Despite 'peacenik' reputation, bonobos hunt and eat other primates too

Unlike the male-dominated societies of their chimpanzee relatives, bonobo society—in which females enjoy a higher social status than males—has a "make-love-not-war" kind of image. While chimpanzee males frequently band together to hunt and kill monkeys, the more peaceful bonobos were believed to restrict what meat they do eat to forest antelopes, squirrels, and rodents.

Not so, according to a study, reported in the October 14th issue of Current Biology, a Cell Press publication, that offers the first direct evidence of wild bonobos hunting and eating the young of other primate species.

"These findings are particularly relevant for the discussion about male dominance and bonding, aggression and hunting—a domain that was thought to separate chimpanzees and bonobos," said Gottfried Hohmann of the Max-Planck-Institute for Evolutionary Anthropology. "In chimpanzees, male-dominance is associated with physical violence, hunting, and meat consumption. By inference, the lack of male dominance and physical violence is often used to explain the relative absence of hunting and meat eating in bonobos. Our observations suggest that, in contrast to previous assumptions, these behaviors may persist in societies with different social relations."

Bonobos live only in the lowland forest south of the river Congo, and, along with chimpanzees, they are humans' closest relatives. Bonobos are perhaps best known for their promiscuity: sexual acts both within and between the sexes are a common means of greeting, resolving conflicts, or reconciling after conflicts.

The researchers made the discovery that these free-loving primates also hunt and kill other primates while they were studying a bonobo population living in LuiKotale, Salonga National Park, in the Democratic Republic of Congo. They had been observing the bonobos there for the last five years, which is what made the new observations possible.

Although Hohmann's team did have prior evidence for monkey hunting by bonobos, it came exclusively from indirect studies of fresh fecal samples—one of which contained the digit of a black mangabey. Yet, in the absence of direct behavioral observations, it was not entirely clear whether the bonobos had hunted the mangabey themselves or had taken it from another predator.

The researchers have now seen three instances of successful hunts in which bonobos captured and ate their primate prey. In two other cases, the bonobo hunting attempts failed. The data from LuiKotale showed that both bonobo sexes play active roles in pursuing and hunting monkeys. The involvement of adult females in the hunts (which is not seen in chimps) may reflect social patterns such as alliance formation and cooperation among adult females, they said.

Overall, the discovery challenges the theory that male dominance and aggression must be causally linked to hunting behavior, an idea held by earlier models of the evolution of aggression in human and non-human primates. Future work on the bonobos of LuiKotale may shed light on the social and ecological conditions that encourage their monkey-hunting expeditions, yielding insight into the evolutionary significance and causes of aggression, hunting, and meat eating in bonobos, chimpanzees, and ourselves.

The researchers include Martin Surbeck and Gottfried Hohmann, of Department of Primatology, Max-Planck Institute for Evolutionary Anthropology, Leipzig, Germany.

Drinking alcohol associated with smaller brain volume

The more alcohol an individual drinks, the smaller his or her total brain volume, according to a report in the October issue of Archives of Neurology, one of the JAMA/Archives journals.

Brain volume decreases with age at an estimated rate of 1.9 percent per decade, accompanied by an increase in white matter lesions, according to background information in the article. Lower brain volumes and larger white matter lesions also occur with the progression of dementia and problems with thinking, learning and memory. Moderate alcohol consumption has been associated with a lower risk of cardiovascular disease; because the brain receives blood from this system, researchers have hypothesized that small amounts of alcohol may also attenuate age-related declines in brain volume.

Carol Ann Paul, M.S., of Wellesley College, Mass., and colleagues studied 1,839 adults (average age 60) who were part of the Framingham Offspring Study, which began in 1971 and includes children of the original Framingham Heart Study participants and their spouses. Between 1999 and 2001, participants underwent magnetic resonance imaging (MRI) and a health examination. They reported the number of alcoholic drinks they consumed per week, along with their age, sex, education, height, body mass index and Framingham Stroke Risk Profile (which calculates stroke risk based on age, sex, blood pressure and other factors).

"Most participants reported low alcohol consumption, and men were more likely than women to be moderate or heavy drinkers," the authors write. "There was a significant negative linear relationship between alcohol consumption and total cerebral brain volume."

Although men were more likely to drink alcohol, the association between drinking and brain volume was stronger in women, they note. This could be due to biological factors, including women's smaller size and greater susceptibility to alcohol's effects.

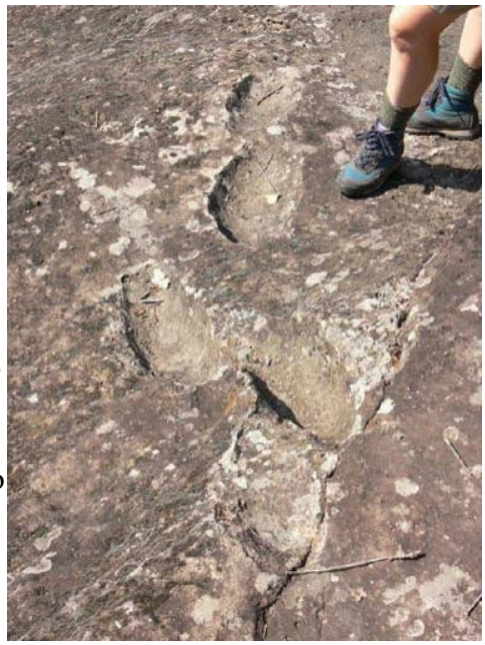
"The public health effect of this study gives a clear message about the possible dangers of drinking alcohol," the authors write. "Prospective longitudinal studies are needed to confirm these results as well as to determine whether there are any functional consequences associated with increasing alcohol consumption. This study suggests that, unlike the associations with cardiovascular disease, alcohol consumption does not have any protective effect on brain volume."

(Arch Neurol. 2008; 65[10]:1363-1367. Available pre-embargo to the media at www.jamamedia.org.)

***Editor's note**: This study was supported by a contract from the National Heart, Lung, and Blood Institute's Framingham Heart Study, National Institutes of Health; grants from the National Institute on Aging; and a grant from the National Institute of Neurological Disorders and Stroke. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

'Devils' trails' are world's oldest human footprints

* 15:28 13 October 2008
* NewScientist.com news service
*** Catherine Brahic**



The "devil's footsteps" were left in volcanic ash 345,000 years ago **(Image: Elsevier / Scaillet)**

It's official: the oldest human footprints ever found are 345,000 years old, give or take 6000. Known as the "devils' trails", they have been preserved in volcanic ash atop the Roccamonfina volcano in Italy.

The prints were first described to the world by Paolo Mietto and colleagues of the University of Padova in Italy in 2003 after amateur archaeologists pointed them out.

At the time, the team estimated that the prints were anywhere between 385,000 and 325,000 years old, based on when the volcano was thought to have last erupted.

Now, Stéphane Scaillet and colleagues at the Laboratory of Climatic and Environmental Sciences, France, have used argon dating techniques to verify the prints' age.

"Their more rigorous methods confirm that these are the oldest human footprints ever found," says Mietto. The new findings also confirm that the owners of the footprints were Homo heidelbergensis.

Trail blazers

Mietto is setting off next week to excavate a second site, some 3 kilometres away. Early visits have convinced him that there are more human footprints, and he says it is highly likely that they are the same age.

The excavations should help reveal a trail that was used by early humans.

Mietto says that based on their stride, the people responsible were walking, not running. What's more, the prints are in both directions: leading to the volcano and away from it. Their owners were therefore not running away from a volcanic eruption and the prints must have been left some time after the event.

Dating experiments have not always confirmed suspicions. In 2003, a team discovered 40,000 year old footprints preserved in volcanic ash in southern Mexico. But when a separate group dated the Mexican prints using the argon technique used by Scaillet, they found that they were 1.3 million years old.

Since this was before modern humans evolved in Africa – the team concluded that they couldn't be human footsteps after all (see the very first Americans.

Journal reference: Earth and Planetary Science Letters (DOI: 10.1016/j.epsl.2008.08.026, in press)

Vitamin D deficiency may be more common in Parkinson's disease patients

Individuals with Parkinson's disease appear more likely to be vitamin D deficient than healthy adults of the same age or patients with Alzheimer's disease, according to a report in the October issue of Archives of Neurology, one of the JAMA/Archives journals.

"Vitamin D is important for maintaining many physiologic functions, and vitamin D deficiency is associated with increased risk of disease," according to background information in the article. "Patients with chronic neurodegenerative diseases frequently have many risk factors for vitamin D insufficiency," including advancing age, obesity, avoidance of sun exposure, residence in northerly latitudes and having darker skin.

Marian L. Evatt, M.D., M.S., and colleagues at the Emory University School of Medicine, Atlanta, compared vitamin D levels of 100 patients with Parkinson's disease to vitamin D levels of 97 Alzheimer's disease patients and 99 healthy individuals matched for age, sex, race, genotype and geographic location.

"Significantly more patients with Parkinson's disease (55 percent) had insufficient vitamin D than did controls (36 percent) or patients with Alzheimer's disease (41 percent)," the authors write. The average vitamin D concentration in the group with Parkinson's disease was considerably lower than the Alzheimer's disease and healthy groups (31.9 nanograms per milliliter vs. 34.8 nanograms per milliliter and 37 nanograms per milliliter, respectively).

"These findings support the previously suggested need for further studies to assess what contribution a low 25(OH)D [a measure of blood vitamin D levels] concentration adds to the risk of developing Parkinson's disease (vs. other neurodegenerative disorders) and to determine whether correction of vitamin D insufficiency and deficiency will improve motor or non-motor symptoms in Parkinson's disease," the authors conclude.

"Finally, the finding of a high incidence of vitamin D deficiency in the Parkinson's disease and other cohorts highlights the importance of routinely checking the level of 25(OH)D, particularly in elderly patients, since deficiency is strongly correlated with a higher incidence of osteoporosis, falls and hip fractures and has been associated with a higher incidence of several forms of cancer and autoimmune disorders."

(Arch Neurol. 2008;65[10]:1348-1352. Available pre-embargo to the media at www.jamamedia.org.)

Worms' nervous system shown to alert immune system in Stanford studies

STANFORD, Calif. — The nervous system and the immune system have something in common. Each has evolved to react quickly to environmental cues. Because the nervous system is able to detect some of these cues - say, a characteristic odor signaling a pathogen's presence - at a distance, it sometimes can sense trouble earlier than the immune system, which has to wait until the pathogen invades the organism.

So it makes sense that the two systems might talk to one another. Stanford University School of Medicine geneticists have shown that, indeed, they do.

In a study to be published online Oct. 14 by the journal Nature Immunology, Man-Wah Tan, PhD, assistant professor of genetics and of microbiology and immunology, and postdoctoral scholar Trupti Kawli have shown that a change in the secretion patterns of nerve cells in the minuscule soil-dwelling worm, Caenorhabditis elegans, induces a change in the worm's susceptibility to a bacterial pathogen, Pseudomonas aeruginosa. In humans, P. aeruginosa is an important pathogen among cystic fibrosis patients and can cause pneumonia.

Importantly, the Stanford investigators have nailed down the connection between the two systems. They identified a particular molecule that, secreted by nerve cells, binds to receptors in the worm's gut cells. When the levels of the secreted molecule fall, this sets off a complicated chain reaction that activates the powerful immune defense against bacterial infection. Since bacteria are what C. elegans mainly eats, this is a handy defense to have.

The notion of crosstalk between our nervous and immune systems is hardly surprising, said Tan. "A person who is undergoing prolonged psychological stress - say, because they're taking care of someone who is sick - is more likely to have reactivation of a latent infection or become more susceptible to new ones," he said. "That stressful situation cannot be changed. But by identifying the pathways through which the nervous system alters immune function in this simple creature C. elegans, we can perhaps start to think about how we can intervene in humans."

The very complexity of the nervous and immune systems would make any interactions between them exceedingly tough to tease out in humans. So Kawli and Tan used C. elegans, because both its nervous and immune systems have been entirely mapped out. This enabled the researchers to manipulate the former, then watch what happened to the latter.

C. elegans has nerve cells that ordinarily secrete bioactive molecules contained within tiny membrane-wrapped bundles, called dense-core vesicles. The rate at which these molecules are secreted is governed by the activity of the nervous system. One of those secreted bioactive molecules is called ins-7. The Stanford team obtained or generated various C. elegans mutants that lacked the ability either to produce or to secrete ins-7, or secreted it excessively.

By using these and other advanced laboratory tools to manipulate the worm's ability to secrete ins-7, the researchers were able to correspondingly alter the readiness of the minuscule creature's innate immune system: a primitive but potent piece of the immune system shared by C. elegans and higher organisms including humans.

People often associate "immune response" with antibodies and roving T-cells dispatched to combat a particular viral or bacterial infection - the so-called adaptive immune response. But that response takes a week or two to develop, said Tan. In contrast, all of our cells have receptors that can recognize molecular patterns common to whole classes of pathogens (for example, characteristic viral DNA snippets, or bacterial cell-wall

constituents), immediately triggering cascades of intracellular reactions, such as the activation of batteries of genes that code for antimicrobial proteins.

Both the innate and adaptive branches of the immune system have to function optimally in order for us to leave a healthy life. "The innate immune system is our first line of defense," said Tan. "If not for the innate immune system, we'd be dead by the time the adaptive immune system raises antibodies to a pathogenic invader we have not encountered before."

It is still a matter of speculation as to how crosstalk between the nervous and immune systems of humans regulates innate immune responses. But now that a clear pathway has been identified in the worm, it will be easier to conduct focused research on higher organisms to see if the phenomenon is universal, Tan said.

Tan acknowledged that it has not yet been proven that the signaling of the nervous system to the immune system of C. elegans, as shown in this experiment, occurs in nature. But there's very good reason to believe it does.

In a separate paper set to be published online on Oct. 17 by another journal, PLoS-Pathogens, Tan and other Stanford associates demonstrate that P. aeruginosa - which is often isolated from the same soil samples in which C. elegans is found and, presumably, co-evolved with C. elegans - has a way of subverting this defense against it. The pathogen induces excess production of ins-7 by the worm to dull its immune responsiveness. In contrast, other human bacterial pathogens such as Salmonella typhimurium and Enterococcus fecalis have no such capability. Nor do abiotic stresses, such as heat or heavy metals.

This suggests to Tan that the fine-tuning of the innate immune response by the nervous system is effective enough in the natural state that some pathogens with which C. elegans coexists have evolved strategies to subvert this system.

An inducible immune response makes more sense - in worms and people - than a state of constantly hyper-elevated immune vigilance. People with hyperactive immune systems suffer from autoimmune and inflammatory conditions. Although worms with downregulated secretion from dense-core vesicles are better at combating infection, they don't move well, which would probably prove lethal in the wild. One of the ins-7-deficient C. elegans mutants used in the Nature Immunology study is called unc, said Kawli, the paper's first author. "That stands for 'uncoordinated,'" she said.

Funding for the Nature Immunology study came from the National Institutes of Health.

'New pathway' for African exodus

By Paul Rincon Science reporter, BBC News

Researchers have found a possible new route taken by early modern humans as they expanded out of Africa to colonise the rest of the world.

A study published in the journal PNAS proposes a "wet corridor" through Libya for ancient human migrations.

Rivers once flowed from the central Saharan watershed all the way to the Mediterranean, the team explains. This might have enabled modern humans to spread beyond their ancestral homeland about 120,000 years ago.

The Sahara then covered most of North Africa, as it does now. So it would have presented a formidable obstacle for early modern humans wishing to cross from the south to the north of the continent.

Researchers had previously focused on the Nile Valley as the principal route of dispersal into other continents by early representatives of our species.

Previous data show there was increased rainfall across the southern part of the Sahara between 130,000 and 170,000 years ago; in a gap between Ice Ages known as the last interglacial period.

The researchers, from the universities of Bristol, Southampton, Oxford, Hull and Tripoli in Libya, investigated whether these wetter conditions had reached a lot further north than previously thought.

A generalized map of the Sahara shows the location of the sample sites and the fossilized river courses. **Anne Osborne**

Radar images from space revealed fossil river channels crossing the Sahara in Libya, flowing north from the central Saharan watershed to the Mediterranean coast.

