structures - must be reading off a different set of the hereditary instructions written into the DNA.

The system is something like a play in which all the actors have the same script but are assigned different parts and blocked from even seeing anyone else's lines. The fertilized egg possesses the first copy of the script; as it divides repeatedly into the 10 trillion cells of the human body, the cells assign themselves to the different roles they will play throughout an individual's lifetime.

How does this assignment process work? The answer, researchers are finding, is that a second layer of information is embedded in the special proteins that package the DNA of the genome. This second layer, known as the epigenome, controls access to the genes, allowing each cell type to activate its own special genes but blocking off most of the rest. A person has one genome but many epigenomes. And the epigenome is involved not just in defining what genes are accessible in each type of cell, but also in controlling when the accessible genes may be activated. In the wake of the decoding of the human genome in 2003, understanding the epigenome has become a major frontier of research.

Since the settings on the epigenome control which genes are on or off, any derangement of its behavior is likely to have severe effects on the cell. here is much evidence that changes in the epigenome contribute to cancer and other diseases. The epigenome alters with age - identical twins often look and behave a little differently as they grow older because of accumulated changes to their epigenomes. Understanding such changes could help address or retard some of the symptoms of aging. And the epigenome may hold the key to the dream of regenerative medicine, that of deriving safe and efficient replacement tissues from a patient's own cells.

Because the epigenome is the gateway to understanding so many other aspects of the cell's regulation, some researchers have criticized the "piecemeal basis" on which it is being explored and called for a large epigenome project similar to the $3 billion program in which the human genome was decoded. At present the National Institutes of Health has a small, $190 million initiative, called the Epigenome Roadmap, with the money going to individual researchers.

As is often the case, academic researchers oppose a large, centralized project if the money seems likely to come out of their grants. But it is also true that such projects often fail unless carefully timed and thought out. "Definitely this is a genome-sized thing, and I believe it will have benefits beyond what are foreseen at present," says Richard A. Young, a biologist at the Whitehead Institute in Cambridge. But Steven Henikoff of the Fred Hutchinson Cancer Research Center in Seattle says the present methods for studying the epigenome are not yet ready to be scaled up. "It's too early to mount a technology development that would be large scale," he says.

The epigenome consists of many million chemical modifications, or marks as they are called, that are made along the length of the chromatin, the material of the chromosomes. The chromatin includes the double-stranded ribbon of DNA and the protein spools around which it is wound. Some of the marks that constitute the epigenome are made directly on the DNA, but most are attached to the short tails that stick out from the protein spools. Marks of a certain kind generally extend through a large region or domain of the DNA that covers one or more genes. They are recognized by chromatin regulator proteins that perform the tasks indicated by each kind of mark.

In some marked domains, the regulators cause the DNA to be wound up so tightly that the genes are permanently inaccessible. The center and tips of the chromosomes are sites of such repressive domains. So is one of the two X chromosomes in every woman's cells, a step that ensures both male and female cells have the same level of activity of the X-based genes.

In other domains, the marks are more permissive, allowing the gene regulators called transcription factors to find their target sites on the DNA. The transcription factors then recruit other members of the complex transcription machinery that begins the process of copying the genes and making the proteins the cell needs. A third kind of domain must be established ahead of the transcription machinery to let it roll along the DNA and transcribe the message in the underlying gene.

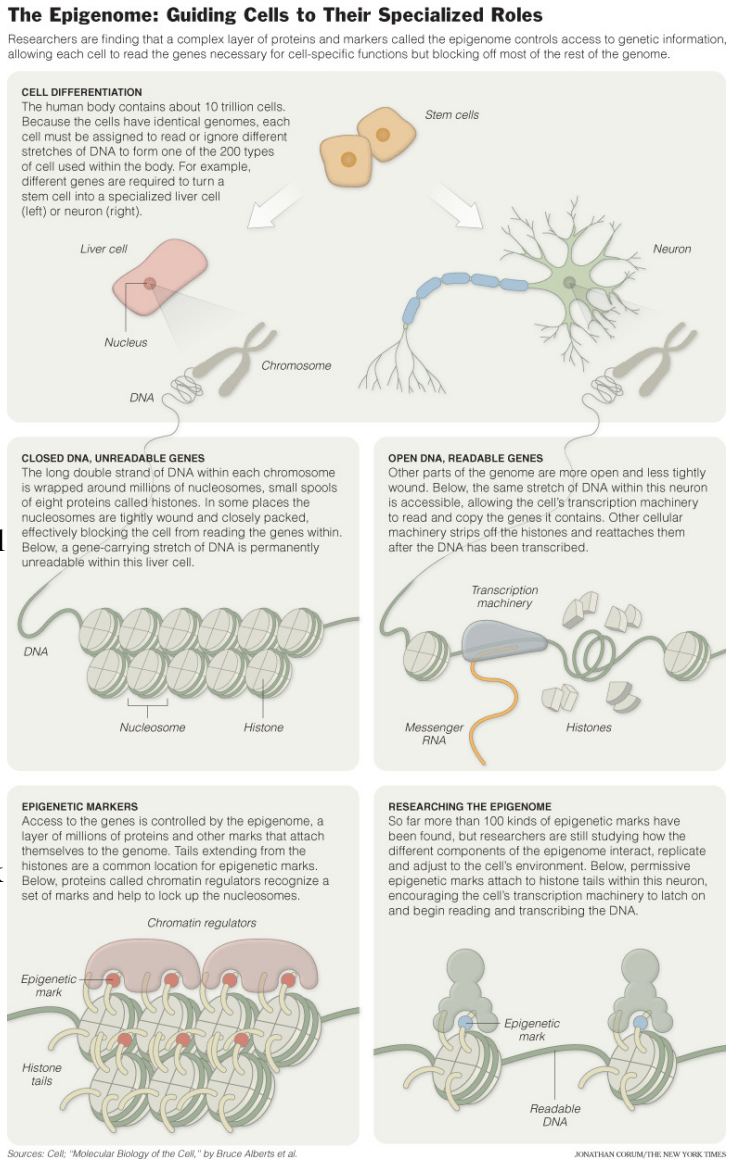
Only a handful of domains are known so far, so it is something of a puzzle that more than 100 kinds of marks have been found in the epigenome, along with specialist protein machines that attach or remove each mark. Some biologists think so many marks are needed to specify a few kinds of domain because the system is full of backups.

The epigenome's role in marking up the genome seems to have been built on top of a more ancient packaging role. The packaging would have been needed by one-celled organisms like yeast that keep their genome in a special compartment, the nucleus. For multi-celled organisms to evolve, the chromatin's packaging system presumably adapted during the course of evolution to index the genome for the needs of different types of cell

The DNA packaging system alone is an extraordinary technical feat. If the nucleus of a human cell were a hollow sphere the size of a tennis ball, the DNA of the genome would be a thin thread some 24 miles long. The thread must be packed into the sphere with no breakages, and in such a way that any region of it can be found immediately.

The heart of the packaging system is a set of special purpose proteins known as histones. Eight histones lock together to form a miniature spool known as a nucleosome. The DNA twists almost twice round each nucleosome, with short spaces in between. Some 30 million nucleosomes are required to package all the DNA of ordinary cells.

For years, biologists assumed that the histones in their nucleosome spools provided a passive framework for the DNA. But, over the last decade, it has become increasingly clear that this is not the case. The histone tails that jut out from the nucleosomes provide a way of marking up the genetic script. Although one kind of mark is attached directly to the bases in the DNA, more than a hundred others are fixed onto specific sites on the histones' tails. When the DNA has to replicate, for cell division, the direct marks pass only to the two parent strands and all the nucleosomes are disassembled, yet the cell has ingenious methods for reconstituting the same marks on the two daughter genomes. The marks are called epigenetic, and the whole system the epigenome, because they are inherited across cell division despite not being encoded in the DNA.



How is the structure of the epigenome determined? The basic blueprint for the epigenomes needed by each cell type seems to be inherent in the genome, but the epigenome is then altered by other signals that reach the cell. The epigenome is thus the site where the genome meets the environment.

The organization of the epigenomes seems to be computed from information inherent in the genome. "Most of the epigenetic landscape is determined by the DNA sequence," says Bradley Bernstein, a chromatin expert at Massachusetts General Hospital. The human genome contains many regulatory genes whose protein products, known as transcription factors, control the activity of other genes. It also has a subset of master regulatory genes that control the lower-level regulators. The master transcription factors act on each other's genes in a way that sets up a circuitry. The output of this circuitry shapes the initial cascade of epigenomes that are spun off from the fertilized egg.

The other shapers of the epigenome are the chromatin regulators, protein machines that read the marks on the histone tails. Some extend marks of a given kind throughout a domain. Some bundle the nucleosomes together so as to silence their genes. Others loosen the DNA from the nucleosome spools so as to ease the path of the transcription machinery along a gene.

Biologists had long assumed that once the chromatin regulators had shaped an epigenome, their work could not be undone because a cell's fate is essentially irreversible. But a remarkable experiment by the Japanese biologist Shinya Yamanaka in June 2007 underlined the surprising power of the master transcription factors.