Using geochemical tests, the scientists showed the channels were active during the last interglacial. This would have created vital water courses across an otherwise arid region, the researchers write in PNAS.

The central Saharan watershed is a range of volcanic mountains formerly considered to be the limit of this wetter region.

Researchers analysed the forms, or isotopes, of different chemical elements in snail shells from two sites in the fossil river channels and from the shells of planktonic microfossils in the Mediterranean.

Despite being hundreds of kilometres from the volcanic rocks of the Saharan watershed, the tests revealed a distinct volcanic signature to these shells, which was quite different to rocks from surrounding sites.

The scientists concluded that water flowing from the volcanic mountains of the central Sahara was the only possible source of this signature.

"It's a possible route that the early modern humans could have taken," lead author Anne Osborne, from the earth sciences group at Bristol, told BBC News.

Similarities in the style of stone tools being made in Chad and Sudan with those manufactured in Libya during this key period, lend the theory some support, say the scientists.

"We now need to focus archaeological fieldwork around the large drainage channels an palaeo-lakes to test these ideas," said co-author Dr Nick Barton, from the University of Oxford.

Although it is unclear which routes they took to get there, Homo sapiens had reached the Levant by around 100,000 years ago, where their remains are known from Es Skhul and Qafzeh in Israel.

However, this appears to have been an early, failed foray outside Africa by modern humans. By 75,000 years ago, Neanderthals had replaced our species in the region.

Then, about 45,000 years ago, modern humans reoccupied the area.

Genetic evidence suggests that populations living outside Africa today are the descendents of a migration which originated in the east of the continent between 60-70,000 years ago.

Some of these pioneers probably crossed the Red Sea at the Bab-el-Mandab straits, taking them from the Horn of Africa across to the Arabian Peninsula.

Haemorrhagic virus carried by common African mouse

* 18:00 13 October 2008
* NewScientist.com news service
*** Debora MacKenzie**

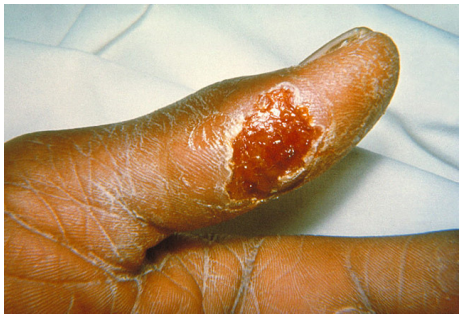
Multimammate mouse

Three people have died and another is seriously ill with a previously unknown strain of a virus carried by a common African rodent. The virus requires close contact to spread, but experts warn that more like it could be circulating.

A 36-year-old woman on a small farm outside the Zambian capital Lusaka developed flu-like symptoms in early September. When they worsened she was taken by air ambulance to South Africa, where she died.

Alarms were raised after the ambulance paramedic and the nurse who attended her also died after developing similar symptoms two weeks later. The nurse who tended the paramedic is also in a serious condition.

On Sunday South Africa's National Institute for Communicable Diseases announced that the victims were infected by an arenavirus, one of a family of viruses carried by rodents.



Viral Hemorrhagic Fever

"They are very widespread," says Bob Swanepoel, former head of the NICD and one of the world's leading experts on haemorrhagic viruses. In Africa, arenaviruses are carried, with no symptoms, by the multimammate mouse, a common farm pest sold in Europe as a "pocket pet".

It is not known whether animals caught in Africa are being sold as pets.

Some of these viruses commonly infect humans. Several related viruses in the Americas cause haemorrhagic fevers, but in Africa only one was known to cause disease: Lassa fever, which kills around 5000 people a year in West Africa.

The rest seemed benign. "We have been testing haemorrhagic fever patients in southern Africa for three decades and we never found an arenavirus," says Swanepoel. "Now suddenly there's this."

The Zambian virus is being sequenced at the US Centers for Disease Control in Atlanta, to see how it is related to other arenaviruses.

This strain may be a new mutant, meaning the Zambian case may herald the start of a new disease. "Or it may always have been out there and we're only recognising it now," says Swanepoel. "It's shocking how little we know about the viruses that are circulating in Africa."

Is there an optimum speed of life?

* 22:00 13 October 2008
* NewScientist.com news service
*** David Robson**

It doesn't matter if it's a tiny bacterium, a growing tree or a gigantic mammal – it seems most groups of organisms favour the same optimum metabolic rate.

Previous studies had shown that, within many groups of organisms, smaller species generally produce more energy within each cell than larger species. But according to Anastassia Makarieva from Petersburg Nuclear Physics Institute in St Petersburg, Russia, no studies had compared resting metabolic rates across the whole range of life on Earth.

Makarieva's team trawled through a database of 3,006 different species, ranging from bacteria to elephants. They found that the average resting metabolic rate per unit mass varied by a factor of 10,000 – despite the fact that body mass varied by a gigantic factor, 1020. For most species, the metabolic range was even narrower, with the majority lying between 1 and 10 Watts per kilogram - a factor of 10 difference. There was no consistent relationship between metabolic rate and body mass.

Elephantine metabolism

"The largest organism we studied is the elephant, which has a metabolic rate of 1 Watt per kilogram, and the smallest is a bacterium with a metabolic rate of 4 Watts/kg," says Makarieva.

Using the formulae that had previously been used to calculate the metabolic rate within separate classes of animals, you would have expected a multimillion-fold difference, she says.

Since such a large number of species falls within this narrow range, she hypothesises there may be an optimum metabolic rate for all organisms. "Organisms that lie close to this value may be the fittest to survive," she says.

Although the team don't yet know what evolutionary advantage it may offer, they believe the need to stay close to this value may help explain certain aspects of evolution, such as the size at which invertebrates needed to evolve a breathing mechanism, or the shape and size of tree leaves.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0802148105

Research Confirms It: Noxious Gas Stove Emissions Worse Asthma Symptoms in Young Children

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October 13, 2008

Johns Hopkins scientists report that high levels of a noxious gas from stoves can be added to the list of indoor pollutants that aggravate asthma symptoms of inner city children, especially preschoolers.

Nitrogen dioxide (NO2), an irritating and toxic form of nitrogen oxide gas, is most prevalent in industrial zones but also found at higher levels in poor homes with unvented gas stoves.

In a report in the October issue of Environmental Health Perspectives, Hopkins researchers say asthma flare-ups were directly related to high concentrations of NO2 in the inner city homes they studied.

Specifically, the researchers compared the frequency and intensity of coughing, wheezing, shortness of breath and chest tightness to NO2 levels inside the inner-city homes of 150 Baltimore City 2- to 6-year-olds. Eighty-three percent of the households had gas stoves, 72 percent were heated by natural gas, and 14 percent used gas stoves for heating in the winter. Forty-two percent of the households had annual incomes under $25,000.

Across the board they found that the pollutant worsened day and night symptoms. Each 20-point increase in nitrogen dioxide levels led to 10 percent more days of cough and 15 percent more days with limited speech due to wheezing.

Use of gas stoves, space heaters or home heating with a stove or an oven, either in combination or alone, each drove up nitrogen dioxide concentrations.

“Because using stoves as heat sources is a hallmark of urban poverty, our study tellingly points to how profound and direct the effects of purely social and environmental factors can be on a child’s health,” says Johns Hopkins lung expert Nadia Hansel, M.D., a lead researcher on the report.

“Doctors caring for children with asthma should always inquire about the home’s heating and cooking appliances and urge those using gas-based stoves and space heaters to switch to electric heating and cooking, if possible, or at least properly vent the exhaust gases.

“Inner-city preschoolers appear especially vulnerable because they spend most of their time indoors and in homes with high levels of nitrogen dioxide,” says study senior investigator and Hopkins pulmonary expert Gregory Diette, M.D. “We knew that but still we were disturbed by what we saw: As nitrogen dioxide levels crept up, so did the frequency and severity of these kids’ symptoms.”

Asthma is the most common pediatric chronic illness, affecting 6.2 million children in the United States. Severe illness is most prevalent in inner-city children, doctors say, because of poor access to regular health care and disproportionate exposure to indoor allergens such as mouse and cockroach dander, dust, cigarette smoke and automobile fumes.

In an earlier study of inner-city children with asthma, Johns Hopkins Children's Center researchers found even mild asthma among this vulnerable group appears to be more unpredictable than ever, with recommendations for at least four check-ups a year in such children to ward off dangerous flare-ups. Current asthma guidelines call for follow-up of one to six months after diagnosis.

Co-investigators in the study: Patrick Breysse, Elizabeth Matsui, M.D. M.H.S.; Meredith McCormack, Jean Courtin-Brosnan, D'Ann Williams, Jennifer Moore and Jennifer Cuhran, all of Hopkins.

The research was funded by the National Institute of Environmental Health Sciences, the National Heart, Lung and Blood Institute and the U.S. Environmental Protection Agency.

Scientists develop new cancer-killing compound from salad plant

Rachel Tompa rtompa@u.washington.edu

Researchers at the University of Washington have updated a traditional Chinese medicine to create a compound that is more than 1,200 times more specific in killing certain kinds of cancer cells than currently available drugs, heralding the possibility of a more effective chemotherapy drug with minimal side effects.

The new compound puts a novel twist on the common anti-malarial drug artemisinin, which is derived from the sweet wormwood plant (Artemisia annua L). Sweet wormwood has been used in herbal Chinese medicine for at least 2,000 years, and is eaten in salads in some Asian countries.

The scientists attached a chemical homing device to artemisinin that targets the drug selectively to cancer cells, sparing healthy cells. The results were published online Oct. 5 in the journal Cancer Letters.

"The compound is like a special agent planting a bomb inside the cell," said Tomikazu Sasaki, chemistry professor at UW and senior author of the study.

In the study, the UW researchers tested their artemisinin-based compound on human leukemia cells. It was highly selective at killing the cancer cells. The researchers also have preliminary results showing that the compound is similarly selective and effective for human breast and prostate cancer cells, and that it effectively and safely kills breast cancer in rats, Sasaki said.

Cancer drug designers are faced with the unique challenge that cancer cells develop from our own normal cells, meaning that most ways to poison cancer cells also kill healthy cells. Most available chemotherapies are very toxic, destroying one normal cell for every five to 10 cancer cells killed, Sasaki said. This is why chemotherapy's side effects are so devastating, he said. "Side effects are a major limitation to current chemotherapies," Sasaki said. "Some patients even die from them."

The compound Sasaki and his colleagues developed kills 12,000 cancer cells for every healthy cell, meaning it could be turned into a drug with minimal side effects. A cancer drug with low side effects would be more effective than currently available drugs, since it could be safely taken in higher amounts.

The artemisinin compound takes advantage of cancer cell's high iron levels. Artemisinin is highly toxic in the presence of iron, but harmless otherwise. Cancer cells need a lot of iron to maintain the rapid division necessary for tumor growth. Since too much free-floating iron is toxic, when cells need iron they construct a special protein signal on their surfaces. The body's machinery then delivers iron, shielded with a protein package, to these signals proteins. The cell then swallows this bundle of iron and proteins.

Artemisinin alone is fairly effective at killing cancer cells. It kills approximately 100 cancer cells for every healthy cell, about ten times better than current chemotherapies. To improve those odds, the researchers added a small chemical tag to artemisinin that sticks to the "iron needed here" protein signal. The cancer cell, unaware of the toxic compound lurking on its surface, waits for the protein machinery to deliver iron molecules and engulfs everything -- iron, proteins and toxic compound.

Once inside the cell, the iron reacts with artemisinin to release poisonous molecules called free radicals. When enough of these free radicals accumulate, the cell dies.

"The compound is like a little bomb-carrying monkey riding on the back of a Trojan horse," said Henry Lai, UW bioengineering professor and co-author of the study.

The compound is so selective for cancer cells partly due to their rapid multiplication, which requires high amounts of iron, and partly because cancer cells are not as good as healthy cells at cleaning up free-floating iron.

"Cancer cells get sloppy at maintaining free iron, so they are more sensitive to artemisinin," Sasaki said.

Cancer cells are already under significant stress from their high iron contents and other imbalances, Sasaki said. Artemisinin tips them over the edge. The compound's modus operandi also means it should be general for almost any cancer, the researchers said.

"Most currently available drugs are targeted to specific cancers," Lai said. "This compound works on a general property of cancer cells, their high iron content."

The compound is currently being licensed by the University of Washington to Artemisia Biomedical Inc., a company Lai, Sasaki and Narendra Singh, UW associate professor of bioengineering, founded in Newcastle, Wash. for development and commercialization. Human trials are at least several years away. Artemisinin is readily available, Sasaki said, and he hopes their compound can eventually be cheaply manufactured to help cancer patients in developing countries.

Other authors of the study are Steve Oh, UW medical student; Byung Ju Kim, UW chemistry instructor; and Singh.
The Washington Technology Center and the Witmer Foundation provided funding for the study.
For more information, contact Sasaki at (206) 543-6590 or sasaki@chem.washington.edu.

UCLA study finds that searching the Internet increases brain function

UCLA scientists have found that for computer-savvy middle-aged and older adults, searching the Internet triggers key centers in the brain that control decision-making and complex reasoning. The findings demonstrate that Web search activity may help stimulate and possibly improve brain function.

The study, the first of its kind to assess the impact of Internet searching on brain performance, is currently in press at the American Journal of Geriatric Psychiatry and will appear in an upcoming issue.

"The study results are encouraging, that emerging computerized technologies may have physiological effects and potential benefits for middle-aged and older adults," said principal investigator Dr. Gary Small, a professor at the Semel Institute for Neuroscience and Human Behavior at UCLA who holds UCLA's Parlow-Solomon Chair on Aging. "Internet searching engages complicated brain activity, which may help exercise and improve brain function."

As the brain ages, a number of structural and functional changes occur, including atrophy, reductions in cell activity, and increases in deposits of amyloid plaques and tau tangles, which can impact cognitive function.

Small noted that pursuing activities that keep the mind engaged may help preserve brain health and cognitive ability. Traditionally, these include games such as crossword puzzles, but with the advent of technology, scientists are beginning to assess the influence of computer use — including the Internet.

Additional details on the study and further research on the impact of computer technologies on the aging brain are highlighted in Small's new book, "iBrain: Surviving the Technological Alteration of the Modern Mind," published today.

For the study, the UCLA team worked with 24 neurologically normal research volunteers between the ages of 55 and 76. Half of the study participants had experience searching the Internet, while the other half had no experience. Age, educational level and gender were similar between the two groups.

Study participants performed Web searches and book-reading tasks while undergoing functional magnetic resonance imaging (fMRI) scans, which recorded the subtle brain-circuitry changes experienced during these activities. This type of scan tracks the intensity of cell responses in the brain by measuring the level of cerebral blood flow during cognitive tasks.

All study participants showed significant brain activity during the book-reading task, demonstrating use of the regions controlling language, reading, memory and visual abilities, which are located in the temporal, parietal, occipital and other areas of the brain.

Internet searches revealed a major difference between the two groups. While all participants demonstrated the same brain activity that was seen during the book-reading task, the Web-savvy group also registered activity in the frontal, temporal and cingulate areas of the brain, which control decision-making and complex reasoning.

"Our most striking finding was that Internet searching appears to engage a greater extent of neural circuitry that is not activated during reading — but only in those with prior Internet experience," said Small, who is also the director of UCLA's Memory and Aging Research Center.

In fact, researchers found that during Web searching, volunteers with prior experience registered a twofold increase in brain activation when compared with those with little Internet experience. The tiniest measurable unit of brain activity registered by the fMRI is called a voxel. Scientists discovered that during Internet searching, those with prior experience sparked 21,782 voxels, compared with only 8,646 voxels for those with less experience.

Compared with simple reading, the Internet's wealth of choices requires that people make decisions about what to click on in order to pursue more information, an activity that engages important cognitive circuits in the brain.

"A simple, everyday task like searching the Web appears to enhance brain circuitry in older adults, demonstrating that our brains are sensitive and can continue to learn as we grow older," Small said.

Small added that the minimal brain activation found in the less experienced Internet group may be due to participants not quite grasping the strategies needed to successfully engage in an Internet search, which is

common while learning a new activity." With more time on the Internet, they may demonstrate the same brain activation patterns as the more experienced group," he said.