By inserting just four of the master regulator genes into skin cells, he showed the transcription factors made by the genes could reprogram the skin cell's epigenome back into that of the embryonic cell from which it had been derived. The skin cell then behaved just like an embryonic cell, not a skin cell. Until then, biologists had no idea that the epigenome with its millions of marks could be recast so simply or that transcription factors could apparently call the shots so decisively.

But subsequent research has shown the chromatin regulators are not pushovers. Only one in a million of the skin cells treated with the four transcription factors reverts fully to the embryonic state. Most get stuck in transitional states, as if the chromatin regulators are resisting a possibly cancerous change in the cell's status. "The take-home story is that yes, the transcription factors are really critical players in determining cellular state, but epigenetics is important, too," Dr. Bernstein said.

The ideal of regenerative medicine is to convert a patient's normal body cells first back into the embryonic state, and then into the specific cells lost to disease. But to prepare such cells safely and effectively, researchers will probably need to learn how to control and manipulate the chromatin of the epigenome as well as the transcription factors that shape cell identity.

The treatment of many diseases may also lie in drugs that manipulate the epigenome. Rett syndrome, a form of autism that affects girls, is caused by a mutation in the gene for an enzyme that recognizes the chromatin marks placed directly on the DNA. At least in mice, the neurons resume normal function when the mutation is corrected. In several forms of cancer, tumor-suppressor genes turn out to have been inactivated not by mutation, the usual known cause, but by the incorrect placement of marks that invite chromatin regulators to silence the genes.

Drugs developed by Peter A. Jones of the University of Southern California reverse the chromatin silencing of these antitumor genes. Two have recently been approved by the Food and Drug Administration for a blood malignancy, myelodysplastic syndrome.

Besides governing access to the genome, the epigenome also receives a host of signals from the environment. A family of enzymes called sirtuins monitors the nutritional state of the cell, and one of them removes a specific mark from the chromatin, providing a possible route for the genome to respond to famine conditions. Accumulating errors in the epigenome's regulation could allow the wrong genes to be expressed, a possible cause of aging.

A principal new technique for studying the marks on an epigenome is to break the chromosomes into fragments, which are then treated with antibodies that bind to a specific mark. The DNA fragments so designated are decoded and matched to sites on the human genome sequence. This provides a genome-wide map of how a particular mark is distributed in a particular epigenomic state. The CHiP-seq maps, as they are called, have been very useful but are far from capturing the full detail of the epigenome, a dynamic structure that can change in minutes.

Individual researchers have made considerable progress but may not be able to assemble the comprehensive set of epigenomic marks and states that would be most useful to those developing new approaches to disease and aging. "I think the effort needs to be organized," Dr. Young said. "It would benefit from being larger than it is."

'Happiness' gene helps you look on the bright side

* 11:03 25 February 2009 **by Andy Coghlan**

Positive people may owe their optimism to a gene variant that helps them dwell on the good and ignore the bad.

That's the conclusion from a study examining people's subliminal preferences for happy, neutral, and threatening images.

Volunteers who had inherited two copies of the "long" variant of 5-HTTLPR - a gene that controls transport of the mood-affecting neurotransmitter serotonin - showed clear avoidance of negative images, such as fierce animals, and a clear preference for positive ones, such as puppies. People with this variant combination are dubbed "LL" carriers.

The effect wasn't seen in volunteers with at least one version of the "short" variant of the same gene - these people showed no strong preference whatever the content of the images.

Time lapse

In repeated tests, the 97 volunteers had less than a second to identify dots hidden in one or other of a pair of adjacent images. Each pair contained a neutral image alongside one that was either positive or negative.

The researchers found that LL volunteers took 18.3 milliseconds longer on average to spot the dots in a negative rather than neutral image, suggesting a subliminal aversion to bad images.

Conversely, they noticed the dots 23.5 milliseconds sooner in the positive images, such as cuddly puppies, than in the neutral ones, suggesting they were subliminally drawn to them. "It sounds very small, but in terms of attentional time, it's consistent," says team leader Elaine Fox of the University of Essex in Colchester, UK.

Optimistic streak

Fox and her colleagues conclude that the LL volunteers may be primed to seek out positive events and ignore negative events. Earlier studies had revealed a tendency for negativity and anxiety among individuals with at least one short variant of the gene, but the study is the first to reveal an optimistic streak in LL individuals.

"A number of mechanisms may contribute to this difference, and the authors have provided good evidence that attentional bias in the processing of emotional stimuli may be one of those mechanisms," says Turhan Canli, who has studied the same phenomenon at Stony Brook University in New York.

Journal reference: Proceedings of the Royal Society B (DOI: 10.1098/rspb.2008.1788)

Why do some people kill themselves?

* 25 February 2009 **by Robert Pool**

FOR a few months in late 2006 and early 2007, the woman who called herself kristi4 was one of the best-known members of the pro-anorexia community. As the administrator of a blog on LiveJournal.com, she dispensed advice, encouraged others and wrote candidly about her own struggles. Then, late one Friday night, after a series of entries describing what she was planning to do, kristi4 killed herself with an overdose of prescription sleeping pills, muscle relaxants and painkillers.

Her death was just one tragic data point in one of the most striking statistics in all of psychology. It has long been known that anorexia has the highest death rate of any mental illness: one out of every five people with anorexia eventually die of causes related to the disease. What has only now been recognised, however, is that a huge number of those deaths are from suicide rather than starvation. Someone who develops anorexia is 50 to 60 times more likely to kill themselves than people in the general population. No other group has a suicide rate anywhere near as high (Archives of General Psychiatry, vol 60, p 179).

Recently, psychologists have tried to explain why anorexia and suicide are so intimately connected, something which is helping to answer the wider question of why anyone would commit suicide. If this explanation holds up, it will give psychiatrists a new tool for screening patients and determining which of them are most likely to kill themselves, perhaps saving lives.

Suicide has always been a conundrum for psychologists and other researchers interested in human behaviour. Self-preservation is one of the strongest human instincts, so the drive to commit suicide must be even more powerful. But what causes it?

A century ago, both the sociologist Emile Durkheim and the psychoanalyst Sigmund Freud came up with sweeping explanations. Durkheim, not surprisingly, saw the roots of suicide in social factors, such as a failure to integrate into society, while Freud rooted his explanation in instinctual drives, particularly what he called the death instinct. More recent explanations have tended to focus on factors such as depression, hopelessness and emotional pain, but none of them have had much success in answering the fundamental question about suicide: why do some people kill themselves while others in seemingly identical circumstances do not?

Some progress has been made by crunching large amounts of data on suicide, says Harvard University psychologist Matthew Nock, who studies suicide and self-harm. Researchers have learned, for example, that suicide rates are rising and now account for 1.5 per cent of all deaths worldwide. Suicide is the second leading cause of death among people aged 15 to 24, after vehicle accidents. Women are more likely than men to attempt suicide, while men are much more likely to succeed.

1 million Approximate number of suicides worldwide each year

Most people who commit suicide have a mental disorder - anorexia, major depressive disorder, bipolar disorder, schizophrenia and borderline personality disorder are the most common, but an elevated suicide risk is part and parcel of many of the others, too. People who kill themselves also generally feel deeply depressed and hopeless at the time.

Every 40 seconds somebody dies by suicide

What the statistics do not tell us - and what psychologists most want to know - is exactly which people are most at risk. The vast majority of depressed, hopeless people do not commit suicide, so why do some do it?

In 2005, psychologist Thomas Joiner, a suicide specialist at Florida State University in Tallahassee whose own father committed suicide, set out to answer that question. By studying suicide statistics and paying particular attention to the groups with above average rates, Joiner believes he has found a common thread others have missed. "It was the first grand theory of suicide in quite a while," says Nock.

In essence, Joiner proposed that people who kill themselves must meet two sets of conditions on top of feeling depressed and hopeless. First, they must have a serious desire to die. This usually comes about when people feel they are an intolerable burden on others, while also feeling isolated from people who might provide a sense of belonging.

Second, and most important, people who succeed in killing themselves must be capable of doing the deed. This may sound obvious, but until Joiner pointed it out, no one had tried to figure out why some people are able to go through with it when most are not. No matter how seriously you want to die, Joiner says, it is not an easy thing to do. The self-preservation instinct is too strong.

There are two ways people who want to die develop the ability to override the self-preservation instinct, Joiner argues. One is by working up to it. In many cases a first suicide attempt is tentative, with shallow cuts or a mild overdose. It is only after multiple attempts that the actions are fatal.

20 Number of failed suicide attempts for each successful one

The other is to become accustomed to painful or scary experiences. Soldiers and police who have been shot at or seen their colleagues injured or killed are known to become inured to the idea of their own death. Both groups also have a higher-than-normal suicide rate. Similarly, doctors and surgeons who witness pain, injury and death are more likely to be able to contemplate it for themselves - the suicide rate for doctors is significantly higher than for the general population. Joiner describes this as a "steeliness" in the face of things that would intimidate most people.

Another group that displays steeliness are people with anorexia. Joiner had noted their heightened suicide rate in his original work, Why people die by suicide (Harvard University Press, 2005), but it wasn't until later that he grasped the importance of the connection.

That realisation began to dawn in 2006, during a seminar in which two of Joiner's graduate students, Jill Holm-Denoma and Tracy Witte, were listening to him describe the risk of suicide among people with anorexia. Witte observed that the high suicide rate had two possible explanations. Perhaps people with anorexia were no more likely to attempt suicide than people with other mental disorders, but the anorexia had so weakened their bodies that their suicide attempts were more likely to succeed. Alternatively, perhaps anorexia had so inured them to pain that they were more capable than others of doing what was necessary to kill themselves.

According to Joiner's hypothesis, the second explanation should be correct. So Holm-Denoma set out to test the prediction. She examined nine suicides chosen randomly, and what she found told a very clear story.

"These people would have died regardless of their body weight," she says. "We were just astounded by the lengths to which they went to make sure they were successful." Three jumped in front of trains. Two hung themselves. Two took large drug overdoses. One poisoned herself with sleeping pills and toilet bowl cleaner. And one locked herself in a gas station restroom and set fire to a trash can that produced enough carbon monoxide to asphyxiate her. Nine cases, of course, are not enough to prove the point, but the fact that all took such drastic measures to kill themselves says something (Journal of Affective Disorders, vol 107, p 231).

Anorexia offers a "perfect storm" of the factors laid out in Joiner's hypothesis, Holm-Denoma says. Social isolation is likely because people with anorexia avoid any interactions that might involve food - so that means not going out for a meal, no movies (the popcorn might be too tempting) and no stopping by a friend's house. The result is the "thwarted belongingness" that Joiner describes as a key factor in suicide.

Then there is the feeling that they have become an intolerable burden to their family and friends. One popular approach to treating anorexia in children, for example, involves having a parent oversee their child full-time.

Most importantly, anorexia means becoming inured to pain. Merciless starvation leads to intense and painful hunger pangs and major headaches. Osteoporosis is common, making fractures more likely, not to mention the chest pains caused by heart damage. Kristi4's blogs in the month leading up to her suicide show this perfect storm at work.

It is one of the strengths of Joiner's explanation, says Nock, that it makes testable predictions such as the one spotted by Witte. For example, it should be possible to develop psychological tests to measure how much of a burden people feel, or how thwarted, and then use them to predict who will commit suicide. It should also be possible to examine rates of suicide among various groups with the characteristics Joiner is talking about.

Those tests are slowly taking shape. Recent work by some of Joiner's students has shown that people who feel they are a burden and also experience thwarted belongingness are more likely to have suicidal thoughts (Journal of Consulting and Clinical Psychology, vol 76, p 72). A second study found that "painful and provocative events", such as shooting a gun or getting into a fight, tend to increase something Joiner calls "acquired capability" - a written test that measures someone's ability to hurt or kill themselves.

Meanwhile, University of Minnesota psychiatrist Scott Crow has studied suicide rates among people with bulimia and found that they, too, kill themselves at a much higher rate than the general population. Crow has found a four to six-fold increase in suicides in this group. Bulimia starves the body at some level, as indicated by various biochemical markers, so people with bulimia may well be inured to pain in much the same way as those with anorexia.

60 per cent increase in worldwide suicide rates since 1965

Even though the evidence is all pointing in the same direction, Joiner says many more tests will be needed before his ideas can be accepted as a general explanation for suicide. "It's a start," he says of the evidence assembled to date. "But we need something much more systematic."

Ultimately, he says, a better understanding of why people commit suicide should help clinicians better assess who is most at risk, and find new ways of preventing people from killing themselves. Long-term psychotherapy, for instance, could help chip away at a person's fearlessness and lessen the likelihood that they will commit suicide.

But as long as people steel themselves to pain, as long as they feel isolated and a burden to others, Joiner's theory predicts that suicide will be with us as well.

Robert Pool is a writer based in Tallahassee, Florida

Asteroid belt may bear scars of planets' migration

* 19:12 25 February 2009 **by Rachel Courtland**

Today's asteroid belt may have been shaped by a tumultuous period in the early solar system when Jupiter and Saturn moved out of their original orbits, a new simulation suggests. Ultimately the work could help refine a picture of how quickly the planets moved and where they got their start.

Recent studies have suggested that many objects in the solar system were reshuffled nearly 4 billion years ago. Jupiter, Saturn, Uranus, and Neptune, are thought to have been born close together before gravitational interactions with numerous pieces of rocky debris changed their trajectories.

Their movement then caused the rocky debris to scatter like bowling pins, potentially explaining what battered the Earth, Moon, and Mars with so many craters some 3.8 billion years ago.

Now, this same reshuffling might explain the appearance of the main asteroid belt between Mars and Jupiter.

Several grooves in the belt seem to be empty of asteroids. Called Kirkwood gaps, they are thought to be cleared of debris by Jupiter's gravity, which causes any objects orbiting there to move chaotically. Saturn's moons have produced similar gaps in the planet's rings.

David Minton and Renu Malhotra at the University of Arizona in Tucson wanted to reproduce the asteroid belt and its gaps in a computer simulation.

Shifting position

Using the current orbits of the giant planets Jupiter, Saturn, Uranus, and Neptune, the team was able to roughly replicate the observed distribution of asteroids over a simulated period of some 4 billion years.

But they had much better luck when they started out with the best estimates of where the giant planets were early in the solar system's history. The four planets are thought to have started out relatively close together. Then, Jupiter moved inward while Saturn, Uranus and Neptune moved outward.

"We're able to produce an asteroid belt that's much more like the observed asteroid belt than a model that only uses the giant planets in their current positions," Minton says.

Eroding belt

In this version of the simulation, two of the belt's gaps showed a distinct signature: a sharp inner edge and a smeared out, relatively empty outer edge.

That is what would be expected if Jupiter carved the gaps as it migrated towards the Sun. In that case, the gaps' inner edges represent where Jupiter stopped in its migration, says Minton. Such a gap "profile" is a closer match to the observed asteroid distribution than the team's other simulation using the planets' current orbits, he adds.

Saturn's outward migration also seems to have left its imprint on the asteroid belt. But in Saturn's case, it was on the inner edge of the entire belt - not the gaps. At the belt's inner edge, asteroids were lost because their orbits were destabilised by the natural wobble of Saturn's orbit over time. This erosion continued as Saturn moved outward, so that the inner edge of the belt is determined by the Ringed Planet's current orbit.

Migration speed

In the simulation, the belt lost 62% of its original population of asteroids due to the migration of the giant planets. But some estimate that the real asteroid belt actually lost some 90 to 95% of its asteroids.

The slower the planets' migration, the more asteroids will be lost due to gravitational interactions with them. "If the planets were migrating too slowly, you wouldn't have an asteroid belt," Minton told New Scientist.

By refining the model, astronomers could get a better sense of how long the migration took and where the planets got their start, he adds. And if cast-out asteroids are responsible for the Late Heavy Bombardment that pounded the Earth, Moon, and Mars 3.8 billion years ago, modelling the belt could also help determine how long the outburst might have lasted. *Journal reference: Nature (vol 457, p 1109)*

Reproductive factors may protect women from Parkinson's disease

SEATTLE – A large new study provides evidence that longer exposure to the body's own hormones may protect women from Parkinson's disease. The study was released today and will be presented at the American Academy of Neurology's 61st Annual Meeting in Seattle, April 25 to May 2, 2009.

The study found that women who have more years of fertile lifespan (number of years from first menstruation to menopause) had a lower risk of developing the disease than women with fewer years of fertile lifespan. The fertile lifespan is a marker for the body's own sex hormone levels. In addition, women with four or more pregnancies were at greater risk of developing the disease than women with fewer pregnancies. Separately, the risk of Parkinson's disease was increased in women who had hysterectomies and had also previously taken hormone replacement therapy compared to those who never took hormone therapy, but it was not increased in women who took the hormones but had not had hysterectomies.

"These findings suggest that longer duration of exposure to the body's own (endogenous) hormones may help protect the brain cells that are affected by Parkinson's disease. Further investigation is necessary to explain why women with four or more pregnancies are at increased risk compared with those with fewer pregnancies. This study does not support a role for treatment with hormone therapy in Parkinson's, but there are still many unanswered questions," said study author Rachel Saunders-Pullman, MD, MPH, MS, of Albert Einstein College of Medicine in Bronx, NY, and Beth Israel Medical Center in New York, NY, and a member of the American Academy of Neurology.

For the study, researchers analyzed the records of the Women's Health Initiative Observational Study to determine who developed Parkinson's disease. The study involved about 74,000 women who underwent natural menopause and about 7,800 women who underwent surgical menopause.

Among women with natural menopause, those who had a fertile lifespan of more than 39 years, which is a time associated with higher levels of the body's own sex hormones, had about a 25-percent lower risk of developing the disease than women with a fertile lifespan shorter than 33 years. Researchers also looked at the number of pregnancies, and women who had four or more pregnancies were about 20 percent more likely to develop Parkinson's disease than women who had three or fewer pregnancies.

Women who had menopause from surgery had almost twice the risk of developing the disease if they had previously taken hormone therapy and stopped than if they had never taken hormone therapy. Taking hormones did not have any effect on Parkinson's risk for women who had natural menopause.

Because Parkinson's disease is more common in men than in women, researchers have long hypothesized about the role of hormones in the disease.

The study was supported by the Thomas Hartman Foundation for Parkinson's Research and the National Institutes of Health.