Researchers noted that additional studies will address both the positive and negative influences of these emerging technologies on the aging brain.

The study was funded by the Parvin Foundation.

Additional study authors include Teena D. Moody, Ph.D., a senior research associate at UCLA's Semel Institute, and Susan Y. Bookheimer, Ph.D., a professor of psychiatry and biobehavioral sciences at the Semel Institute.

Tribendimidine shows promise against intestinal worms

Researchers have reported positive results from a safety and efficacy study pertaining to tribendimidine, a broad-based treatment for intestinal worm infections. The group's results demonstrate the success of the new drug from China versus that of the standard albendazole for the treatment of hookworm, large roundworm, whipworm, and, for the first time, threadworm and tapeworm. The study was jointly implemented by researchers from the Swiss Tropical Institute in Basel, the National Institute of Parasitic Diseases (IPD) in Shanghai, the Yunnan Institute of Parasitic Diseases in Simao, China, and the Jiangsu Institute of Parasitic Diseases in Wuxi, China. Details are published October 15th in the open-access journal PLoS Neglected Tropical Diseases.

Globally, more than one billion people are infected with intestinal worms. These chronic infections negatively impact on child and maternal health, nutritional status, physical performance, and cognitive development. The current control strategy relies on drugs to reduce morbidity, ideally complemented by the provision of safe water and sanitation to curb transmission. Only four drugs are currently recommended by the World Health Organization for treating soil-transmitted helminth infections, making the potential development of drug resistance a concern. Tribendimidine belongs to a different chemical class than current worm treatments. The drug had been developed at IPD and Shandong Xinhua Pharmaceutical in Zibo, China, and was approved by the China State Food and Drug Administration in 2004.

The community-based study involved 123 individuals who were screened for intestinal helminth infections, and randomly allocated to tribendimidine or the widely used albendazole treatment (both at 200 mg for children aged 5-14 years and 400 mg for individuals aged 15 years and above). The researchers' administration of a single oral dose of tribendimidine cured up to 92% of the common soil-transmitted helminth infections in humans in a highly endemic setting in China. Encouraging results were also found against threadworm and tapeworm infections. After treatment, these two parasites were absent in 55% and 67% of those initially infected, respectively. The infection intensity of large roundworms and hookworms was significantly reduced by both drugs, and no adverse treatment-related events were noted among the final study cohort.

The obtained results need to be validated in larger patient cohorts and different epidemiological settings, and repeated dosing should be tested to further improve treatment outcomes.

http://dx.plos.org/10.1371/journal.pntd.0000322 (links will go live on Wednesday, October 15)

***CITATION**: Steinmann P, Zhou X-N, Du Z-W, Jiang J-Y, Xiao S-H, et al. (2008) Tribendimidine and Albendazole for Treating Soil-Transmitted Helminths, Strongyloides stercoralis and Taenia spp.: Open-Label Randomized Trial. PLoS Negl Trop Dis 2(10): e322. doi:10.1371/journal.pntd.0000322*

Vitamin B supplementation did not slow cognitive decline in patients with Alzheimer's disease

High-dose vitamin B supplementation for patients with mild to moderate Alzheimer disease did not slow the rate of cognitive decline, according to a study in the October 15 issue of JAMA.

Evidence of homocysteine (an amino acid produced by the body) elevation in Alzheimer disease (AD) and the involvement of homocysteine in neuropathological mechanisms suggest that reduction of homocysteine may offer an approach to altering the disease. B vitamins that influence homocysteine metabolism have been considered as a therapeutic option to reduce risk of AD or slow its progression, according to background information in the article. According to the authors, prior studies of B vitamins to reduce homocysteine in AD have not had sufficient size or duration to assess their effect on cognitive decline.

Paul S. Aisen, M.D., of the University of California, San Diego, and colleagues conducted a clinical trial to determine if reduction of homocysteine levels with high-dose supplementation with folic acid and vitamins B6 and B12 for 18 months would slow the rate of cognitive decline in 409 individuals with mild to moderate AD. Participants were randomly assigned to two groups of unequal size to increase enrollment (60 percent treated with high-dose supplements [5 mg/d of folate, 25 mg/d of vitamin B6, 1 mg/d of vitamin B12] and 40 percent treated with identical placebo). A total of 340 participants (202 in active treatment group and 138 in placebo group) completed the trial while taking study medication. Cognitive abilities were measured via testing with the Alzheimer Disease Assessment Scale (ADAS-cog).

The researchers found that even though the vitamin supplement regimen was effective in reducing homocysteine levels, it had no beneficial effect on the primary cognitive measure: the rate of change in ADAS-cog score did not differ significantly between treatment groups. The authors did find that symptoms of depression were more common in the high-dose supplement group.

"Many studies suggest that relative elevation of homocysteine is characteristic of AD, and laboratory research implicates homocysteine in neurodegenerative mechanisms. High-dose B vitamin supplementation in individuals with normal levels of B vitamins was effective in reducing homocysteine levels. However, our study does not support the treatment of individuals with mild to moderate AD and normal vitamin levels with B vitamin supplements," the authors conclude.

(JAMA. 2008;300[15]:1774-1783. Available pre-embargo to the media at www.jamamedia.org)

***Editor's Note**: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

Editorial: B Vitamins for Prevention of Cognitive Decline - Insufficient Evidence to Justify Treatment

In an accompanying editorial, Robert J. Clarke, M.D., F.R.C.P., and Derrick A. Bennett, Ph.D., of the University of Oxford, England, comment on the findings regarding B vitamin supplementation.

"The precise reasons the [study by Aisen and colleagues] failed to detect any beneficial effect of B vitamins on the rate of cognitive decline remain unclear," they write. "However, until and unless new data suggest otherwise, there is insufficient evidence to justify routine use of homocysteine-lowering vitamin supplements for the prevention of Alzheimer disease and cognitive decline among individuals with normal vitamin status."

(JAMA. 2008;300[15]:1819-1821. Available pre-embargo to the media at www.jamamedia.org)

***Editor's Note**: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

Northerners' hands up to 3 times dirtier than those living in the South

The further north you go, the more likely you are to have faecal bacteria on your hands, especially if you are a man, according to a preliminary study conducted by the London School of Hygiene & Tropical Medicine.

But women living in the South and Wales have little to feel smug about. In London, they are three times as likely as their men folk to have dirty hands, and in Cardiff, twice as likely. The men of London registered the most impressive score among all those surveyed, with a mere 6% found to have faecal bugs on their hands. Overall more than one on four commuters have bacteria which come from faeces on their hands.

The Dirty Hands Study was conducted in order to provide a snapshot of the nation's hand hygiene habits, as part of the world's first Global Handwashing Day today. Commuters' hands were swabbed at bus stops outside five train stations around the UK (Newcastle, Liverpool, Birmingham, Euston and Cardiff).

The results indicated that commuters in Newcastle were up to three times more likely than those in London to have faecal bacteria on their hands (44% compared to 13%) while those in Birmingham and Cardiff were roughly equal in the hand hygiene stakes (23% and 24% respectively). Commuters in Liverpool also registered a high score for faecal bacteria, with a contamination rate of 34%.

In Newcastle and Liverpool, men were more likely than women to show contamination (53% of men compared to 30% of women in Newcastle, and 36% of men compared to 31% of women in Liverpool), although in the other three centres, the women's hands were dirtier. Almost twice as many women than men in Cardiff were found to have contamination (29% compared to 15 %) while in Euston, they were more than three times likelier than the men to have faecal bacteria on their hands (the men here registered an impressive 6%, compared to a rate of 21% in the women). In Birmingham, the rate for women was slightly higher than the men (26% compared to 21%).

The bacteria that were found are all from the gut, and do not necessarily always cause disease, although they do indicate that hands have not been washed properly.

Dr Val Curtis, Director of the Hygiene Centre at the London School of Hygiene & Tropical Medicine, comments: 'We were flabbergasted by the finding that so many people had faecal bugs on their hands. The figures were far higher than we had anticipated, and suggest that there is a real problem with people washing their hands in the UK. If any of these people had been suffering from a diarrhoeal disease, the potential for it to be passed around would be greatly increased by their failure to wash their hands after going to the toilet'.

Global Handwashing Day was initiated by the Public-Private Partnership for Handwashing (www.globalhandwashing.org), which is dedicated to promoting handwashing with soap to reduce diarrhoea in developing countries and implement large-scale handwashing interventions by combining the expertise and resources of the soap industry with the facilities and resources of governments. Global Handwashing Day activities are being implemented in more than forty countries and focus on raising awareness among policymakers and the public about the role handwashing plays in public health.

Biotech experts urge industry to work with researchers or risk federal action

New report calls for reform of the intellectual property system

WASHINGTON, DC—(14 October 2008) - The intellectual property (IP) system in the United States is broken and must be transformed if it is to foster biotechnological advances and ensure that treatments and cures for diseases reach patients, national and international IP and biotech leaders said today.

At a briefing on Capitol Hill, McGill University's Richard Gold, SJD, and Duke University's Robert Cook-Deegan, MD, revealed the results of a case study that documents for the first time mistakes made by a US company in protecting and enforcing patent rights on breast cancer genes in the United States and abroad. And contrary to what industry has argued, they said, Myriad Genetics' "hardball" tactics are the norm in the biotech and pharmaceutical industry.

"Our findings suggest that patent holders are not doing a good job of sharing information and biotechnological tools to foster innovation and access to vital genetic data," said Cook-Deegan, "and government must be prepared to intervene when they do not."

The conclusions presented by Gold and Cook-Deegan today are echoed in a new groundbreaking report - Toward a New Era of Intellectual Property: From Confrontation to Negotiation - from the International Expert Group on Biotechnology, Innovation and Intellectual Property, chaired by Gold, and in a series of new case studies prepared by the Expert Group and by Duke University, chronicling the development and commercialization of several genetic diagnostic tests.

The authors of the report say that the pharmaceutical and biotechnology industries' heavy reliance on patents and aggressive enforcement of IP—the era of "Old IP"—are creating an environment of intimidation that prevents scientists from using tools that are vital to innovation, while blocking access to diagnostic tests that may have important implications for science and for public health.

Based on consultations with more than 100 researchers and other representatives of industry, government, academic research centers and non-governmental organizations, and more than 10 years of data from 17 countries, the Montreal-based International Expert Group found "there is universal acknowledgment that the biopharmaceutical innovation system is broken," Gold said.

"As a result, the biopharmaceutical industry has fewer and fewer products in their pipelines," he added, "and more and more of those products are 'me-too' drugs, which target diseases for which treatments have already been developed."

According to Gold and Cook-Deegan, if patent holders don't change their behavior and government agencies don't act, pressure will grow on legislators to intervene.

"The solution in the United States is not to prevent patenting activity, but for government to make clear it will step in and exercise rights it has already," said Cook-Deegan, director of the Center for Genome Ethics, Law & Policy at the Duke Institute for Genome Sciences & Policy. He notes that under the 1980 Bayh-Dole Act, universities, small businesses and non-profits are allowed to control their inventions and other IP that results from federal funding. But the government retains the right to "march-in," or intervene on behalf of the public and grant additional licenses, if it sees the need.

"The fact is, in the 28 years since the Bayh-Dole Act was enacted, the government has never asserted its right to 'march-in,' whether for health or safety reasons, or to push for action to achieve practical application of a given invention," said Cook-Deegan. "And industry knows that."

When Aggressive Tactics Backfire

Cook-Deegan and Gold point to the case studies discussed in Washington today as illustrations of the fundamental problems of "Old IP." In Myriad Genetics: In the Eye of the Policy Storm, they follow the story of Utah-based company, Myriad Genetics, and document mistakes the company made in protecting and enforcing patent rights on breast cancer genes in the United States and abroad.

"The mistakes in the Myriad case were not illegal actions, but political and strategic errors," said McGill's Gold. "In the United States this meant the company failed to reassure those conducting research on breast cancer that they would not be sued. Internationally, in nations with public health care systems, Myriad's hardball tactics led to resistance from governments and in most places prevented Myriad from being able to license its diagnostic tests."

Instead of securing international markets, he added, aggressive tactics undermined Myriad's interests—not only for the breast cancer test, but for future products the company might want to market abroad.

And contrary to what industry says, according to the new research discussed today, the Myriad model of fiercely protecting patents is being replicated throughout the biotech and pharmaceutical industry. Cook-Deegan presented preliminary observations based on studies in progress about the behavior of a number of

companies and institutions with patents on genes and diagnostic tests. He observed that companies are ignoring at their peril the lessons of Myriad and of the other examples cited in the International Expert Group's report.

"Some of the same tactics that damaged Myriad's reputation and harmed its business interests are being repeated by other companies, which are aggressively enforcing patents against university laboratory testing services," Cook-Deegan said. "Such actions are affecting genetic testing for several diseases, including Alzheimer's disease and Long QT syndrome, a condition that can make carriers extremely vulnerable to sudden cardiac death."

Based on their research, Gold and Cook-Deegan conclude that such actions are decreasing the size of potential markets and alienating the payers that reimburse for testing, as well as the physicians who order tests and the consumers who seek them.

"In the end, the companies are undermining their long-term viability," said Cook-Deegan. "Rather than treating their patents as clubs, the companies should use them as tools to foster collaboration with other companies, physicians, disease-group constituencies, reference laboratories, universities and academic researchers, as well as attending to the needs and expectations of purchasers of health care services both in the United States and around the world."

'Don't Mess with Natural Allies'

Cook-Deegan notes that patents alone are not enough to guarantee the success of a patent holder. At least as important, he said, are the reimbursement policies of payers such as Medicare and Medicaid, the behavior of physician specialists who order genetic tests, collaborations with academic researchers and the support of advocacy groups.

"One lesson emerging from the case studies is that patents are important, but they are not enough to ensure financial success," said Cook-Deegan. "Indeed, if patents tempt companies to overplay their hand, they can damage their own long term business interests. The warning to industry is, 'Do not mess with your natural allies.'"

And patients, physicians, and payers are likely to push for access to the results of diagnostic tests, and greater and more flexible licensing of patents, Gold said. The report he and his team produced, drawing on the work of an extensive team of contributors, concludes that innovation occurs best when all parties – researchers, companies, NGOs, and governments - work collaboratively. They point to information technology as a model for how a new system might be designed.

"This doesn't mean we don't need a system for protecting intellectual knowledge," Gold said. "But we need a system that is flexible enough to allow research to encourage innovation and benefit those who need it most.

"If companies adapt to the needs of consumers and payers through more open and flexible licensing, the biotechnology industry will thrive. Look at the way that change has swept through the world of information technology and brought benefits to millions, merely by engaging in broad and transparent licensing that results in a great deal of creativity and new products that address existing problems."

Other recommendations from the International Expert Group report for national and international IP systems include:

* Fostering greater trust between actors: A lack of trust has blocked collaborations to deliver lifesaving technologies, such as diagnostic tests, and has led to ineffective legislative reform. Independent trust builders who educate and encourage dialogue between industry, government, researchers and non-governmental organizations are essential.

* Creating better ways to develop and deliver biotechnology products: This will require governments, researchers, industry and NGOs to collaborate through partnerships designed to:

=> encourage the sharing of molecular libraries and basic environmental technologies;

=> allow for exchanges of data, materials, and patents;

=> overcome concerns about high risk through joint public and private funding of promising avenues of research;

=> create patent pools to unblock the development, production and sale of medicines and technologies that the developing world needs to have a sustainable and secure economy.

* Promoting more transparency and communication: Because the stakes are so high, the level of conversation about IP and science and technology policy must be raised and objectives and motives clearly stated.

* Improving how data are collected and measured: Right now, the United States measures the wrong things about IP, particularly at public institutions and universities. The U.S. needs to figure out what it wants from innovation and how to measure it. New computer tools and digital information, much of it available on-line, will allow policy makers to explore a variety of factors in deciding how to proceed in patenting—or not—a piece of federally-funded research.