BUSM researchers encourage use of potassium iodide

Researchers from Boston University School of Medicine (BUSM) are strongly encouraging prenatal vitamin manufacturers to use only potassium iodide and not other sources of iodine in their products. According to the researchers, potassium iodide is the best way to ensure that prenatal vitamins given to expectant mothers receive 150µg of supplemental daily iodine as recommended by the American Thyroid Association. The researchers' recommendation appears as a research letter in the February 26th issue of the New England Journal of Medicine.

Normal thyroid function in fetuses and breastfed infants, which is dependent on sufficient maternal dietary intake of iodine, is crucial for normal neurocognitive development. Iodine deficiency affects more than 2.2 billion persons and is the leading cause of preventable mental retardation worldwide. Even mild iodine deficiency may have adverse effects on the cognitive function of children.

Using the Internet, the BUSM researchers identified 127 nonprescription and 96 prescription prenatal multivitamins currently marketed in the U.S. Of these multivitamins, 114 (87 nonprescription and 27 prescription) contained iodine. According to the label, 89 percent contained 150µg or more of iodine per serving. The iodine was in the form of kelp in 42 multivitamins, potassium iodide in 67, or another ingredient in five.

The researchers then measured the iodine content in 60 randomly selected iodine-containing prenatal multivitamins and compared the results with the values on their labels. They found that the iodine measured in those containing potassium iodide was approximately 75 percent of that stated on their labels. In contrast, the multivitamins containing kelp had large variations in their iodine content.

"The American Thyroid Associated has recommended that women receive prenatal vitamins containing 150µg of iodine daily during pregnancy and lactation. However, the iodine content of prenatal vitamins is not mandated in the United States," said author Elizabeth Pearce, MD, an assistant professor of medicine at BUSM, on behalf of her co-authors, Angela Leung, MD and Lewis Braverman, MD.

"In order to maintain consistency of labeling and to ensure these vitamins contain the recommended dosage, we strongly propose that the manufacturers of these products use only potassium iodide at a dose of 200µg per serving," she added.

Crab claws pack strengthening bromide-rich biomaterial

University of Oregon-led study is part of effort to tap nature's secrets for building tiny tools

Next time you have an unlucky encounter with a crab's pinchers, consider that the claw tips may be reinforced with bromine-rich biomaterial 1.5 times harder than acrylic glass and extremely fracture resistant, says a University of Oregon scientist.

Residents on the U.S. West Coast may have had close encounters with the biomaterial -- detailed by a seven-member team in a paper published online in advance of regular publication in the Journal of Structural Biology. The translucent substance empowers the claw tips of the striped (or lined) shore crab (Pachygrapsus cassipes) as the pinchers pick and hold prey. It also is present on the walking legs of Dungeness crabs (Cancer magister), a dining delicacy in the Pacific Northwest.

"The types of crabs that use this trick for their claw tips rely on the tips fitting together like forceps in order to pick and hold bits of food, and fracture damage could make the tips useless," said the study's lead author Robert Schofield, a researcher in the UO physics department. "These crabs include many common crabs such as hermit crabs, which have one large claw for crushing, and a small claw tipped with this newly discovered biomaterial for finer work."

The claws of the Dungeness crab, he noted, are designed for crushing instead of fine manipulations, and are not tipped with this material. But their legs are, he said.

"The next time you are eating a Dungeness crab, notice that the sharp tip of the leg is a cap of translucent material that is very different from the rest of the crab," he said. "Notice how difficult it is to break the tip, even though it is very thin. This biomaterial can bend six times further before breaking than the material used in other regions. If the tip were made of the same material as the rest of the crab, it could never stay sharp and the crab would have difficulty clinging."

This bromine-rich material at the tips of crab claws and legs is a new member of a class of structural biomaterials that employ heavy atoms like zinc, iodine and iron. "It's not yet clear why heavy elements are used," Schofield said. "Perhaps the mass of the atoms themselves plays a role in damping vibrations that can lead to fracture."

These heavy-element biomaterials had escaped notice until now because they are typically employed by small organisms such as insects. Schofield was lead author of a study published in 2001 that had identified their presence in mandibular teeth, tarsal claws, stings and other such tools of small organisms.

In order to measure the mechanical properties of these tiny structures, the researchers had to develop machines and techniques that would work for tiny samples.

"It turns out that fracture tends to be a bigger problem for small organisms than for large ones," Schofield said. "Humans are just starting to try to engineer tiny machines and tools, and we have a lot still to learn from organisms that have coped with being small for millions of years."

Co-authors with Schofield on the National Science Foundation-supported research were UO undergraduate student Jack C. Niedbala, Michael H. Nesson of Oregon State University, Ye Tao of the Chinese Academy of Sciences in Beijing, Jacob E. Stokes and Robert A. Scott of the University of Georgia, and Matthew J. Latimer of the Stanford Synchrotron Radiation Laboratory.

Earliest 'human footprints' found

The earliest footprints showing evidence of modern human foot anatomy and gait have been unearthed in Kenya.

The 1.5-million-year-old footprints display signs of a pronounced arch and short, aligned toes, in contrast to older footprints. The size and spacing of the Kenyan markings - attributed to Homo erectus - reflect the height, weight, and walking style of modern humans. The findings have been published in the journal Science.

The footprints are not the oldest belonging to a member of the human lineage. That title belongs to the 3.7 million-year-old Australopithecus afarensis prints found in Laetoli, Tanzania, in 1978.

Those prints, however, showed comparatively flat feet and a significantly higher angle between the big toe and the other toes, representative of a foot still adapted to grasping.

Exactly how that more ape-like foot developed into its modern version has remained unclear.

The fossil record is distinctly lacking in foot and hand bones, according to lead author Matthew Bennett of Bournemouth University, UK.

"The reason is that carnivores like to eat hands and feet," Professor Bennett told BBC News.

"Once the flesh is gone there's a lot of little bones that don't get preserved, so we know very little about the evolution of hands and feet on our ancestors."

The footprints were found near Ileret in northern Kenya. The site, on a small hill, is made up of metres of sediment which the researchers carefully cleared away.

What they found was two sets of footprints, one five metres deeper than the other, separated by sand, silt, and volcanic ash.

The team dated the surrounding sediment by comparing it with well-known radioisotope-dated samples from the region, finding that the two layers of prints were made at least 10,000 years apart.

Another critical feature that the series of footprints makes clear is how Homo erectus walked.

There is evidence of a heavy landing on the heel with weight transferred along the outer edge of the foot, progressing to the ball of the foot and lifting off with the toes.

"That's very diagnostic of the modern style of walking, and the Laetoli prints don't give that same character," Professor Bennett said.

The finding is a critical clue for mapping out the evolution of modern humans, both in terms of physiology and also how H. erectus fared in its environment.

H. erectus was a great leap in evolution, showing increased variety of diet and of habitat, and was the first Homo species to make the journey out of Africa.

"There's some suggestion out there that Homo erectus was able to scour the landscape for carcasses and meat...and was able to get there very quickly, had longer limbs and was much more efficient in terms of long distance travel," Professor Bennett added.

"Now we're also saying it had an essentially modern foot anatomy and function, which also adds to that story."

Psychologists shed light on origins of morality: study suggests bad behaviour really does leave a "bad taste in your mouth"

Feb. 26/09 **By Kim Luke**

In everyday language, people sometimes say that immoral behaviours "leave a bad taste in your mouth". But this may be more than a metaphor according to new scientific evidence from the University of Toronto that shows a link between moral disgust and more primitive forms of disgust related to poison and disease.

"Morality is often pointed to as the pinnacle of human evolution and development," says lead author Hanah Chapman, a graduate student in the Department of Psychology. "However, disgust is an ancient and rather primitive emotion which played a key evolutionary role in survival. Our research shows the involvement of disgust in morality, suggesting that moral judgment may depend as much on simple emotional processes as on complex thought." The research is being published in Science on February 27, 2009. A complete press package, including images is available on Eureka Alert.

In the study, the scientists examined facial movements when participants tasted unpleasant liquids and looked at photographs of disgusting objects such as dirty toilets or injuries. They compared these to their facial movements when they were subjected to unfair treatment in a laboratory game. The U of T team found that people make similar facial movements in response to both primitive forms of disgust and moral disgust.

The research employed electromyography, a technique that uses small electrodes placed on the face to detect electrical activation that occurs when the facial muscles contract. In particular, they focused on movement of the levator labii muscle, which acts to raise the upper lip and wrinkle the nose, movements that are thought to be characteristic of the facial expression of disgust.

"We found that people show activation of this muscle region in all three situations – when tasting something bad, looking at something disgusting and experiencing unfairness," says Chapman.

"These results shed new light on the origins of morality, suggesting that not only do complex thoughts guide our moral compass, but also more primitive instincts related to avoiding potential toxins," says Adam Anderson, principal investigator on the project and the Canada Research Chair in Affective Neuroscience. "Surprisingly, our sophisticated moral sense of what is right and wrong may develop from a newborn's innate preference for what tastes good and bad, what is potentially nutritious versus poisonous."