Copies of the report Toward a New Era of Intellectual Property: From Confrontation to Negotiation, can be obtained at http://www.theinnovationpartnership.org/en/ieg/report/. A copy of Myriad Genetics: In the Eye of the Policy Storm, can be obtained at: http://www.theinnovationpartnership.org/ieg/documents/cases/TIP_Myriad_Report.pdf

The Innovation Partnership (TIP)

The Innovation Partnership (http://www.theinnovationpartnership.org/en/) is an independent non-profit consultancy with experts in developed and developing countries specializing in the understanding, use and management of intellectual property. TIP's mission is to foster innovation and creativity through the better use of intellectual property and its alternatives

TIP was created in 2007 by a group of experts, who spent seven years working together on a study of the role that patents and other intellectual property rights play in determining social, economic and cultural outcomes of biotechnology. Funded by the Canadian government and organized through McGill University's Centre for Intellectual Property Policy (www.cipp.mcgill.ca), the International Expert Group on Biotechnology, Innovation and Intellectual Property concluded that government, industry and NGOs lack independent, empirically-based expertise on how best to adapt intellectual property to the needs of modern society. The research of the International Expert Group on Biotechnology, Innovation and Intellectual Property was conducted with financial support from Social Sciences and Humanities Research Council of Canada (http://www.sshrc.ca/) and the Canadian Institutes of Health Research (www.cihr-irsc.gc.ca/).

The Duke Institute for Genome Sciences & Policy/Duke Center for Public Genomics

The Duke Institute for Genome Sciences and Policy (http://www.genome.duke.edu/) represents the university's comprehensive response to the broad challenges of the Genomic Revolution. Because advances in genome science and its applications raise a broad spectrum of ethical, legal and policy issues, the IGSP comprises -- in addition to scientists, engineers and physicians -- scholars in law, business, economics, public policy, ethics, religion, environmental studies and other humanities and social sciences. The Duke Center for Public Genomics (http://www.genome.duke.edu/centers/cpg/) is housed at the IGSP. It was established to explore the value of "open science" norms and practices as well as to study the benefits and risks of intellectual property protections in genomics, through historical, legal, economic, and empirical research. The Center is composed of three mutually dependent research projects and three cores that provide support for the projects. Work of the Center for Public Genomics is funded by the National Human Genome Research Institute http://www.genome.gov/ and US Department of Energy. http://www.genome.duke.edu/centers/cpg/

Earliest known human TB found in 9,000-year-old skeletons

The discovery of the earliest known cases of human tuberculosis (TB) in bones found submerged off the coast of Israel shows that the disease is 3000 years older than previously thought. Direct examination of this ancient DNA confirms the latest theory that bovine TB evolved later than human TB.

The new research, led by scientists from UCL (University College London) and Tel-Aviv University and published today in PLoS One, sheds light on how the TB bacterium has evolved over the millennia and increases our understanding of how it may change in the future.

The bones, thought to be of a mother and baby, were excavated from Alit-Yam, a 9000 year-old Pre-Pottery Neolithic village, which has been submerged off the coast of Haifa, Israel for thousands of years. Professor Israel Hershkovitz, from Tel-Aviv University's Department of Anatomy, noticed the characteristic bone lesions that are signs of TB in skeletons from the settlement, one of the earliest with evidence of domesticated cattle.

An international collaborative team, led by Dr Helen Donoghue and Dr Mark Spigelman, UCL Centre for Infectious Diseases & International Health, conducted detailed analyses of the bones using scientific techniques that revealed DNA and cell wall lipids from Mycobacterium tuberculosis, the principal agent of human TB. The DNA was sufficiently well-preserved for molecular typing to be carried out and the analysis of the bacterial cell wall lipids by high performance liquid chromatography provided direct, confirmatory evidence of tuberculosis.

Dr Donoghue said: "What is fascinating is that the infecting organism is definitely the human strain of tuberculosis, in contrast to the original theory that human TB evolved from bovine TB after animal domestication. This gives us the best evidence yet that in a community with domesticated animals but before dairying, the infecting strain was actually the human pathogen. The presence of large numbers of animal bones shows that animals were an important food source, and this probably led to an increase in the human population that helped the TB to be maintained and spread.

"We were also able to show that the DNA of the strain of TB in these skeletons had lost a particular piece of DNA which is characteristic of a common family of strains present in the world today. The fact that this deletion had occurred 9000 years ago gives us a much better idea of the rate of change of the bacterium over time, and indicates an extremely long association with humans."

Dr Spigelman added: "Examining ancient human remains for the markers of TB is very important because it helps to aid our understanding of prehistoric tuberculosis and how it evolved. This then helps us improve our understanding of modern TB and how we might develop more effective treatments."

Worrisome Infection Eludes a Leading Children's Vaccine

By LAURA BEIL

A highly drug-resistant germ has become a common cause of meningitis, pneumonia and other life-threatening conditions in young children. The culprit — a strain of strep bacteria — can conquer almost all antibiotics in pediatrics, and has dodged a vaccine otherwise credited with causing the number of serious infections in children to plummet.

Since 2000, American toddlers have been immunized against Streptococcus pneumoniae, or pneumococcus, an organism that preys largely on children younger than 5 and the elderly. Pneumococcal meningitis can be fatal, and survivors are often left with deafness and other lifelong neurological problems.

And by most measures, the vaccine has worked: by 2002, rates of infection from these bacteria had dropped as much as 80 percent in some places. But progress has now stalled, and infection with a particular type of pneumococcus, Serotype 19A, is steadily rising.

"It's very much a concern," said Bernard Beall, a pneumococcal expert at the federal Centers for Disease Control and Prevention. Last year, in The Journal of the American Medical Association, pediatricians described an outbreak of Serotype 19A ear infections in Rochester that could be cured only by surgically implanting tubes, or by turning to adult medicines not yet tested for safety in children.

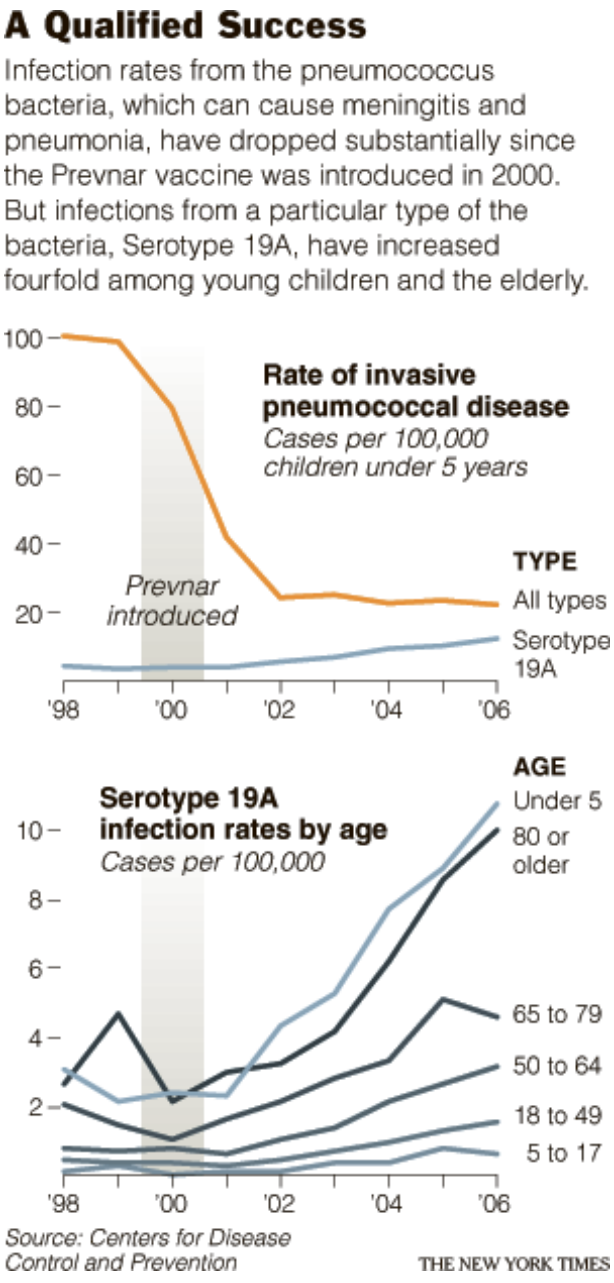
A greater worry, however, is the frequency of meningitis, pneumonia and bloodstream infections from Serotype 19A. Since 2001, rates of these and other invasive pneumococcal diseases have crept upward, to more than 10 per 100,000 children from about 2 per 100,000. A fourfold increase in life-threatening infections has also occurred among the elderly.

The vaccine, Prevnar, is aimed at seven types of bacteria that were responsible for 70 to 80 percent of pneumococcal illness during the 1990s. Because pneumococci come in 91 forms, experts have worried from the start whether bacteria that were just as deadly, but not wiped out by the vaccine, might move in as opportunists when the competition suddenly vanished.

"Nature abhors a vacuum," said Dr. Steven Black of Cincinnati Children's Hospital. Indeed, almost all pneumococcal infections among American children today are caused by versions not covered by the vaccine, and 19A is leading the way. "People hoped against hope it wouldn't happen," he said.

The vaccine's manufacturer, Wyeth, says it has been working quickly to develop a new product to counter 19A and five other pneumococcal variations, along with the original seven. The company will release results of the first large studies of the newer version this month at an infectious disease meeting in Washington.

"There was no point where we said to ourselves, 'We missed it, we need to put in 19A,' " said Emilio A. Emini, head of vaccine research and development for Wyeth. The company was always prepared to remake the product, he said.



Once a new vaccine demonstrates that it can protect against pneumococcus, it must work its way through the approval process — passing tests of effectiveness and safety — before it can be licensed. Researchers will also try to determine whether young children who have been immunized with the old Prevnar should be revaccinated to protect themselves from 19A.

The remodeling of a vaccine so soon after its approval is highly unusual, but so was the effort to tackle pneumococcus.

The bacteria live in the nose and throat, usually as microbial freeloaders of no consequence. Occasionally — often after a simple viral infection — pneumococci slip into inner areas of the body and cause disease. Weaker immune systems in the very young and the very old leave them most vulnerable. (The pneumonia shot in older people includes 19A, but many elderly people have not received the immunization.)

Not all of the 91 incarnations of pneumococcal bacteria are dangerous. They developed so much variety by mingling in the back of the throat, exchanging genetic material as eagerly as children trading Halloween candy. The variation in genes slightly alters how the bacteria function and how they are received by the immune system.

For vaccine manufacturers, pneumococci's diversity presented a challenge: how to teach the immune system to recognize a target that may look a little different from child to child. "This is the most complex biological product ever made," Dr. Emini said.

Serotype 19A was around in the 1990s, though uncommon, and the vaccine includes a similar version called 19F. The hope in 2000 was that 19F looked enough like 19A to set off an immune reaction. It did not.

Experts say it is hard to know what role the introduction of Prevnar may have played in the rise of the bacteria, which was gaining momentum in some countries before the vaccine's adoption. For example, researchers from GlaxoSmithKline, which is introducing its own pneumococcal vaccine, reported last month that Serotype 19A became more common in Belgium from 2001 to 2004 — years when pneumococcal vaccination was rare in that country. Similar reports have emerged from China, South Korea and Israel.

Pneumococci ebb and flow in natural cycles, and some types have gained a survival advantage by growing resistant to a host of drugs. The vaccine may have simply amplified natural trends..

"I don't think anyone can tell you the relative contributions of these factors," said Dr. Sheldon L. Kaplan of Texas Children's Hospital in Houston. This summer, he and his colleagues described a growing number of cases of drug-resistant mastoiditis, an infection of an inner-ear bone, from 19A.

Experts are now watching to see how forcefully the organism will spread before the new immunization arrives. Wyeth says it hopes to file an application with the Food and Drug Administration in 2009.

Disease experts also wonder what organisms like 19A mean for the future of pneumococcal infections. Public health experts once hoped the infection could be defeated, but it now appears that pneumococci may be playing a game of cat and mouse.

"The pneumococcus has shown an extraordinary ability to evolve to our strategies," said Dr. Beall of the C.D.C.

Yet he and others are quick to say that immunization remains highly effective, even if it leaves some children behind. "This is not a failure of the vaccine," said Dr. George H. McCracken Jr. of the University of Texas Southwestern Medical Center at Dallas. Even with the rise of 19A, children are much less likely to become ill from pneumococcal infections.

Dr. McCracken hopes that researchers will one day avoid threats like 19A entirely by developing a vaccine that primes the immune system to recognize some element common to all 91 types of pneumococci — in the way a quiche, an omelet and a custard pie are all versions of eggs. But until such an immunization comes along, he said, pediatricians will be forced to battle the pneumococcus as they always have, by trying to stay one strain ahead of its game.

New Study Reveals Details Of Evolutionary Transition From Fish To Land Animals

Head skeleton sheds light on intermediate steps

PHILADELPHIA. New research by scientists at The Academy of Natural Sciences provides the first detailed look at the internal head skeleton of Tiktaalik roseae, the 375-million-year-old fossil animal that represents an important intermediate step in the evolutionary transition from fish to animals that walked on land.

The study, published in the Oct. 16 issue of Nature shows that the transition from aquatic to terrestrial lifestyles involved complex changes not only to the appendages (fins to limbs) but also to the internal head skeleton. This is the first report on Tiktaalik roseae since the original description in 2006 made international news.

A team co-led by the Academy's Dr. Ted Daeschler discovered Tiktaalik roseae (tik-TAHL-ik RO-zay) in 2004 within Devonian-age rock on Ellesmere Island in Canada, more than 700 miles above the Arctic Circle. The creature was a large aquatic predator with a flattened head and body. The body plan and nature of the deposits where the fossils were found suggest an animal that lived on the bottom in shallow water and perhaps even out of the water for short periods. Tiktaalik roseae has features of the skull, neck, ribs and appendages that are shared with the earliest limbed animals (tetrapods), as well as fishlike features such as scales and fin rays. This mosaic of features makes it a textbook example of a transitional fossil.

Dr. Jason Downs, a postdoctoral research fellow at the Academy and lead author of the latest study, said the examination of the internal head skeleton further demonstrates the intermediacy of Tiktaalik roseae. "The

braincase, palate and gill arches of Tiktaalik help reveal the pattern of evolutionary change in this part of the skeleton," said Downs. "We see that cranial features once associated with land-living animals were first adaptations for life in shallow water."

"The new study reminds us that the gradual evolutionary transition from fish to tetrapod and the transition from aquatic to terrestrial lifestyles required much more than the evolution of limbs," said Daeschler. "Our work demonstrates that the head of these animals was becoming more solidly constructed and, at the same time, more mobile with respect to the body across this transition."

Along the lineage of lobe-finned fish that leads to tetrapods, trends in head shape include a flattening of the skull and a lengthening of the snout. With several well-preserved specimens of Tiktaalik roseae, this study helps document the relative timing of the particular skeletal changes associated with these changes in head shape.

The head skeleton of Tiktaalik. **Ted Daeschler, Academy of Natural Sciences**

"We used to think of this transition of the neck and skull as a rapid event largely because we lacked information about the intermediate animals," said Dr. Neil Shubin of the University of Chicago, who co-lead the team that discovered Tiktaalik roseae. "Tiktaalik neatly fills this morphological gap, and so it helps to resolve the relative timing of this complex transition."

During this time of transition, the interactions among the different parts of the head skeleton also were changing. An example is the gradual reduction of the hyomandibula, a bone that, in fish, links the braincase, palate and gill skeletons and coordinates their relative motions during underwater feeding and respiration. In the transition to life on land, the hyomandibula gradually lost these functions, and the bone became available for an eventual role in hearing. In humans, as in other mammals, the hyomandibula, or stapes, is one of the tiny bones in the middle ear.

"The bony part of Tiktaalik's hyomandibula is greatly reduced from the primitive condition," said Downs. "This could indicate that these animals, in shallow-water settings, were already beginning to rely less on gill respiration." Correlated with the changes to the hyomandibula was the dramatic loss of rigid gill-covering bones; this allowed for increased mobility in the neck region.

"Fish in deep water move and feed in three-dimensional space and can easily orient their body in the direction of their prey," said Dr. Farish Jenkins, Jr., a Harvard University evolutionary biologist and a co-author of the study. "A mobile neck is advantageous in settings where the body is relatively fixed, as is the case in shallow water and on land."