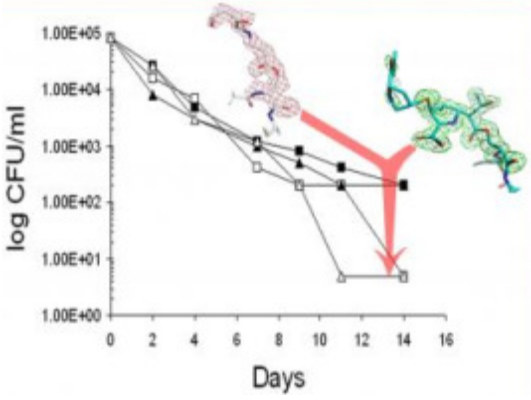
The research was supported by the National Sciences and Engineering Research Council of Canada (NSERC) and the Canada Research Chairs program. In addition to Anderson and Chapman, the U of T team included David Kim and Joshua Susskind.

Antibiotic combination defeats extensively drug-resistant TB

Clinical trials planned for late 2009

BRONX, NY – A combination of two FDA-approved drugs, already approved for fighting other bacterial infections, shows potential for treating extensively drug resistant tuberculosis (XDR-TB), the most deadly form of the infection. This finding is reported by scientists from Albert Einstein College of Medicine of Yeshiva University in the February 27 issue of Science.

TB is caused by the bacterium Mycobacterium tuberculosis (Mtb). An estimated one-third of the world's population is infected with TB. Active disease develops in approximately 10 percent of infected people over a lifetime - particularly those with weak immune systems such as infants, the elderly, and people infected with HIV. Globally, cases of active TB have increased significantly since the 1980s due to the AIDS pandemic and the emergence of Mtb strains resistant to standard antibiotic treatment.



The combination of the beta-lactamase inhibitor (Structure on left) and meropenem (Structure shown on right) lead to rapid sterilization of cultures of TB. **Albert Einstein College of Medicine**

In the Science paper, Einstein researchers and collaborators at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, describe a two-drug combination that inhibited both the growth of susceptible laboratory strains and 13 XDR-TB strains isolated from TB patients in laboratory culture medium. The drugs truly work in tandem: one of them (clavulanate) inhibits a bacterial enzyme, β-lactamase, which normally shields TB bacteria from the other antibiotic (meropenem, a member of the β-lactam class of antibiotics).

The idea of inhibiting β-lactamase to make β-lactam antibiotics effective isn't new - which is why β-lactamase inhibitors, such as clavulanate, already exist. The strategy finally proved effective against XDR-TB because Einstein researchers conducted a detailed, methodical investigation of the β-lactamase enzyme to find the ideal combination of β-lactamase inhibitor and β-lactam antibiotic. β-lactam antibiotics include penicillin, the first antibiotic discovered and one of the safest. Amoxicillin/clavulanic acid and meropenem have excellent safety profiles and are FDA-approved for adult and pediatric use.

"This is a great example of how, in a collaborative environment, basic, old-fashioned, hypothesis-driven science can lead to timely clinical applications," said John S. Blanchard, Ph.D., Dan Danciger Professor of Biochemistry at Einstein and senior author of the Science paper, whose research was funded by NIAID.

In parts of Asia, 70 percent of new TB cases are multi-drug resistant, meaning they don't respond to the two antibiotics most commonly used against TB. Recently, an even greater health threat has emerged: extensively drug-resistant (XDR) bacteria that resist at least four of the drugs used to treat TB and can prove deadly. The cure rate for patients infected with XDR-TB ranges from 12 percent to 60 percent.

XDR-TB is still rare in the United States - 83 cases were documented by the Centers for Disease Control and Prevention between 1993 and 2007. However, worldwide, the figures are much larger and on the rise. In 2004, the World Health Organization (WHO) estimated a half-million people were infected with multi-drug resistant TB, and in some countries the percentage of XDR-TB cases is growing. In the only global TB study to date, the WHO reported in 2008 that 15 percent of multi-drug resistant TB cases in Ukraine, for example, were XDR-TB.

Current TB therapy requires four antibiotics that must be taken for at least six months. "If proven in human subjects, the ability to simplify treatment to just two drugs that work against drug-susceptible, multi-drug resistant and XDR-TB could help patients better adhere to therapy," said Dr. Blanchard, whose laboratory has conducted pioneering studies of fundamental aspects of antibiotic resistance.

"This discovery could be one of the most promising developments in TB research since the discovery of isoniazid - it is very exciting," said William Jacobs, Ph.D., referring to the first effective antituberculosis medication discovered in the 1950s. Dr. Jacobs is a Howard Hughes Investigator and professor of microbiology & immunology at Einstein and associate director of the Einstein-Montefiore Center for AIDS Research.

Currently, clavulanate is not commercially available, except in combination with β-lactam antibiotics, such as amoxicillin. This combination of clavulanate and amoxicillin has been used against other types of bacteria to inhibit β-lactamase activity and make β-lactams more effective. But it has rarely been used against TB, which is why the β-lactamase inhibitor/β-lactam approach had not been comprehensively analyzed until now.

NIAID researcher Clifton E. Barry, III, Ph.D., a co-author of the new paper, is leading plans to launch a phase two clinical study of the clavulanate potassium-meropenem drug combination in South Korea by the end

of 2009 involving approximately 100 TB patients. NIAID investigators are currently working with manufacturers to provide the drugs needed for the trial.

Additionally, as part of a joint collaboration between Montefiore Medical Center, The University Hospital and Academic Medical Center for Albert Einstein College of Medicine, and the Nelson Mandela School of Medicine in Durban, South Africa, a separate trial slated for 2009 will test the potency of the drug combination in a smaller number of TB patients. If the results are successful and funding is available, a trial involving a larger number of XDR-TB patients will be conducted. Montefiore researchers chose South Africa for the clinical studies because of its disproportionately high number of XDR-TB cases. In some areas of South Africa, one in four TB cases is extensively drug resistant.

"We see tremendous potential for treating not only XDR-TB cases, but also routine TB cases," said Brian Currie, M.D., M.P.H., assistant dean for clinical research, and professor of medicine and of clinical epidemiology and population health at Einstein. Dr. Currie is also vice president and medical director for research at Montefiore. He will serve as U.S. leader for the planned clinical studies in Durban.

With the hope that the meropenem/clavulanate combination proves highly effective in the planned clinical trials, Einstein has filed a patent application on this novel TB treatment method as an incentive for commercial drug manufacturers to support expanded clinical trials and to develop with Einstein an improved combination clavulanate-β-lactam drug formulation that may be optimized for routine use in TB treatment.

The research and clinical components of these studies will help fulfill the mission of a $22 million Clinical and Translational Science Award given to Einstein and Montefiore by the National Center for Research Resources of the NIH in 2008. The grant supports the new Einstein-Montefiore Institute for Clinical and Translational Research (ICTR) whose goal is to collaboratively expedite the transfer of research discoveries to patient care.

Do doodle: Research shows doodling can help memory recall

Doodling while listening can help with remembering details, rather than implying that the mind is wandering as is the common perception. According to a study published today in the journal Applied Cognitive Psychology, subjects given a doodling task while listening to a dull phone message had a 29% improved recall compared to their non-doodling counterparts.

40 members of the research panel of the Medical Research Council's Cognition and Brain Sciences Unit in Cambridge were asked to listen to a two and a half minute tape giving several names of people and places, and were told to write down only the names of people going to a party. 20 of the participants were asked to shade in shapes on a piece of paper at the same time, but paying no attention to neatness. Participants were not asked to doodle naturally so that they would not become self-conscious. None of the participants were told it was a memory test.

After the tape had finished, all participants in the study were asked to recall the eight names of the party-goers which they were asked to write down, as well as eight additional place names which were included as incidental information. The doodlers recalled on average 7.5 names of people and places compared to only 5.8 by the non-doodlers.

"If someone is doing a boring task, like listening to a dull telephone conversation, they may start to daydream," said study researcher Professor Jackie Andrade, Ph.D., of the School of Psychology, University of Plymouth. "Daydreaming distracts them from the task, resulting in poorer performance. A simple task, like doodling, may be sufficient to stop daydreaming without affecting performance on the main task."

"In psychology, tests of memory or attention will often use a second task to selectively block a particular mental process. If that process is important for the main cognitive task then performance will be impaired. My research shows that beneficial effects of secondary tasks, such as doodling, on concentration may offset the effects of selective blockade," added Andrade. "This study suggests that in everyday life doodling may be something we do because it helps to keep us on track with a boring task, rather than being an unnecessary distraction that we should try to resist doing."

(27th February 2009 is National Doodle Day - http://www.nationaldoodleday.org.uk/)

Youths are most influenced by negative family members and by positive adults outside the family

While children look up to and aspire to be like a positive family member or peer, they are more likely to imitate traits of other role models -- including negative role models, which can lead to behavioral problems, according to a Kansas State University researcher.

Brenda McDaniel, assistant professor of psychology at K-State, worked with colleagues at Oklahoma State University-Tulsa to study the relationship of moral traits shared by youths and their role models to find predictors of outcomes like youth conduct problems.

"Understanding the relationship between youths' view of self, youths' view of role models and youths' behavioral and psychological outcomes provides the knowledge to foster healthy, successful youth," McDaniel said.

The researchers surveyed 30 boys and girls, ages 7 to 14, from Boys and Girls clubs in Manhattan and in Tulsa, Okla. McDaniel said all of the participants in the study were categorized as having a lower socioeconomic status, lower academic outcomes and being at-risk.

The study asked students who they considered to be their role models or wanted to be like, and who they considered to be their anti-role models or didn't want to be like. Students rated their choices and themselves on 10 sets of moral constructs using a five-point scale, like being unfair versus fair and forgiving versus not forgiving. The youths also measured themselves on their pro-social behavior and relational aggression, and provided parenting styles experienced in their home.

Though the youths reported their ideal selves being most like a positive family member and a positive peer, results showed students were most similar to a positive adult outside the family. This provides support for programs such as Big Brothers Big Sisters where an adult outside the home spends time with the youth, McDaniel said.

The researchers also found that negative family members are a strong influence on the moral traits of youths. McDaniel said children who in actuality were more like a family member they didn't want to be like had higher reports of relational aggression and also received higher forms of corporal punishment in the home, such as spanking.

"Youths' inability to incorporate positive role model behaviors into their self-concept relates to youth conduct problems, such as acting out and starting fights," McDaniel said. "Positive parenting and mother involvement seem to be key components, which aid this ability."

The researchers also found that immoral traits, like lying and being unfriendly, shared between youths and all role models was significantly predictive of youth witnessing anti-social behaviors in their neighborhood, such as vandalism.

In addition, the youths were asked to name a celebrity they look up to, but the researchers found that the famous individuals had little influence on the youths' moral traits.

The study was funded by the Oklahoma Agricultural Experiment Station. McDaniel said future research includes laboratory-site studies where interaction between youth and a role model will be recorded and coded for important information, such as interpersonal emotional exchange and physiological stress levels.

McDaniel's colleagues for the project are Amanda Sheffield Morris, associate professor of human development and family science and Benjamin Houltberg, a doctoral student in human development and family science, both at Oklahoma State University-Tulsa.

Fossilised fish are proof of ancient sex

* 26 February 2009 **by Rachel Nowak**

Video: ***See virtual fish having sex***

SEXUAL intercourse was far more common in early vertebrates than anyone imagined. So suggests a new study of ancient shark-like creatures called placoderms.

Last year, John Long of Museum Victoria in Melbourne, Australia, and colleagues found an embryo complete with umbilical cord inside a placoderm fossil from the Gogo formation in Kimberley, Western Australia. This "mother fish" pushed back evidence of internal fertilisation and live birth by 200 million years to 380 million years ago. But how placoderms managed to mate, considering some orders could grow to be 6 metres long and all were heavily armoured, had been a mystery.

Now, Long and a different team think they have the answer. They examined the pelvic anatomy of three 380-million-year-old placoderm fossils belonging to the order Arthrodira and found a previously unnoticed "extra long bone" with "a long lobe projecting backwards", says Long. The shape of the lobe indicates that it articulates with cartilage, similar to the erectile claspers of modern-day sharks, he says (Nature, DOI: 10.1038/nature07732). These claspers would have been used to channel sperm into the female's cloaca, a posterior opening also used for expelling waste, in a similar way to today's sharks, says Long.

The team also re-examined two other arthrodire fossils from the same region. Small skeletons inside the specimens had been thought to be the debris of a cannibalistic dinner. But Long's team now thinks that they

were growing embryos. "The fish bones and armoury were not broken and crushed, as you'd expect if they were stomach contents," says Long.

While the original "mother fish" was from an obscure placoderm order, the arthrodires are from the largest. This raises the question of whether sexual intercourse evolved once, prior to the orders branching off, or many times independently, says Gavin Young, an expert on fish evolution at the Australian National University in Canberra.

'Oldest English words' identified

Some of the oldest words in English have been identified, scientists say.

Reading University researchers claim "I", "we", "two" and "three" are among the most ancient, dating back tens of thousands of years.

Their computer model analyses the rate of change of words in English and the languages that share a common heritage.

The team says it can predict which words are likely to become extinct - citing "squeeze", "guts", "stick" and "bad" as probable first casualties.

"We use a computer to fit a range of models that tell us how rapidly these words evolve," said Mark Pagel, an evolutionary biologist at the University of Reading.

"We fit a wide range, so there's a lot of computation involved; and that range then brackets what the true answer is and we can estimate the rates at which these things are replaced through time."

Sound and concept

Across the Indo-European languages - which include most of the languages spoken from Europe to the Asian subcontinent - the vocal sound made to express a given concept can be similar.

New words for a concept can arise in a given language, utilising different sounds, in turn giving a clue to a word's relative age in the language.

At the root of the Reading University effort is a lexicon of 200 words that is not specific to culture or technology, and is therefore likely to represent concepts that have not changed across nations or millennia.

"We have lists of words that linguists have produced for us that tell us if two words in related languages actually derive from a common ancestral word," said Professor Pagel.

"We have descriptions of the ways we think words change and their ability to change into other words, and those descriptions can be turned into a mathematical language," he added.

The researchers used the university's IBM supercomputer to track the known relations between words, in order to develop estimates of how long ago a given ancestral word diverged in two different languages.

They have integrated that into an algorithm that will produce a list of words relevant to a given date.

"You type in a date in the past or in the future and it will give you a list of words that would have changed going back in time or will change going into the future," Professor Pagel told BBC News.

"From that list you can derive a phrasebook of words you could use if you tried to show up and talk to, for example, William the Conqueror."

That is, the model provides a list of words that are unlikely to have changed from their common ancestral root by the time of William the Conqueror.

Words that have not diverged since then would comprise similar sounds to their modern descendants, whose meanings would therefore probably be recognisable on sound alone.

However, the model cannot offer a guess as to what the ancestral words were. It can only estimate the likelihood that the sound from a modern English word might make some sense if called out during the Battle of Hastings.

Dirty business

What the researchers found was that the frequency with which a word is used relates to how slowly it changes through time, so that the most common words tend to be the oldest ones.

For example, the words "I" and "who" are among the oldest, along with the words "two", "three", and "five". The word "one" is only slightly younger.

The word "four" experienced a linguistic evolutionary leap that makes it significantly younger in English and different from other Indo-European languages.

Meanwhile, the fastest-changing words are projected to die out and be replaced by other words much sooner.

For example, "dirty" is a rapidly changing word; currently there are 46 different ways of saying it in the Indo-European languages, all words that are unrelated to each other. As a result, it is likely to die out soon in English, along with "stick" and "guts".

Verbs also tend to change quite quickly, so "push", "turn", "wipe" and "stab" appear to be heading for the lexicographer's chopping block.

Again, the model cannot predict what words may change to; those linguistic changes are according to Professor Pagel "anybody's guess".

High fidelity

"We think some of these words are as ancient as 40,000 years old. The sound used to make those words would have been used by all speakers of the Indo-European languages throughout history," Professor Pagel said.

"Here's a sound that has been connected to a meaning - and it's a mostly arbitrary connection - yet that sound has persisted for those tens of thousands of years."

The work casts an interesting light on the connection between concepts and language in the human brain, and provides an insight into the evolution of a dynamic set of words.

"If you've ever played 'Chinese whispers', what comes out the end is usually gibberish, and more or less when we speak to each other we're playing this massive game of Chinese whispers. Yet our language can somehow retain its fidelity."

US shiitake market mushrooming

Mushroom growers report increased consumer demand

COLUMBA, MO - Shiitake mushrooms are the third most popular mushroom species in the U.S. In addition to taste, shiitake have a multitude of health benefits. Low in calories, glucose and sodium, shiitake are high in potassium, phosphorus, copper, and zinc.

Beyond those positive nutritional factors, shiitake also contain elements that lower blood cholesterol and improve the immune system. It's no wonder that demand is increasing for these nutritional powerhouses.

Native to Asian forests, shiitake are cultivated in two ways in the United States. The first takes place in forests, often applying an agroforestry technique known as forest farming, in which the forest canopy is altered to provide the appropriate amount of shade to grow crops below. The mushrooms grow on hardwood logs. This method results in a higher-quality product with minimal capital investment. The disadvantages of this method are weather dependence, seasonal production with lower yields, longer production cycles, and a heavier workload.

Shiitake can also be cultivated indoors, grown on logs or blocks of sawdust in environmentally controlled buildings. The distinct advantage of this process is the ability to produce shitake year-round with shorter production cycles and higher yields. The downside to indoor cultivation is increased cost and a lower-quality product.

Michael A. Gold, Mihaela M. Cernusca, and Larry D. Godsey from the University of Missouri surveyed 104 shiitake producers throughout the U.S. to learn about production and marketing in the field, and published the results of their study in the American Society for Horticultural Science journal HortTechnology.

According to the report based on 36 survey responses, 40% of shiitake growers had been in business less than 5 years, and only 17% had been growing for 20 or more years. The growers cited low start-up costs and the existence of potential markets as reasons for choosing this business. They chose shiitake because of their nutritional benefits as well as being an environmentally friendly crop. Eighty-eight percent of the growers who responded produced organically, while 40% were certified organic by the USDA.

However, respondents considered growing shiitake mushrooms to be labor-intensive, especially since it takes a full year to reach the point of harvest. Some of the producers felt that the income was not high enough compared to the time invested. A general lack of production and marketing information and the lack of dependable labor were cited as reasons some would not choose to grow shiitake again.