It took more than a year for fossil preparators C. Frederick Mullison, of the Academy in Philadelphia, and Bob Masek, of the University of Chicago, to expose and preserve the delicate details in the head skeleton of Tiktaalik roseae. The Academy has co-led six expeditions to the Arctic sites, including this past summer The public can see a cast and a reconstruction of Tiktaalik roseae on permanent display in the Academy's museum.

The fossil research in Nunavut is carried out with authorization from the Department of Culture, Language, Elders and Youth, Government of Nunavut. All fossils are the property of the people of Nunavut and will be returned to Canada after they are studied. The research was supported by private donors, The Academy of Natural Sciences, the Putnam Expeditionary Fund (Harvard University), The University of Chicago, The National Science Foundation, and The National Geographic Society Committee for Research and Exploration.

Blindsight: How brain sees what you do not see

Blindsight is a phenomenon in which patients with damage in the primary visual cortex of the brain can tell where an object is although they claim they cannot see it. A research team led by Prof. Tadashi Isa and Dr. Masatoshi Yoshida of the National Institute for Physiological Sciences, Japan, provides compelling evidence that blindsight occurs because visual information is conveyed bypassing the primary visual cortex. Japan Science and Technology Agency supported this study. The team reports their finding in the Journal of Neuroscience on Oct 15, 2008.

The researchers recorded eye movements of Japanese monkeys that had damage in one side of the primary visual cortex. Training with an eye movement task for 2-3 months enabled the monkeys to move their eyes to the correct direction where an object was even in the affected side of their visual fields. Brain became able to feel where an object was without 'seeing' it. After the training, their eye movements looked almost normal; they

discriminated five different directions even in the affected visual field. To investigate how eyes move, the monkeys' eye movements to targets in their affected visual field were compared with those to dark targets in their normal visual field. Both were 'equally difficult to see'. By this trick, the researchers found two differences from the normal: 1) the trajectory of their eye movements was straight and 2) the response time of their eye movement was short. These differences were thought to be due to the damage of eye movement control and decision making, not purely on that of vision. Therefore, the researchers concluded that the monkeys' eye movements after damage in the primary visual cortex were mediated by a qualitatively different vision which is supported by alternative brain circuits bypassing the primary visual cortex.

"Our finding will provide a new strategy for rehabilitation of these patients with damage in the primary visual cortex. That will be a rehabilitation training to activate alternative brain circuits to see what you do not see", said Dr. Yoshida. "A similar training may help the patients to know where an object is even without 'seeing' it."

Being altruistic may make you attractive

Tue, 14 Oct 2008 15:54:00 GMT

Displays of altruism or selflessness towards others can be sexually attractive in a mate. This is one of the findings of a study carried out by biologists and a psychologist at The University of Nottingham.

In three studies of more than 1,000 people Dr Tim Phillips and his fellow researchers discovered that women place significantly greater importance on altruistic traits in all three studies. Their findings have been published in the British Journal of Psychology.

Dr Phillips said: “Evolutionary theory predicts competition between individuals and yet we see many examples in nature of individuals disadvantaging themselves to help others. In humans, particularly, we see individuals prepared to put themselves at considerable risk to help individuals they do not know for no obvious reward.”

Participants in the studies were questioned about a range of qualities they look for in a mate, including examples of altruistic behaviour such as ‘donates blood regularly’ and ‘volunteered to help out in a local hospital’. Women placed significantly greater importance on altruistic traits in all three studies.

Yet both sexes may consider altruistic traits when choosing a partner. One hundred and seventy couples were asked to rate how much they preferred altruistic traits in a mate and report their own level of altruistic behaviour. The strength of preference in one partner was found to correlate with the extent of altruistic behaviour typically displayed in the other, suggesting that altruistic traits may well be a factor both men and women take into account when choosing a partner.

Dr Phillips said: “For many years the standard explanation for altruistic behaviour towards non-relatives has been based on reciprocity and reputation — a version of ‘you scratch my back and I’ll scratch yours’. I believe we need to look elsewhere to understand the roots of human altruism. The expansion of the human brain would have greatly increased the cost of raising children so it would have been important for our ancestors to choose mates both willing and able to be good, long-term parents. Displays of altruism could well have provided accurate clues to this and genes linked to altruism would have been favoured as a result.”

Dr Phillips concluded: “Sexual selection could well come to be seen as exerting a major influence on what made humans human.”

Dr Tom Reader in the School of Biology said: “Sexual preferences have enormous potential to shape the evolution of animal behaviour. Humans are clearly not an exception: sex may have a crucial role in explaining what are our most biologically interesting and unusual habits.”

Importance of sex-specific testing shown in anxiety study

An Australian study has flagged an important truth for the medical research community. Like their human counterparts, male and female mice are not only different, their respective genetic responses can often be the reverse of what you'd expect from pharmacological results. This has important ramifications for laboratory and clinical testing.

Dr Tim Karl, behavioural neuroscientist at the Garvan Institute of Medical Research, found the opposite of what he expected in female mice when he investigated the anxiety behaviours of males and females in specific mouse models. His results were reported recently in the European Journal of Neuroscience.

"There's a neurotransmitter in the brain known as NPY, and we know that it buffers behavioural consequences of stress, lowering anxiety levels," explained Karl. "Pharmacological tests show that when you introduce NPY to an animal in a stressful situation, its stress levels decrease."

"Studies in the past have shown that male mice created without NPY are more anxious than normal mice, which is hardly surprising. What is surprising is that female mice without NPY, while still more anxious than normal mice, are less anxious than the males without NPY."

"Knowing that normal female mice respond in a different way to stress than normal male mice, in the same way that women respond differently to stress than men - they are at least twice as prone to anxiety disorders for example - we didn't expect what we found."

"The outcomes tell us that you have to do both genetic studies and pharmacological studies to get the whole picture and see what your gene of interest is really doing."

"You also have to look at males and females because we operate differently. Women show a better response to certain antipsychotics than men, for example."

"Using female mice in research is complicated by the females' oestrus cycle - it impacts on neuro-physiological parameters, including behaviour and perception of stress. For these reasons, and because of the additional time and cost involved in taking such variations into account, people often avoid using females in their research."

"But when a sexual difference has bearing on the physiological response under investigation, it becomes vital to look at males and females, both in animals and in humans."

Note to Editors *While not directly relevant to the above study, Dr Tim Karl's work while at Garvan has also been supported by the Schizophrenia Research Institute.*

Pharmaceutical freebies may harm children

THE practice of using free drug samples to treat some children in the US may be causing more harm than good.

In many countries, doctors are allowed to obtain free samples of new drugs from companies so that they can familiarise themselves and their patients with them. Critics argue that this can divert prescribing away from the best clinical practice.

A team led by Sarah Cutrona of the Cambridge Health Alliance in Massachusetts has now revealed the extent to which free drug samples are given to children in the US. In 2004, 4.9 per cent of the 10,295 children in a nationally representative survey were given at least one free drug sample (Pediatrics, DOI: 10.1542/peds.2007-2928).

Among the 15 drugs most frequently distributed were some with safety risks. These include stimulants to treat attention-deficit hyperactivity disorder that the US government lists as controlled substances because of their addictive potential. ...

Free Drug Samples in the United States: Characteristics of Pediatric Recipients and Safety Concerns

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OBJECTIVES. Free drug samples frequently are given to children. We sought to describe characteristics of free sample recipients, to determine whether samples are given primarily to poor and uninsured children, and to examine potential safety issues.

METHODS. We analyzed data on 10295 US residents <18 years of age from the 2004 Medical Expenditure Panel Survey, a nationally representative survey that includes questions on receipt of free drug samples. We performed bivariate and multivariate analyses to evaluate characteristics associated with receipt of ≥1 free drug sample in 2004. We identified the most frequently reported sample medications and reviewed potential safety issues.

RESULTS. Ten percent of children who received prescription medications and 4.9% of all children received ≥1 free drug sample in 2004. In bivariate analyses, poor children (family incomes of <200% of the federal poverty level) were no more likely to receive free samples than were those with incomes of ≥400% of the poverty level (3.8% vs 5.9%). Children who were uninsured for part or all of the year were no more likely to receive free samples than were those who were insured all year (4.5% vs 5.1%); 84.3% of all sample recipients were insured. In multivariate analyses, routine access to health care (≥3 provider visits in 2004) was associated with free sample receipt. The 15 most frequently distributed pediatric free samples in 2004 included 2 schedule II controlled medications, Strattera (atomoxetine) and Adderall (amphetamine/dextroamphetamine), and 4 medications that received new or revised black box warnings between 2004 and 2007, Elidel (pimecrolimus), Advair (fluticasone/salmeterol), Strattera (atomoxetine), and Adderall (amphetamine/dextroamphetamine).

CONCLUSIONS. Poor and uninsured children are not the main recipients of free drug samples. Free samples do not target the neediest children selectively, and they have significant safety considerations.

Polio could be wiped out in Nigeria thanks to improved vaccine, says study

A recently introduced polio vaccine is four times more effective at protecting children than previous vaccines and has the potential to eradicate type 1 polio in Nigeria if it reaches enough children, according to a study published today in the New England Journal of Medicine.

Nigeria is one of only four countries in the world where polio has yet to be eliminated and 82% of global cases so far this year have been in Nigeria. Polio is highly infectious and it primarily affects children under five years of age. A small minority of infected people develop permanent paralysis, which can be fatal.

The monovalent oral poliovirus vaccine, known as mOPV1, has been used in Nigeria since February 2006 and the number of reported cases of polio in the country fell by 75% between 2006 and 2007.

With each dose of mOPV1 received, a child in Nigeria has a 67% chance of being protected against type 1 paralytic poliomyelitis, according to the new study, which was carried out by researchers from the MRC Centre for Outbreak Analysis and Modelling at Imperial College London, working with international colleagues. The standard trivalent vaccine in the same setting had an efficacy of 16%.

Although the monovalent vaccine is proving very effective, many more children need to be immunised against polio if the virus is to be eliminated in Nigeria, say the researchers. In the North West zone of the country, where the majority of new cases are found, 21% of children report never having received a single dose of the vaccine and a further 55% have received fewer than the recommended four doses.

The new research comes just 4 months after the World Health Assembly expressed alarm over a dramatic increase in type 1 cases in Nigeria because of poor immunisation in the north of the country. The Government of Nigeria subsequently established a Presidential Task Force to identify barriers to immunisation and potential solutions.

A previous study, published in the Lancet in 2007, looked at how well polio vaccines were working in Northern India and revealed that there, although mOPV1 was three times more effective than the trivalent vaccine, environmental factors compromised the efficacy of both the trivalent and monovalent oral vaccines. The researchers behind today's study say that the mOPV1's effectiveness is not as badly compromised by environmental conditions in Nigeria. This means that the key to eliminating polio in Nigeria is reaching sufficient numbers of children with the vaccine, demonstrating the feasibility of elimination in Africa.

Helen Jenkins, the corresponding author of the study from the MRC Centre for Outbreak Analysis and Modelling at Imperial College London, said: "Nigeria and India are responsible for the vast majority of new global polio cases. In Nigeria, we now have an effective vaccine to use and we've seen the start of improvements in vaccine uptake. These last pockets of unvaccinated children now need to be reached to achieve elimination in Nigeria and this in turn will have a dramatic impact on the prospects of worldwide eradication."

The researchers reached their conclusions after analysing the vaccination histories of 21,815 children with acute flaccid paralysis, 14% of whom had polio, collected between January 2001 and December 2007.

This study was supported by the Medical Research Council and the Royal Society.

Bugs in the gut trigger production of important immune cells, NYU study finds

The finding may lead to new treatments for inflammatory bowel disease

NEW YORK CITY, NY - October 15, 2008 – A new study reveals that specific types of bacteria in the intestine trigger the generation of pro-inflammatory immune cells, a finding that could eventually lead to novel treatments for inflammatory bowel disease and other diseases. The study by NYU Langone Medical Center researchers is published in the October 16 issue of the journal Cell Host and Microbe. The new finding adds to the growing body of research showing that the kinds of bacteria in our intestine, and in our stomach, have an impact on our health.

"There is more and more evidence that gut flora have a tremendously important influence on human health," says Yasmine Belkaid, Ph.D., chief of the mucosal immunology unit in the laboratory of parasitic diseases at the National Institutes of Health "If some set of microbes induces a specific immune response, this points to a way to manipulate the immune system," says Dr. Belkaid. "This new study is the first report that has associated a defined set of gut flora with the induction of specific immune cells."

The new research is from the laboratory of Dan Littman, M.D., Ph.D., the Helen L. and Martin S. Kimmel Professor of Molecular Immunology at NYU School of Medicine and a Howard Hughes Medical Institute Investigator. "It's not the amount of microbial flora but the kind of microbial flora that seems to count," says Dr. Littman.

The new study found that cytophaga-flavobacter-bacteroidetes (CFB) bacteria were associated with the creation of Th17 cells in mice. Typically, in both mice and humans, most of the bacteria found in the gut fall

into the CFB phylum or another phylum called Firmicutes. These bacteria play many roles, such as aiding in digestion and protecting against pathogens by outcompeting harmful bacteria.

Inflammatory bowel disease (IBD) affects as many as 700,000 people each year and is one of the most prevalent gastrointestinal diseases in the United States. Treatment with antibiotics has had limited success. But pinpointing the specific species of bacteria that influence the balance of inflammatory cells, says Dr. Littman, could lead to more sophisticated treatments that fine-tune bacteria in the intestine and, in turn, dampen the production of inflammatory cells.

The Yin and Yang of Immunity

A healthy immune system is a balancing act between two opposing yet intimately connected forces, one calming, the other inflammatory. Sometimes called the yin and yang of adaptive immunity, pro-inflammatory cells (the "yang") dominate when the body needs protection, and regulatory cells (the "yin") soothe the immune system when it doesn't.

When this balance is disrupted and there is an overload of fiery yang cells, inflammatory disease results. In recent years, scientists have linked a striking number of autoimmune disorders to excess pro-inflammatory cells, including psoriasis, inflammatory bowel disease, and multiple sclerosis. "The number of inflammatory diseases known to involve T helper 17 (Th17) cells," – the fiery yang cells – "seems to be growing every week," says Dr. Littman.

For this reason, Dr. Littman has been studying the molecular pathways that stimulate the production of these cells. Recently, his team reported on a promising potential therapeutic target that may help ameliorate diseases associated with overproduction of Th17 cells.

In the new study, Dr. Littman's team observed that newborn mice that remain isolated from bacteria never generate any of these cells. Normally, newborn mice are born without any bacteria or Th17 cells in their intestines. They begin to generate the cells only after they begin to eat food and ingest bacteria. These observations suggested that the introduction of bacteria in the gut is associated with the creation of Th17 cells.

To determine if the bacteria actually cause the generation of Th17 cells, the team gave normal, bacteria-filled mice antibiotics that selectively killed some of the bacteria in their small intestine. Some of these antibiotics also depleted their Th17 cells, indicating for the first time a causal link between specific bacteria and the generation of inflammatory cells.

Littman's team then found a colony of mice that have intestinal bacteria but do not have Th17 cells. This colony, it turned out, had different bacteria in their guts than other colonies. "The same way people from different countries have different bacteria in their guts, mice from different colonies will have different bacteria," explains Dr. Ivaylo Ivanov, an author of the study and a post-doctoral fellow in Dr. Littman's laboratory. In this case, "one colony has the bacterial species associated with Th17 cells and the other doesn't."

By comparing the intestinal bacteria in mice, the team discovered that cytophaga-flavobacter-bacteroidetes (CFB) bacteria were associated with the creation of Th17 cells. Dr. Littman's team is now working to determine the specific bacteria that induce pro-inflammatory immune cells in mice. They will use this information to help determine the bacterial species in the intestines of humans that trigger the overproduction of these cells.

Dr. Littman also is interested in identifying the signals emitted by bacteria that influence the innate immune system, which responds to immediate threats from foreign pathogens and produces substances that spur naive or unspecialized T cells to develop into Th17 cells. Manipulation of the bacteria or their products, says Dr. Littman, could then be used to shift the balance of pro-inflammatory and regulatory immune cells.