The study found that 75% of the survey respondents sold shiitake to restaurants, 69% sold to farmers markets, and 61% sold through on-farm outlets. Wholesale prices reported by respondents were between $5 and $7 per pound.

Nearly 40% of respondents noted an increase in demand over the past 5 years, and more than 40% expected an additional increase in demand for log-grown shiitake in the next 5 years. "Importantly, no respondent believed that demand will decrease over the next 5 years", the study authors concluded.

The complete study is available on the ASHS HortTechnology electronic journal web site:
http://horttech.ashspublications.org/cgi/content/abstract/18/3/489

Artificial disc replacement as good or better than spinal fusion surgery

By Jim Dryden

Spine surgeons at Washington University School of Medicine in St. Louis and other U.S. centers are reporting that artificial disc replacement works as well and often better than spinal fusion surgery.

The two procedures are performed on patients with damaged discs in the neck. Researchers found patients who received an artificial disc lost less motion in the neck and recovered faster than those who had a disc removed and the bones of the spine fused.

"Those who received the artificial disc either did equally as well or a little bit better than those who had fusion surgery," says K. Daniel Riew, M.D., a cervical spine surgeon at Washington University Orthopedics and Barnes-Jewish Hospital. "One of the most important findings was that people who got the artificial disc were able to preserve all of their motion."

A disc in the spine is similar to a jelly donut, with a squishy center surrounded by a tough outer portion. It functions like a shock absorber between the vertebrae. When a disc ruptures, or becomes herniated, the squishy disc tissue can spread into the spinal canal and press against nerves, causing numbness, weakness or pain.
For years, the surgery to treat cervical disc disease relieved pressure by removing the offending disc and then fusing the bones of the spine together. Surgery to implant an artificial disc also removes the damaged disc, but instead of using metal rods, screws and bone grafts to fuse bones together, the surgeon replaces the disc with an implant.

Patients in the study were randomly assigned to receive either the BRYAN Cervical Disc or standard fusion surgery. Ultimately, 242 received the artificial disc, and 221 had spinal fusion. Improvement following surgery was measured with a tool called the neck disability index (NDI). Two years post surgery, patients in both groups had improved NDI scores. Both had less neck and arm pain and were less likely to experience numbness. Overall, the surgery was rated as successful in 83 percent of the patients who received artificial discs and 73 percent of those who had fusion surgery (230 vs. 194). Part of that difference, Riew says, can be explained by better motion in the neck for those who had artificial discs implanted.

He says the neck is always slightly restricted following spinal fusion surgery. Since bones in the neck have been fused together, it is impossible to regain full range of motion. But the defect is subtle.

"Fusion adds a small amount of stress in the spine above and below the fusion site, so bone can break down a little faster than normal," Riew explains. "If the patient is a young person, then they may need another operation in 20 or 30 years. The hope with artificial cervical disc replacement is the preserved motion may protect against additional stress at other levels of the spine."

In the short term, Riew says most patients receiving artificial disc replacement surgery recovered faster and got back to normal life sooner than fusion surgery patients.

"They didn't need to wear a neck brace after surgery," he says. "If they had a job, they returned to work faster. And many had a resolution of their pain faster than fusion patients. With a spinal fusion, there are some pain and activity restrictions until the bone is fully incorporated, but with an artificial disc, as soon as the disc is in, it's 'good to go.'"

Riew, the Mildred B. Simon Distinguished Professor of Orthopaedic Surgery, professor of neurological surgery and chief of the cervical spine service for Washington University Orthopedics, says people from outdoorsmen to couch potatoes have seemed to do well following implantation of artificial discs. Last summer, he implanted an artificial disc into a professional baseball player's cervical spine. That player plans to return to the diamond and continue his career this season.

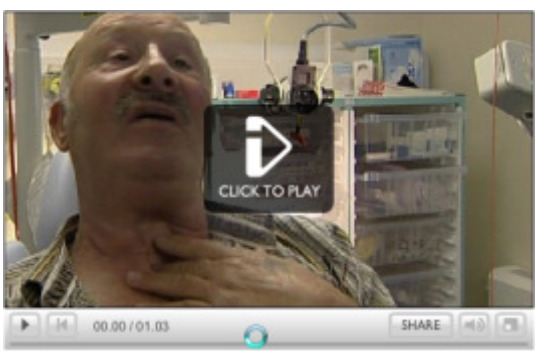
But at the moment, the discs are not an option for some patients. Those with arthritis or disc disease at multiple levels in the spine are not good candidates. A barrier for those who are good candidates is that many insurance companies don't yet cover them.

The study was supported by Medtronic Sofamor Danek, which manufactures the BRYAN Cervical Disc. Riew has received or will receive financial benefits from Medtronic. The researchers reported their findings in the January issue of the journal Spine.
Heller JG, Sasso RC, Papadopoulos SM, Anderson PA, Fessler RG, Jacker, RJ, Coric D, Cauthen JC, Riew KD. Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled clinical trial. Spine, vol 34 (2), pp. 101-107. Jan. 2009

Doctors plan voice box transplant

By Matthew Hill BBC West health correspondent

British doctors are debating whether it is ethical to start clinical trials to allow voice box transplantation. The task force has been set up as developments in stem cell technology make the development a possibility.



A team of scientists believe they may be able to transplant a voice box in such a way that the patient would not need to take anti-rejection drugs.

Each year around 1,000 patients in the UK will lose their voice box - the larynx - because of cancer or trauma. The larynx creates and controls sound through muscle and cartilage interacting with the vocal cords.

But when it is removed - in a procedure known as a laryngectomy - the patient is left with a permanent breathing hole in their neck.

The difficulty of restoring the complicated nerve and muscle functions has, to date, been beyond surgery.

So the only option to them is to have an artificial voice, either through a vibrating machine they put on their throat, or placing a small device in a permanent breathing hole in their neck which is activated by putting their finger over the hole.

Tom Foot, from Weston-Super-Mare, uses this technique to talk. He lost his voice box because he used to smoke. He said: "The easiest part was recovering from the surgery. "The most difficult bit is getting used to not being able to have meaningful conversations - and that it was a different voice, it wasn't my voice."

New hope

Despite years of research, there has only ever been one voice box transplant in the US, and the patient still needed to breathe through a hole in his neck.

But now there is the possibility that improved stem cell technology could make it a possibility to develop a voice box for transplantation.

A similar technique was used last year to give Claudia Castillo an artificial windpipe. She was given a donated organ which was covered with her own stem cells to trick her body into thinking the organ was part of her.

She can now live a normal life without having to take powerful anti-rejection drugs.

The international scientists behind the new project are now applying for funding to try to do the same thing with voice boxes.

One of the team, Professor Anthony Hollander, from Bristol University, said they faced a big challenge. He said: "In addition to windpipe tissue which will have to be created - the cartilage and the epithelium - we also have to create muscle because the voice box is a moving part and needs to move in co-ordination with breathing.

"We don't yet have a good way of taking stem cells and creating muscle and we need to figure out exactly how to do that and then how to implant that muscle and have it co-ordinate with the moving voice box."

Task force consideration

The Royal College of Surgeons is about to debate these technical challenges, the potential benefits of such surgery and ethical dilemmas they throw up. For instance, since these are not a life-saving procedures, do the benefits outweigh the significant risks of harm from surgery?

Among the members of the task force is Professor Martin Birchall, from University College London, who led the team on the windpipe transplant.

He said: "We, as a task force, have to ask ourselves whether we are finally entering the right window where a marriage of technology and of need mandates that we can go forward with this procedure.

"Before now, the prevailing view has been that the balance has been strongly in favour of not going ahead. But we feel there have been sufficient technological advances to make us seriously revisit the case for developing and making routine this procedure. We have to ask ourselves is it right to subject a patient to the risks of surgery for a procedure which is not life-saving."

Patient support

Another patient who lost his voice box, Dave Williams from Bristol, would welcome a transplant.

He said he often has to come into hospital because of complications from his implant.

Mr Williams said: "What people don't realise is when they have this operation there are a few things you can't do - one thing is smell, another is swim, and another is shout."

The pan-European team that has developed the stem cell technique should find out by April whether they have secured the 6m euros they need for the project to begin.

If they get the go-ahead, then laboratory work should start this year.

Vegetable-based drug could inhibit melanoma

Compounds extracted from green vegetables such as broccoli and cabbage could be a potent drug against melanoma, according to cancer researchers. Tests on mice suggest that these compounds, when combined with selenium, target tumors more safely and effectively than conventional therapy.

"There are currently no drugs to target the proteins that trigger melanoma," said Gavin Robertson, associate professor of pharmacology, pathology and dermatology, Penn State College of Medicine. "We have developed drugs from naturally occurring compounds that can inhibit the growth of tumors in mice by 50 to 60 percent with a very low dose."

Robertson and his colleagues previously showed the therapeutic potential of targeting the Akt3 protein in inhibiting the development of melanoma. The search for a drug to block the protein led them to a class of compounds called isothiocyanates.

These naturally occurring chemicals found in cruciferous vegetables are known to have certain cancer-fighting properties. However, the potency of these compounds is so low that a successful drug would require large impractical amounts of these compounds.

Instead, the Penn State researchers rewired the compounds by replacing their sulfur bonds with selenium. The result, they believe, is a more potent drug that can be delivered intravenously in low doses.