Genetic 'fingerprint' shown to predict liver cancer's return

Finding flows from enhanced genomic method for reading genes' activity in clinical specimens

Scientists have reached a critical milestone in the study of liver cancer that lays the groundwork for predicting the illness's path, whether toward cure or recurrence. By analyzing the tissue in and around liver tumors, an international research team has identified a kind of genetic "fingerprint" that can help predict if patients' cancers will return. The findings appear in the October 15 advance online edition of the New England Journal of Medicine and were made possible by a large-scale method for revealing genes' activity, which the researchers show can be applied to tissues that have been chemically preserved instead of frozen. This technical triumph promises to unlock biological information within millions of clinical samples previously intractable to genomic study.

"In most hospitals and clinics, the prevailing method of storing patient tissue involves a chemical fixative, which often precludes future genome-scale analyses. That means the vast majority of patient samples have effectively been off-limits to a variety of important questions," said senior author Todd Golub, who directs the Cancer Program at the Broad Institute of MIT and Harvard and is the Charles A. Dana Investigator in Human

Cancer Genetics at the Dana-Farber Cancer Institute. "Our work reveals that it is indeed possible to access this biological trove, a step we hope will bolster future genomic discoveries throughout the scientific community."

Unlike many cancers, hepatocellular carcinoma, a form of liver cancer, is often detected early. That is because in the developed world, doctors can identify and closely monitor individuals at highest risk — those with a history of liver damage due to infection or chronic alcohol abuse, for example. Yet even with early diagnosis and treatment, the disease often recurs. And that development often proves fatal. The ability to pinpoint in advance those most at risk of suffering recurring cases could improve treatment, perhaps helping doctors choose more aggressive therapies for patients whose disease is most likely to return and identifying patients whose health should be carefully followed.

Genome-scale technologies are a powerful means to help develop such predictors, particularly methods that measure the activity (or "expression") of every human gene. However, a major obstacle to applying such methods to hepatocellular carcinoma, as well as other cancers, has been the technical requirements — samples must be frozen, not preserved, or "fixed," in the chemical formalin.

An international team of researchers from the Broad Institute, Harvard Medical School, Dana-Farber Cancer Institute, Mount Sinai School of Medicine, and elsewhere came together to develop an enhanced method for measuring gene expression in formalin-fixed tissues and applied it to samples from more than 300 liver cancer patients. Their work uncovered a striking pattern — a characteristic signature of more than 180 active and inactive genes linked with increased patient survival. Interestingly, this putative predictor was discovered not within the tumors per se, but within the normal tissue surrounding them.

In the future, the telltale gene signature could help distinguish patients whose tumors are likely to return. "Our findings underscore the potential of genomic signatures to help identify treatments that will be most beneficial to individual patients," said Golub, who is also an investigator at the Howard Hughes Medical Institute.

The discovery flows from an existing gene expression method that works on formalin-fixed tissues yet extracts information on just a few hundred genes. The researchers redesigned the technique to analyze roughly 6,000 genes — a subset that yields sufficient data to either directly measure or infer the expression levels of nearly all ~20,000 human genes.

Although further work is needed before the liver cancer findings can be used in the clinic, the current study marks a key step toward accelerating genomic discoveries with medical promise. Indeed, most patient tissue banks, especially those with valuable clinical data such as disease severity and course that are so vital to retrospective studies, are built from fixed samples and up until now have been largely inaccessible to genomic analysis. "In the Boston-area hospitals alone, we estimate that there are more than one million archived samples that can be analyzed with this approach," said Golub. "There's a wealth of information waiting to be explored."

Paper cited: *Hoshida Y. et al. Gene expression in fixed tissues and outcome in hepatocellular carcinoma. New England Journal of Medicine DOI: 10.1056/NEJMoa0804525.*

Scientists restore movement to paralyzed limbs through artificial brain-muscle connections

Researchers in a study funded by the National Institutes of Health (NIH) have demonstrated for the first time that a direct artificial connection from the brain to muscles can restore voluntary movement in monkeys whose arms have been temporarily anesthetized. The results may have promising implications for the quarter of a million Americans affected by spinal cord injuries and thousands of others with paralyzing neurological diseases, although clinical applications are years away.

"This study demonstrates a novel approach to restoring movement through neuroprosthetic devices, one that would link a person's brain to the activation of individual muscles in a paralyzed limb to produce natural control and movements," said Joseph Pancrazio, Ph.D., a program director at the National Institute of Neurological Disorders and Stroke (NINDS).

The research was conducted by Eberhard E. Fetz, Ph.D., professor of physiology and biophysics at the University of Washington in Seattle and an NINDS Javits awardee; Chet T. Moritz, Ph.D., a post-doctoral fellow funded by NINDS; and Steve I. Perlmutter, Ph.D., research associate professor. The results appear in the online Oct. 15 issue of Nature. The study was performed at the Washington National Primate Research Center, which is funded by NIH's National Center for Research Resources.

In the study, the researchers trained monkeys to control the activity of single nerve cells in the motor cortex, an area of the brain that controls voluntary movements. Neuronal activity was detected using a type of brain-computer interface. In this case, electrodes implanted in the motor cortex were connected via external circuitry to a computer. The neural activity led to movements of a cursor, as monkeys played a target practice game.

After each monkey mastered control of the cursor, the researchers temporarily paralyzed the monkey's wrist muscles using a local anesthetic to block nerve conduction. Next, the researchers converted the activity in the

monkey's brain to electrical stimulation delivered to the paralyzed wrist muscles. The monkeys continued to play the target practice game—only now cursor movements were driven by actual wrist movements—demonstrating that they had regained the ability to control the otherwise paralyzed wrist.

The group's approach is one of several lines of current neuroprosthetic research. Some investigators are using brain-computer interfaces to record signals from multiple neurons and convert those signals to control a robotic limb. Other researchers have delivered artificial stimulation directly to paralyzed arm muscles in order to drive arm movement—a technique called functional electrical stimulation (FES). The Fetz study is the first to combine a brain-computer interface with real-time control of FES.

"A robotic arm would be better for someone whose physical arm has been lost or if the muscles have atrophied, but if you have an arm whose muscles can be stimulated, a person can learn to reactivate them with this technology," says Dr. Fetz.

Until now, brain-computer interfaces were designed to decode the activity of neurons known to be associated with movement of specific body parts. Here, the researchers discovered that any motor cortex cell, regardless of whether it had been previously associated with wrist movement, was capable of stimulating muscle activity. This finding greatly expands the potential number of neurons that could control signals for brain-computer interfaces and also illustrates the flexibility of the motor cortex.

"The cells don't have to have a preordained role in the movement. We can create a direct link between the cell and the motor output that the user can learn to control and optimize over time," says Dr. Fetz.

Dr. Fetz and his colleagues found that the monkeys' control over neuronal activity—and the resulting control over stimulation of their wrist muscles—improved significantly with practice. Practice time was limited by the duration of the nerve block. Comparing the monkeys' performance during an initial two-minute practice and a two-minute peak performance period, the scientists found the monkeys successfully hit the target three times more frequently and with less error during the peak performance. In the future, greater control could be gained by using implanted circuits to create long-lasting artificial connections, allowing more time for learning and optimizing control, Dr. Fetz says.

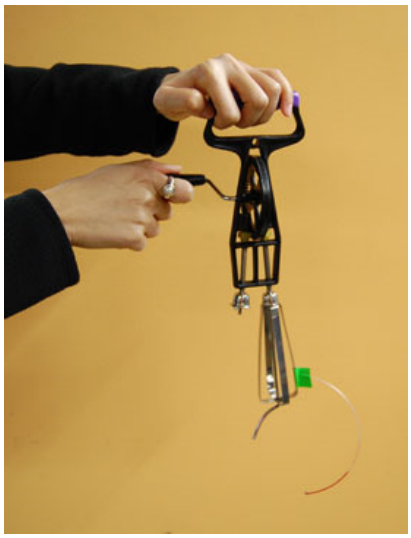
The researchers also found that the monkeys could achieve independent control of both the wrist flexor and extensor muscles. "An important next step will be to increase the number of direct connections between cortical cells and muscles to control coordinated activation of muscles," says Dr. Fetz.

If researchers are able to establish a connection between the motor cortex and sites in the spinal cord below the injury, people with spinal injuries may be able to achieve coordinated movements.

Clinical applications are still probably at least a decade away, according to Dr. Fetz. Better methods for recording cortical neurons and for controlling multiple muscles must be developed, along with implantable circuitry that could be used reliably and safely, he says.

$2 egg-beater could save lives in developing countries

Plastic tubing taped to a handheld egg-beater could save lives in developing countries, the Royal Society of Chemistry's journal Lab on a Chip reports.



Whitesides' egg beater centrifuge requires no special training, electricity or maintenance

The low-cost centrifuge replacement can separate plasma from blood in minutes, which is used in tests to detect lethal infectious diseases responsible for half of all deaths in developing countries.

George Whitesides and colleagues at Harvard University, US, say the plasma obtained is easily good enough to use in tests to detect diseases such as Hepatitis B and cysticercosis.

"The object was to separate serum [plasma] from blood using readily-obtained materials in a resource-constrained environment," explains Whitesides.

The equipment can be bought from shops for around two dollars. It needs no special training to use, no electricity or maintenance, and can be sterilised with boiling water and reused.

The user can even prepare several samples at once - just by taping more lengths of tubing to the beater.

Contrast this with the bulky, sensitive commercial centrifuges, costing thousands of dollars and requiring extensive operation training, and it's easy to see how this development could save lives.

"This technique is simple and works remarkably well," says Doug Weibel, an expert in microbiology at the University of Wisconsin-Madison, US. "This technique complements several other 'simple solutions' that the Whitesides group has developed to tackle point-of-care diagnostics in resource-poor settings."

Man 'roused from coma' by a magnetic field

* 15 October 2008
* NewScientist.com news service
*** Linda Geddes**

JOSH VILLA was 26 and driving home after a drink with a friend on 28 August 2005 when his car mounted the kerb and flipped over. Villa was thrown through the windscreen, suffered massive head injuries and fell into a coma.

Almost a year later, there was little sign of improvement. "He would open his eyes, but he was not responsive to any external stimuli in his environment," says Theresa Pape of the US Department of Veterans Affairs in Chicago, who helped treat him.

Usually there is little more that can be done for people in this condition. Villa was to be sent home to Rockford, Illinois, where his mother, Laurie McAndrews, had volunteered to care for him.

But Pape had a different suggestion. She enrolled him in a six-week study in which an electromagnetic coil was held over the front of his head to stimulate the underlying brain tissue. Such transcranial magnetic stimulation (TMS) has been investigated as a way of treating migraine, stroke, Parkinson's disease and depression, with some promising results, but this is the first time it has been used as a potential therapy for someone in a coma-like state.

The rapidly changing magnetic fields that the coil creates can be used either to excite or inhibit brain cells - making it easier or harder for them to communicate with one another. In Villa's case, the coil was used to excite brain cells in the right prefrontal dorsolateral cortex. This area has strong connections to the brainstem, which sends out pulses to the rest of the brain that tell it to pay attention. "It's like an 'OK, I'm awake' pulse," says Pape.

At first, there was little change in Villa's condition, but after around 15 sessions something happened. "You started talking to him and he would turn his head and look at you," says McAndrews. "That was huge."

Villa started obeying one-step commands, such as following the movement of a thumb and speaking single words. "They were very slurred but they were there," says Pape, who presented her findings this month at an international meeting on brain stimulation at the University of Göttingen, Germany. "He'd say like 'erm', 'help', 'help me'."

After the 30 planned sessions the TMS was stopped. Without it, Villa became very tired and his condition declined a little, but he was still much better than before. Six weeks later he was given another 10 sessions, but there were no further improvements and he was sent home, where he remains today.

Villa is by no means cured. But he is easier to care for and can interact with visitors such as his girlfriend, who has stuck by him following the accident. "When you talk to him he will move his mouth to show he is listening," McAndrews says. "If I ask him, 'Do you love me?' he'll do two slow eye blinks, yes. Some people would say it's not much, but he's improving and that's the main thing."

John Whyte of the Moss Rehabilitation Research Institute in Philadelphia, Pennsylvania, cautions that as intriguing as Villa's case is, it alone does not show that TMS is a useful treatment. "Even after eight months, it is not uncommon for patients to transition from the vegetative to the minimally conscious state without any particular intervention," he points out. He says TMS merits further investigation, along with other experimental treatments such as drugs which have temporarily roused three men from a coma, and deep brain stimulation, an invasive technique that roused a man out of a minimally conscious state.

"This is the first and very interesting use of repetitive TMS in coma," says Steven Laureys of the Coma Research Group at the University of Liège in Belgium. Our understanding of disorders of consciousness is so limited that even a single study can provide new insights, he says.

Pape acknowledges that further studies are needed to demonstrate that TMS really is beneficial, though she is convinced that it helped Villa. He had only been given a 20 to 40 per cent chance of long-term recovery, and until he was given TMS his functioning had not improved since about four months after the accident. What's more, after the 15th TMS session, he improved incrementally with each session - further evidence that TMS was the cause.

Pape hopes to begin treating a second patient in a coma-like state later this year. This time she plans to adjust the number of pulses of TMS in each train, and to alter the gap between pulses to see if there is an optimum interval.

McAndrews is also in no doubt that her son's quality of life has improved as a result of TMS. "Before I felt like he was not responsive, that he was depressed almost. Now you move him around and he complains - he can show emotions on that level."

A gentle current helps when words are hard to find

People with Alzheimer's disease got better at a word-recognition task after their brains were stimulated with an electric current.

Like transcranial magnetic stimulation or TMS (see main story), transcranial direct current stimulation (tDCS) aims to activate or inhibit areas of the brain by making it easier or harder for the brain cells to fire. While TMS involves holding a current-carrying coil over the subject's head, tDCS, which has previously shown promise in treating pain and depression (New Scientist, 5 April 2006, p 34), uses electrodes to send a current of 1 to 2 milliamps through the skull.

In Alzheimer's, the temporoparietal areas of the brain, which are involved in memory and recognition, are known to be less active than in healthy people. So Alberto Priori at the University of Milan, Italy, and his colleagues used tDCS to stimulate these areas. They asked 10 people with mild to moderate Alzheimer's to perform a word-recognition and a visual-attention task, before and after receiving tDCS or a sham treatment.

With tDCS, word recognition improved by 17 per cent, but there was no improvement in visual attention. Word recognition worsened when tDCS was used to inhibit neurons, and there was no change when the sham treatment was applied (Neurology, vol 71, p 493).

"Our findings are consistent with evidence that tDCS improves cognitive functions in healthy subjects and in patients with neurological disorders," Priori says. He is now running a larger study to confirm the results, and to find out how long the improvement lasts.

Estimate Soil Texture-by-Feel

How good are you at estimating soil texture-by-feel? Read about how to learn this skill in the Journal of Natural Resources and Life Sciences Education.

MADISON, WI, October 14, 2008 -- The ability to estimate soil texture-by-feel is an important skill that students and registered soil scientists should learn.

Many soil properties depend largely on soil texture, and texture impacts most land-use decisions. Soil texture strongly influences the nutrient holding ability of a soil, the amount of water the soil can store, the amount of this water that is available to plants, how fast water moves through the soil, the effectiveness of soil in cleaning up waste water, the shrink-swell nature of soil, and many other properties.

D.P. Franzmeier and P.R. Owens, Purdue University, write about how soil texture can be determined by using the texture-by-feel method in an article published in the 2008 Journal of Natural Resources and Life Sciences Education.

"Soil texture can be determined in the field using the texture-by-feel method or the samples may be sent to a laboratory for particle-size analysis. The laboratory option is more accurate, but it is more expensive and slower because it can take weeks or months to get the results," explains Owens.

The field method is less accurate but much faster. Soil scientists use texture-by-feel to provide quick reliable estimates of soil texture in the field. This method is used by researchers where numerous samples are required to capture variability, developing soil surveys, and consultants for sizing on-site wastewater disposal systems.

When the texture-by-feel method is used, the estimator takes a soil sample about the size of a marble up to the size of a golf ball. The person estimates the texture by rolling, squeezing, flattening, and pressing the soil between his fingers. Each person develops his own technique for estimating texture. The important point is that while learning the technique, he must always compare his results with laboratory data.

A computer program assesses student performance for estimating particle-size distribution and soil texture. If the estimate coincides exactly with laboratory results, the score is 100%. If the estimate and laboratory results are as far apart as possible, at opposite corners of the texture triangle, the score is zero.

"Students appreciate the fairness of grading. Also, we can use the method to let a student or professional know if their estimates are consistently above or below the laboratory values, which helps them calibrate their fingers," says Owens.

"We have used this tool to help registered soil scientists improve their field skills and they seem to enjoy the challenge," says Franzmeier.

The program is available on the IRSS website: http://www.isco.purdue.edu/irss/. Select Resources, then Texture Estimate Calculator.

The full article is available for no charge for 30 days following the date of this summary. View the abstract at http://www.jnrlse.org/pdf/2008/E08-0018.pdf. After 30 days it will be available at the Journal of Natural Resources and Life Sciences Education website, www.jnrlse.org. Go to http://www.jnrlse.org/issues/ (Click on the Year, "View Article List," and scroll down to article abstract).

10 years on, high-school social skills predict better earnings than test scores

Ten years after graduation, high-school students who had been rated as conscientious and cooperative by their teachers were earning more than classmates who had similar test scores but fewer social skills, said a new University of Illinois study.

The study's findings challenge the idea that racial, ethnic, and socioeconomic gaps in educational attainment and earnings can be narrowed solely by emphasizing cognitive skills, said Christy Lleras, a University of Illinois assistant professor of human and community development.

"It's important to note that good schools do more than teach reading, writing, and math. They socialize students and provide the kinds of learning opportunities that help them to become good citizens and to be successful in the labor market," she said.

"Unless we address the differences in school climates and curriculum that foster good work habits and other social skills, we're doing a huge disservice to low-income kids who may be entering the labor market right after high school, especially in our increasingly service-oriented economy," Lleras added.

She cited responses to employer surveys that stress the need for workers who can get along well with each other and get along well with the public.

The U of I study analyzed data from the National Educational Longitudinal Study, which followed a diverse group of 11,000 tenth graders for 10 years, tracking not only their scores on standard achievement tests but teacher appraisals of such qualities as the students' work habits, their ability to relate well to peers, and their participation in extracurricular activities, a proxy for the ability to interact well with both students and adults.

The teachers' assessments were then compared with the students' self-reported educational attainments and earnings 10 years after high-school graduation.

Even after controlling for students' achievement test scores, family socioeconomic status, and educational attainment, Lleras found that such social skills as conscientiousness, cooperativeness, and motivation were as important as test scores for success in the workplace.

"You could argue that the reason these behaviors matter is that kids who display them are more likely to obtain a college degree and in turn have higher earnings. Certainly that is part of it, but even after I controlled for educational attainment, there were still significant effects," she said.

To measure conscientiousness, the researcher ranked teacher responses to such questions as: Does this student usually work hard for good grades? How often does the student complete homework assignments? How often is this student tardy to class?

To measure cooperativeness and sociability, she ranked teacher assessments of how well a student related to other students. Teachers were also asked to rank a student's motivation or passivity.

Participation in sports and school organizations also had strong effects on a student's future educational and occupational success.

"For African American and Hispanic students only, participation in fine arts led to significantly better earnings compared to whites. This suggests that different activities teach kids different kinds of skills and learned behaviors," she said.

Lleras also emphasized the importance of improving school quality. "Low-income and racial minority students continue to be concentrated in lower-quality schools with fewer opportunities for extracurricular participation, larger class sizes, and lower teacher quality, all factors that are correlated with poorer school-related attitudes and behavior," she said.

"If the few resources that low-performing schools have are used solely for testing and preparing students for tests, which is what many schools are doing to meet the requirements set forth in No Child Left Behind, these schools will continue to face challenges," she said. "My findings show that the most successful students are those who have not only high achievement test scores but also the kinds of social skills and behaviors that are highly rewarded by employers in the workplace," she said.

The study appeared in the September issue of Social Science Research.

Cancer fighting human immune cells to be grown in pigs

By Richard Alleyne, Science Correspondent
Last Updated: 6:01pm BST 15/10/2008

Cancer patients could have immune cells removed and cultivated in piglets before being injected back into them to boost the body's natural defences, new research claims.

Scientists have long been excited by the prospect of 'turbo-charging' patients immune systems by injecting them with their own cancer fighting cells grown outside the body.

But the process of cloning the immune or T- cells is extremely expensive and difficult for all but a few patients.

Now the researchers believe pigs could hold the answer. They have successfully injected human cells into developing pig foetuses and found that they multiplied and matured as the pig grew.

The new stem cells, which would then be implanted back into the patient, could even be modified in the piglet so as to boost their disease fighting powers, experts believe.

They said the new system could mark a major breakthrough in the process which is known as cell transfer immunotherapy or T-cell treatment.

The new research, detailed in New Scientist, was undertaken by Jeffrey Platt at the University of Michigan, Ann Arbor.

To see if growing a human immune system inside pigs is possible, Dr Platt and his colleagues extracted stem cells from human umbilical cord blood and bone marrow, and injected them into developing pig foetuses.

Lacking a mature immune system, the foetuses accepted the foreign tissue as their own, and when the piglets were born the injected cells had multiplied and matured into a diverse range of human T-cells, alongside the pig's own immune cells.

The team were then able to extract the T-cells and while they have yet to re-introduce them to humans they have tested them to see if they are active and safe.

The researchers separated out the human cells from the pig's blood and mixed some of them with ordinary cells from the person whose cells had been injected into the foetus.

The extracted cells did not mount an immune attack, indicating that it should be possible to implant them back into the donor, but they did attack cells from other people, showing they were functional.

Dr Platt believes the cells reared in the piglets are so young they could even be modified to fight specific diseases. "If I had HIV, I could put my stem cells in pigs and immunise them with an HIV vaccine," said Dr Platt. "You would get immunity in the pig that you would never get in my body."

Dr Platt, who believes miniature varieties of pigs would be the most efficient way to cultivate cells, now wants to persuade the regulatory authorities to allow testing in humans.

Immunotherapy is thought to work because usually there are too few of the cells naturally in a patient's body to fight cancer effectively but by boosting them, it boosts natural defences.

In its most successful use to date one American patient suffering from advanced skin cancer even made a full recovery following the treatment. This was even though the disease had already spread to the lymph nodes and lungs.

The new techniques raise the hope of fighting the disease, which claims 150,000 lives in Britain every year.

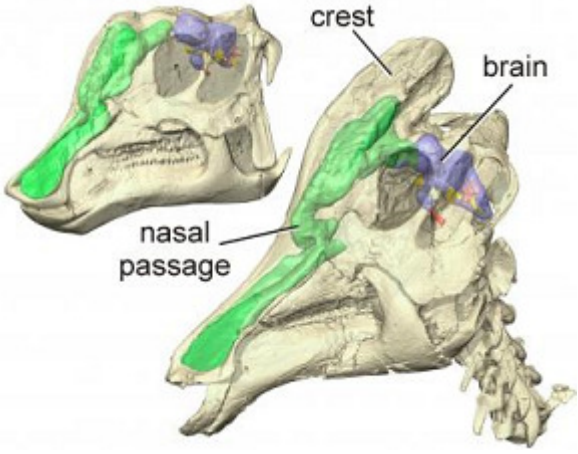
Brain structure provides key to unraveling function of bizarre dinosaur crests

High-tech imaging reveals inner structure of duck-billed dinosaur skulls

ATHENS, Ohio (Oct. 16, 2008) — Paleontologists have long debated the function of the strange, bony crests on the heads of the duck-billed dinosaurs known as lambeosaurs. The structures contain incredibly long, convoluted nasal passages that loop up over the tops of their skulls.

Scientists at the University of Toronto, Ohio University and Montana State University now have used CT-scanning to look inside these mysterious crests and reconstruct the brains and nasal cavities of four different lambeosaur species. At the annual meeting of the Society for Vertebrate Paleontology in Cleveland, Ohio, on Oct. 16, the team will present new study findings that suggest the crests were used for communication.

"The shape of the brain can tell us a lot about what senses were important in a dinosaur's everyday life, and give insight into the function of the crests," said study lead author David Evans, a paleontologist at the Royal Ontario Museum and the University of Toronto.



Reconstructions of the skull in a juvenile and sub-adult Corythosaurus created using CT scanning. The nasal cavity is highlighted in green, and the brain appears in purple. The complicated nasal passage within the showy crest functioned as resonating chambers during vocalization. The structure of the inner ear and expanded brain confirms that duck-billed dinosaurs were capable of perhaps sophisticated behavioral communication. **Courtesy of Witmer & Ridgely, Ohio University.**

Some paleontologists have suggested that the crests heightened the sense of smell by increasing the surface area of the sensory tissue. Others have argued that they regulated temperature, and still others have speculated that the crests acted as sound resonators for communication.

"It's difficult to infer the function of structures in an extinct dinosaur when there is so little resemblance to any living animal," said Jack Horner, a member of the team and paleontologist at Montana State University.

By analyzing CT scans, conducted by Lawrence Witmer and Ryan Ridgely of Ohio University's College of Osteopathic Medicine, the scientists were able to circumvent the problems of fossilization.

"Even though the soft tissues are not preserved in the fossils, the shape of the bones that encase the brain and nasal passages are," said Evans. "From there, the anatomy of these missing soft parts is easily interpreted."

A life reconstruction of the helmet-crested lambeosaur Corythosaurus.

The CT scan results revealed a mismatch between the external shape of the crest (which no doubt functioned as a visual display) and the internal shape of the nasal passages in closely related species, suggesting a special function for the nasal cavity. The portion of the brain responsible for the sense of smell was relatively small and primitive, indicating that the crest did not evolve to improve that sense.

Computer models done by other researchers suggest that the crests could have been used to make low, eerie bellowing calls that could have been used in communication, perhaps to call for mates or warn others of predators. The CT scans documented a delicate inner ear that confirms that the dinosaurs could hear the low-frequency calls produced by the crest.

"We were surprised to see just how large the centers of the brain associated with higher cognitive functions were," said Witmer, Chang Professor of Paleontology in Ohio University's College of Osteopathic Medicine. "We suspected that the crested duck-billed dinosaurs used both vocal and visual displays, but now we see that they had the brain power and hearing to pull off these behaviors."

The diversity of crests in the lambeosaurine dinosaurs Parasaurolophus, Corythosaurus, and Lambeosaurus.

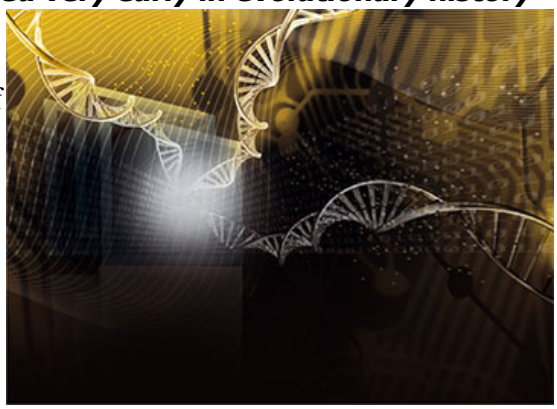
When all the available information is put together, including the digital brain and ear casts, the evolutionary relationships of the species, and the growth pattern of the crest and its high degree of variability in different co-existing species, it supports the idea that the elaborate nasal cavity was likely used to produce sounds for communication. This study demonstrates the power of using an integrated approach combining 3D imaging, growth studies, and phylogenetic sampling to test ideas about the function and evolution of unusual structures in extinct animals.

The research was funded by the National Science and Engineering Research Council of Canada and the National Science Foundation. This study also will be published in part in an upcoming issue of the journal The Anatomical Record.

Genetic based human diseases are an ancient evolutionary legacy

Evolutionary geneticists reveal that disease genes emerged very early in evolutionary history

Tomislav Domazet-Lošo and Diethard Tautz from the Max Planck Institute for Evolutionary Biology in Plön, Germany, have systematically analysed the time of emergence for a large number of genes - genes which can also initiate diseases. Their studies show for the first time that the majority of these genes were already in existence at the origin of the first cells. The search for further genes, particularly those which are involved in diseases caused by several genetic causes, is thus facilitated. Furthermore, the research results confirm that the basic interconnections are to be found in the function of genes - causing the onset of diseases - can also be found in model organisms (Molecular Biology and Evolution).



Artistic illustration of a phylostratigraphy. **Image: Irena Andreic, Ruđer Bošković Institute, Zagreb**

The Human Genome Project that deciphered the human genetic code, uncovered thousands of genes that, if mutated, are involved in human genetic diseases. The genomes of many other organisms were deciphered in parallel. This now allows the evolution of these disease associated genes to be systematically studied.

Tomislav Domazet-Lošo and Diethard Tautz from the Max Planck Institute for Evolutionary Biology in Plön (Germany) have used for this analysis a novel statistical method, "phylostratigraphy" that was developed by Tomislav Domazet-Lošo at the Ruđer Bošković Institute in Zagreb (Croatia). The method allows the point of origin for any existing gene to be determined by tracing the last common ancestor in which this gene existed. Based on this information, it is then possible to determine the minimum age for any given gene.

Applying this method to disease genes, the scientists from Plön came to surprising findings. The vast majority of these genes trace back to the origin of the first cell. Other large groups emerged more than one

billion years ago around the first appearance of multi-cellular organisms, as well as at the time of origin of bony fishes about 400 million years ago. Surprisingly, they found almost no disease associated genes among those that emerged after the origin of mammals.

These findings suggest that genetic diseases affected primarily ancient cellular processes, which emerged already during the early stages of life on Earth. This leads to the conclusion that all living organisms today, i.e. not only humans, will be affected by similar genetic diseases. Furthermore, this implies that genetically caused diseases will never be beaten completely, because they are linked to ancient evolutionary processes.

Although it was already known that many disease associated genes occur also in other organisms distant to humans, such as the fruitfly Drosophila or the round worm Caenorhabditis, the analysis of Domazet-Lošo and Tautz shows now for the first time that this is systematically true for the vast majority of these genes. At present it remains unknown why the more recently evolved genes, for example those involved in the emergence of the mammals, do not tend to cause diseases when mutated.

The research results of the scientists from Plön also have some practical consequences. It will now be easier to identify candidates for further disease genes, in particular for those involved in multi-factorial diseases. Furthermore, the results confirm that the functional knowledge gained about such genes from remote model organisms is also relevant for understanding the genes in humans.

[1] Free access to journal article

Original work:

Tomislav Domazet-Lošo und Diethard Tautz
An ancient evolutionary origin of genes associated with human genetic diseases.
Molecular Biology and Evolution, September 26, 2008; doi 10.1093/molbev/msn214

New solar energy material captures every color of the rainbow

Columbus, Ohio -- Researchers have created a new material that overcomes two of the major obstacles to solar power: it absorbs all the energy contained in sunlight, and generates electrons in a way that makes them easier to capture.

Ohio State University chemists and their colleagues combined electrically conductive plastic with metals including molybdenum and titanium to create the hybrid material.

"There are other such hybrids out there, but the advantage of our material is that we can cover the entire range of the solar spectrum," explained Malcolm Chisholm, Distinguished University Professor and Chair of the Department of Chemistry at Ohio State.

The study appears in the current issue of the Proceedings of the National Academy of Sciences (PNAS).

Sunlight contains the entire spectrum of colors that can be seen with the naked eye -- all the colors of the rainbow. What our eyes interpret as color are really different energy levels, or frequencies of light. Today's solar cell materials can only capture a small range of frequencies, so they can only capture a small fraction of the energy contained in sunlight.

This new material is the first that can absorb all the energy contained in visible light at once.

The material generates electricity just like other solar cell materials do: light energizes the atoms of the material, and some of the electrons in those atoms are knocked loose.

Ideally, the electrons flow out of the device as electrical current, but this is where most solar cells run into trouble. The electrons only stay loose for a tiny fraction of a second before they sink back into the atoms from which they came. The electrons must be captured during the short time they are free, and this task, called charge separation, is difficult.