"Selenium deficiency is common in cancer patients, including those diagnosed with metastatic melanoma," explained Robertson, whose findings appear in the March edition of Clinical Cancer Research. "Besides, selenium is known to destabilize Akt proteins in prostate cancer cells."

To study the effectiveness of the new drug -- isoselenocyanate -- researchers injected mice with 10 million cancer cells. Six days later, when the animals developed large tumors, they were divided into two groups and treated separately with either the vegetable compounds or the compounds supplemented with selenium. "We found that the selenium-enhanced compounds significantly reduced the production of Akt3 protein and shut down its signaling network," explained Robertson, who is also associate director of translational research and leader of the experimental therapeutics program at Penn State Hershey Cancer Institute. The modified compounds also reduced the growth of tumors by 60 percent, compared to the vegetable-based compounds alone.

When the researchers exposed three different human melanoma cell lines to the two compounds, the selenium-enhanced drug worked better on some cell lines than others. The efficiency was from 30 to 70 percent depending on the cell line.

The exact mechanism of how selenium inhibits cancer remains unclear. However Robertson, who has a filed provisional patent on the discovery, is convinced that the use of naturally occurring compounds that target cancer-causing proteins could lead to more effective ways of treating melanoma.

"We have harnessed something found in nature to target melanoma," said Robertson. "And since we only need tiny amounts to kill the cancer cells, it means even less toxic side-effects for the patient."

Human trials of the new drug are still some years away, but the Penn State researcher envisions a drug that could be delivered either intravenously to treat melanoma, or added to sunscreen lotion to prevent the disease.
Other researchers on the paper include Arati Sharma and Arun K. Sharma, both assistant professors; Subbarao V. Madhunapantula, postdoctoral scholar; Dhimant Desai, associate professor; Sung Jin Huh, graduate student, and Shantu Amin, professor, all in the department of pharmacology, and Paul Mosca, assistant professor of surgery, Lehigh Valley and Health Network.

USC researchers identify gene variant associated with both autism and gastrointestinal dysfunction

Altered expression of MET gene may contribute to increased risk of co-occurring medical conditions

A study led by researchers at the University of Southern California (USC) and Vanderbilt University have identified a specific gene variant that links increased genetic risk for autism with gastrointestinal (GI) conditions.

The findings suggest that disrupted signaling of the MET gene may contribute to a syndrome that includes autism and co-occurring gastrointestinal dysfunction, says principal investigator Pat Levitt, Ph.D., director of the Zilkha Neurogenetic Institute at the Keck School of Medicine of USC and chair-designate of the Department of cell and neurobiology.

The study will appear in the March Issue of the journal Pediatrics and is now available online.

Autism is a developmental disorder characterized by deficits in communication abilities, social behavior disruption and inflexible behavior. While gastrointestinal conditions are common among individuals with autism, researchers have long debated whether co-occurring GI dysfunction represents a unique autism subgroup, Levitt and lead author Daniel Campbell, Ph.D., say.

"Gastrointestinal disorders don't cause autism. Autism is a disorder of brain development," Levitt says. "However, our study is the first to bring together genetic risk for autism and co-occurring GI disorders in a way that provides a biologically plausible explanation for why they are seen together so often."

In the brain, the MET gene is expressed in developing circuits that are involved in social behavior and communication. Disturbances in MET expression result in alterations in how these critical circuits develop and mature, Levitt explains. Research indicates that MET also plays an important role in development and repair of the GI system.

Researchers analyzed medical history records from 214 families in the Autism Genetic Resource Exchange (AGRE). They found that a variant in the MET gene was associated with autism specifically in those families where an individual had co-occurring autism and a GI condition.

The study brings researchers closer to understanding the complex genetic risks for autism. However, further research is needed, as different combinations of genes are likely to result in different types of autism features, Levitt says.

"We believe that there are other genes that will help identify different subgroups of individuals who have autism spectrum disorder," he says. "We also believe that there needs to be research looking at whether the children with co-occurring GI dysfunction and autism have unique features that will help us predict what treatments will be best for them."

The study was funded by the Simons Foundation, the Nancy Lurie Marks Foundation, the Dan Marino Foundation's Marino Autism Research Institute, the National Institute of Mental Health and the National Institute of Child Health and Human Development.

Daniel B. Campbell, Timothy M. Buie, Harland Winter, Margaret Bauman, James S. Sutcliffe, James M. Perrin, Pat Levitt. "Distinct Genetic Risk Based on Association of MET in Families With Co-occurring Autism and Gastrointestinal Conditions." Pediatrics. Doi: 10.1542/peds.2008-0819.

Experts trying to decipher ancient language

The Associated Press Sunday, March 1, 2009

ALMODOVAR, Portugal: When archaeologists on a dig in southern Portugal last year flipped over a heavy chunk of slate and saw writing not used for more than 2,500 years, they were elated.

The enigmatic pattern of inscribed symbols curled symmetrically around the upper part of the rough-edged, yellowish stone tablet and coiled into the middle in a decorative style typical of an extinct Iberian language called Southwest Script.

"We didn't break into applause, but almost," says Amilcar Guerra, a University of Lisbon lecturer overseeing the excavation. "It's an extraordinary thing."

For more than two centuries, scientists have tried to decipher Southwest Script, believed to be the peninsula's oldest written tongue and, along with Etruscan from modern-day Italy, one of Europe's first. The stone tablet features 86 characters and provides the longest-running text of the Iron Age language ever found.

About 90 slate tablets bearing the ancient inscriptions have been recovered, most of them incomplete. Almost all were scattered across southern Portugal, though a handful turned up in the neighboring Spanish region of Andalucia.

A stone tablet engraved with symbols at least 2,500 years old is seen at the Southwest Script Museum on Feb. 5, 2009 in Almodovar, southern Portugal. The museum has on display 20 tablets engraved with symbols of the Iron Age extinct Iberian language called Southwest Script. **(Armando Franca / AP)**

Some of the letters look like squiggles. Others are like crossed sticks. One resembles the number four and another recalls a bow-tie. They were carefully scored into the slate. The text is always a running script, with unseparated words which usually read from right to left.

The first attempts to interpret this writing date from the 18th century. It aroused the curiosity of a bishop whose diocese encompassed this region where the earth keeps coughing up new fragments.

Almodovar, a rural town of some 3,500 people amid a gentle landscape of meadows punctuated by whitewashed towns, sits at the heart of the Southwest Script region. It created a museum two years ago where 20 of the engraved tablets are on show.

Though the evidence is gradually building as new tablets are found, researchers are handicapped because they are peering deep into a period of history about which they know little, says professor Pierre Swiggers, a Southwest Script specialist at the University of Leuven, Belgium. Scientists have few original documents and hardly any parallel texts from the same time and place in readable languages.

"We hardly know anything about (the people's) daily habits or religious beliefs," he says.

Southwest Script is one of just a handful of ancient languages about which little is known, according to Swiggers. The obscurity has provided fertile ground for competing theories about who wrote these words.

It is generally agreed the texts date from between 2,500 and 2,800 years ago. Most experts have concluded they were authored by a people called Tartessians, a tribe of Mediterranean traders who mined for metal in these parts — one of Europe's largest copper mines is nearby — but disappeared after a few centuries. Some scientists have proposed that the composers were other pre-Roman tribes, such as the Conii or Cynetes, or maybe even Celts who roamed this far south.

Another translation difficulty is that the writing is not standardized. It seems certain that it was adapted from the Phoenician and Greek alphabets because it copied some of their written conventions. However, it also tweaked some of those rules and invented new ones.

Experts have identified characters that represent 15 syllables, seven consonants and five vowels. But eight characters, including a kind of vertical three-pronged fork, have confounded attempts at comprehension.

There's also the problem of figuring out what messages the slate tablets are intended to convey. Even when they can read portions of text, scientists don't really understand what it is saying — like a child mouthing the words of a Shakespeare play.

"We have a lot of doubts," says Guerra, who has written scholarly articles about Southwest Script. "We can read characters and see the phonetics in action ... but when we try to understand what they actually mean we have a lot of problems."

There are clues, however.

The symmetrical, twisting text gives the impression of a decorative flourish. Some stones also feature crudely rendered figures, such as a warrior carrying what appear to be spears. The lower part of the rectangular stones is left blank as if intended to be stuck in the ground.

That has led experts to a supposition: The tablets were gravestones for elite members of local Iron Age society. Repeated sequences of words perhaps mean "Here lies..." or "Son of...," Guerra explains. Since most people probably couldn't read, the ornamental elements lent distinction.

These are educated guesses, says Guerra, as he surveys the hilltop dig by a small river where the big stone was found last year. His team here has excavated through centuries of occupation: Islamic (Almodovar is a corruption of the Arabic word al-mudura, meaning encirclement or enclosure), Roman and pre-Roman. Nowadays, it is within view of a wind farm's turbines.

Last year's find has helped, but it wasn't the breakthrough scientists had hoped for, Guerra says. If all the Southwest Script found so far were transcribed onto paper, it would still barely fill a single sheet. Without an equivalent of the Rosetta stone, which helped unlock the secrets of hieroglyphic writing, efforts to reconstruct the ancient language are doomed to slow progress.

"We have to be patient — and hopeful," Guerra says.