In the new hybrid material, electrons remain free much longer than ever before.

Today's solar cell materials can only capture a small range of frequencies, so they can only capture a small fraction of the energy contained in sunlight. This new material is the first that can absorb all the energy contained in visible light at once.

To design the hybrid material, the chemists explored different molecular configurations on a computer at the Ohio Supercomputer Center. Then, with colleagues at National Taiwan University, they synthesized molecules of the new material in a liquid solution, measured the frequencies of light the molecules absorbed, and also measured the length of time that excited electrons remained free in the molecules.

They saw something very unusual. The molecules didn't just fluoresce as some solar cell materials do. They phosphoresced as well. Both luminous effects are caused by a material absorbing and emitting energy, but phosphorescence lasts much longer.

To their surprise, the chemists found that the new material was emitting electrons in two different energy states -- one called a singlet state, and the other a triplet state. Both energy states are useful for solar cell applications, and the triplet state lasts much longer than the singlet state.

Electrons in the singlet state stayed free for up to 12 picoseconds, or trillionths of a second -- not unusual compared to some solar cell materials. But electrons in the triplet state stayed free 7 million times longer -- up to 83 microseconds, or millionths of a second.

When they deposited the molecules in a thin film, similar to how they might be arranged in an actual solar cell, the triplet states lasted even longer: 200 microseconds.

"This long-lived excited state should allow us to better manipulate charge separation," Chisholm said.

At this point, the material is years from commercial development, but he added that this experiment provides a proof of concept -- that hybrid solar cell materials such as this one can offer unusual properties.

The project was funded by the National Science Foundation and Ohio State's Institute for Materials Research.

Chisholm is working with Arthur J. Epstein, Distinguished University Professor of chemistry and physics; Paul Berger, professor of electrical and computer engineering and physics; and Nitin Padture, professor of materials science and engineering to develop the material further. That work is part of the Advanced Materials Initiative, one Ohio State's Targeted Investment in Excellence (TIE) programs.

The TIE program targets some of society's most pressing challenges with a major investment of university resources in programs with a potential for significant impact in their fields. The university has committed more than $100 million over the next five years to support 10 high-impact, mostly interdisciplinary programs.

Co-authors on the PNAS paper from Ohio State included: Gotard Burdzinski, a postdoctoral researcher; Yi-Hsuan Chou, a postdoctoral researcher; Florian Fiel, a former postdoctoral researcher; Judith Gallucci, a senior research associate; Yagnaseni Ghosh, a graduate student; Terry Gustafson, a professor; Yao Liu, a postdoctoral researcher; Ramkrishna Ramnauth, a former postdoctoral researcher; and Claudia Turro, a professor; all of the Department of Chemistry. They collaborated with Pi-Tai Chou and Mei-Lin Ho of National Taiwan University.

New spark in classic experiments

By Roland Pease BBC Radio Science Unit

There's a new spark of life in iconic experiments first done in the 1950s, on the kind of primordial "soup" that may have predated life itself on Earth.

Ageing vials of chemicals have been discovered in a Californian lab, surviving samples from the legendary experiments performed by chemist Stanley Miller.

The Bada Lab at Scripps holds the original samples used by Stanley Miller to study the origins of life. Credit: Scripps Institution of Oceanography, University of Calif., San Diego

They hold evidence that life may have born violently, in erupting volcanoes in the midst of a thunderstorm.

Miller was just 22 years old and studying for his PhD when he carried out his original, groundbreaking experiments (under his University of Chicago mentor, Harold Urey).

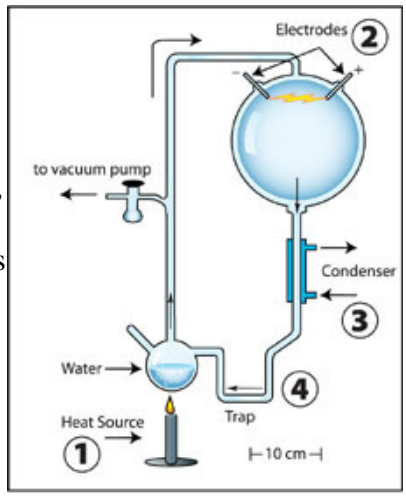
He wanted to test the current ideas for the origin of life, by striking electric sparks in a mixture of gases thought to resemble the atmosphere of the young Earth.

When his analysis of the products in the experiments revealed traces of the building blocks of life, amino acids (which combine to make proteins), Stanley Miller became an instant celebrity - though the 1950s newspapers were overstating the case when they claimed he had actually recreated life in the lab.

When Stanley Miller died in May last year, his former student, Jeffrey Bada, inherited his materials; including, it turns out, several boxes containing vials of dried samples from those 1950s experiments, and the accompanying notebooks

"We started going through some of the stuff that was piled up in the corner, and here were several little cardboard boxes, taped shut and all dusty, carefully labelled with all of these little vials with dried material from his experiments," Professor Bada, of the University of California, San Diego, told the BBC.

Miller's well-known experiments first done in 1952 used water along with methane, ammonia and hydrogen, the kinds of gases then thought to have dominated the Earth's oxygen-free atmosphere more than two billion years ago.



The apparatus used for Miller's original experiment. Boiled water (1) creates airflow, driving steam and gases through a spark (2). A cooling condenser (3) turns some steam back into liquid water, which drips down into the trap (4), where chemical products also settle. **Credit: Ned Shaw, Indiana University**

His sparks turned the mixture red, then yellow-brown, and made a number of amino acids, including glycine and alanine, commonly found in proteins.

But soon after, Miller had revised those experiments by injecting hot steam into the gas mixture, so that conditions resembled those you might find in an erupting volcano.

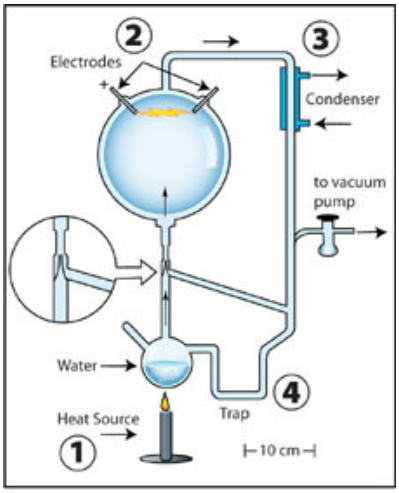
These experiments were the ones that intrigued Jeffrey Bada. Because not long after Miller's original experiments, it became clear the Earth's early atmosphere was nothing like the "reducing" mixture simulated in his apparatus.

The first experiments remained iconic in their attempt at simulating pre-biotic chemistry, but became irrelevant in detail.

But conditions locally in volcanoes, says Professor Bada, might not have been so different. The trouble was, Miller published only the sketchiest of details of those tests, and the apparatus was lost. It had looked like a dead end, until those dusty boxes turned up with their 200 vials.

"We started sorting through these, and lo and behold, we found a whole collection, almost a complete collection, of the extract samples from the volcanic experiments. And so we just went at it, using the state-of-the-art techniques we have today and analysed these samples.

"We found not only did these make more of certain amino acids than in the classic experiment, but they made a greater diversity of amino acids."



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The apparatus used for Miller's "second," initially unpublished experiment. Boiled water (1) creates airflow, driving steam and gases through a spark (2). A tapering of the glass apparatus (inlay) creates a spigot effect, increasing air flow. A cooling condenser (3) turns some steam back into liquid water, which drips down into the trap (4), where chemical products also settle. **Credit: Ned Shaw, Indiana University**

Miller, using the old methods, had found five amino acids; Jeffrey Bada and his teams tracked down 22. What is more, the overall chemical yields were often higher than in the first set of experiments - the mixture appeared to be more fertile.

Professor Bada points out that today, almost all volcanic eruptions are accompanied by violent electric storms. The same could have been true on the young Earth.

"What we suggest is that volcanoes belched out gases just like the ones Stanley had used, and were immediately subjected to intense volcanic lightning.

"And so each one of those volcanoes could have been a little, local prebiotic factory. And so all of that went into making the material that we refer to as the prebiotic soup."

That material could then have been washed down the flanks of volcanoes into pools or coastal bays, where the building blocks of life might have kick-started evolution.

Jeffrey Bada and colleagues report their latest work in the journal Science.

Better beer: college team creating anticancer brew

Rice students enter 'BioBeer' in synthetic biology's iGEM contest

College students often spend their free time thinking about beer, but a group of Rice University students are taking it to the next level. They're using genetic engineering to create beer that contains resveratrol, a chemical in wine that's been shown to reduce cancer and heart disease in lab animals.

Rice's "BioBeer" will be entered in the International Genetically Engineered Machine (iGEM) competition Nov. 8-9 in Cambridge, Mass. It's the world's largest synthetic biology competition, a contest where teams use a standard toolkit of DNA building blocks - think genetic LEGO blocks - to create living organisms that do odd things.

Notable past iGEM creations include sheets of bacteria that behave like photographic film and bacteria that smell like mint while they're growing but like bananas when they stop growing. Rice's student-led iGEM team -- the Rice BiOWLogists -- are returning for a third year. Their entry last year, a bacterial virus that fought antibiotic resistance, was well-received but finished out of the prize running.

"After last year's contest, we were sitting around talking about what we'd do this year," said junior Taylor Stevenson. "(Graduate student) Peter Nguyen made a joke about putting resveratrol into beer, but none of us took it seriously."

But when the team began looking in earnest for a new project this spring, they discovered a good bit of published literature about modifying yeast with resveratrol-related genes. When they looked further, they found two detailed accounts by teams that had attacked both halves of the metabolic problem independently.

"That was when we said, 'You know, we could actually do this,'" said junior Thomas Segall-Shapiro.

Ironically, most of the team's undergraduate members aren't old enough to legally drink beer. But the reality is that with less than a month to go until the competition, the team has yet to brew a drop. All their work to date has gone into creating a genetically modified strain of yeast that will ferment beer and produce resveratrol at the same time. While the team does plan to brew a few test batches in coming weeks, these will contain some unappetizing chemical "markers" that will be needed for the experiments.

"There's no way anyone's drinking any of this until we get rid of that, not to mention that there's only one genetically modified strain of yeast that's ever been approved for use in beer, period," said Segall-Shapiro. "In short, it will be a long time before anybody consumes any of this."

So why would someone want to make beer with resveratrol in the first place? It's a naturally occurring compound that some studies have found to have anti-inflammatory, anticancer and cardiovascular benefits for mice and other animals. While it's still unclear if humans enjoy the same benefits, resveratrol is already sold as a health supplement, and some believe it could play a role in the "French paradox," the seemingly contradictory observation that the French suffer from relatively low rates of heart disease despite having a diet that's rich in saturated fats.

"I have seen some studies where it's been shown to activate the same proteins that are known to play a role in extending the life span of lab animals that are kept on low-calorie diets," said junior David Ouyang.

Ouyang said the team is working with a strain of yeast that's used commercially to make wheat beer. They got a sample of the yeast from Houston's Saint Arnold Brewing Company, and they are modifying it with two sets of genes. The first set allows the yeast to metabolize sugars and excrete an intermediate chemical that the second set can later convert into resveratrol.

"One set of genes gets you from A to B, and the other gets you from B to C," said Stevenson. "We've already created a strain that has the B-to-C genes, but our genes for the A-to-B part are still on order."

With some luck and hard work, the team said it will finish the full A-to-C yeast in time to get some data before heading to Cambridge. But even if they don't have this final piece of the puzzle, they're confident they'll have plenty of data from other experiments and computer models.

Faculty adviser Jonathan Silberg said the iGEM competition provides a unique educational experience for undergraduates.

"In terms of education value, the great thing about synthetic biology research is that it stimulates undergraduate creativity and gives them an opportunity to work collaboratively at an early stage of their science and engineering education," said Silberg, assistant professor of biochemistry and cell biology. "While students work collaboratively in other undergraduate research endeavors, they typically are not given the pie-in-the-sky opportunity to pursue their own ideas."

Regardless of how the BiOWLogists fare with BioBeer, they are already looking ahead to next year. Team members recently filed the necessary paperwork to create the Rice Synthetic Biology Club. Ouyang said the official recognition will help ensure Rice's annual presence at iGEM, even after the current team members graduate.

The other 2008 Rice BiOWLogists are sophomore Selim Sheikh, junior Arielle Layman, senior Sarah Duke, graduate student Justin Judd and faculty advisers Silberg, George Bennett and Beth Beason, all of Biochemistry and Cell Biology; Oleg Igoshin and Junghae Suh, both of Bioengineering; and Ken Cox of Chemical and Biomolecular Engineering.

Scientists discover bacteria that can cause bone infections

Scientists have discovered that a bone infection is caused by a newly described species of bacteria that is related to the tuberculosis pathogen. The discovery may help improve the diagnosis and treatment of similar infections, according to an article published in the October issue of the International Journal of Systematic and Evolutionary Microbiology.

Some rare genetic diseases can make patients susceptible to infections with Mycobacterium species, the bacteria that amongst other diseases, cause tuberculosis and leprosy. These patients often suffer from recurring mycobacterial infections throughout their whole lives. Because of this, researchers are trying to identify unusual species that cause disease in order to improve treatment strategies.

"We isolated an unknown species of bacteria from a 7 year old child who has a genetic immune defect," said Dr Didi Bang from Statens Serum Institut in Copenhagen, Denmark. "The infection had caused bone lesions and this is where we found the newly described bacteria."

Mycobacterial infections can be very difficult to treat. The bacteria have unique cell walls that protect them from several antibiotics. As well as being resistant to treatment, they can also survive attack with acids, alkalis and detergents. Most mycobacterial infections can be treated with antibiotics such as clarithromycin and rifamycins, but some species are becoming resistant to these antibiotics, so new drugs for treatments must be developed.

"Initial tests suggested we had found a Mycobacterium. By sequencing some of the bacterium's genes we showed that we had discovered an undescribed species," said Dr Bang. "We called the bacterium Mycobacterium arosiense. The name comes from Arosia, the Latin name of the city of Aarhus in Denmark, which is where the bacterium was first found. We showed the position of the new bacterium on the Mycobacterium family tree by sequencing genes and comparing them to related bacteria."

The new pathogen is closely related to Mycobacterium intracellulare and Mycobacterium avium, which cause a lung disease similar to tuberculosis in people, especially those with weak immune systems such as HIV patients that are immunologically suppressed. It is rod-shaped and grows slowly.

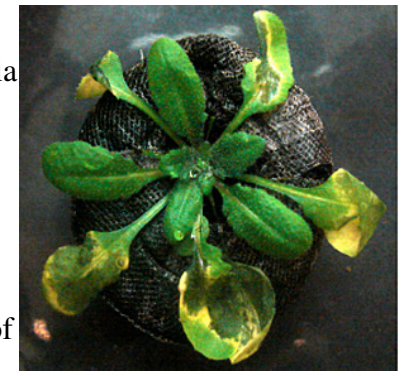
"Mycobacterium arosiense can be killed by several antibiotics in the lab, including clarithromycin and rifamycins. However, resistance to fluoroquinolones and isoniazid was observed," said Dr Bang. "Little knowledge is available on performing resistance tests on mycobacteria other than tuberculosis."

"We hope that this discovery will help doctors to diagnose similar diseases in the future and that further investigation may improve the treatment of people with similar infections."

When under attack, plants can signal microbial friends for help

Article by Tracey Bryant

Researchers at the University of Delaware have discovered that when the leaf of a plant is under attack by a pathogen, it can send out an S.O.S. to the roots for help, and the roots will respond by secreting an acid that brings beneficial bacteria to the rescue.



The finding quashes the misperception that plants are “sitting ducks”--at the mercy of passing pathogens--and sheds new light on a sophisticated signaling system inside plants that rivals the nervous system in humans and animals.

The research was led by Harsh Bais, assistant professor of plant and soil sciences at UD, former postdoctoral researcher Thimmaraju Rudrappa, who is now a research scientist at the DuPont Co., Kirk Czymmek, associate professor of biological sciences and director of UD's Bio-Imaging Center, and Paul Paré, a biochemist at Texas Tech University.

***This Arabidopsis plant infected with the pathogen Pseudomonas syringae shows typical yellowing and disease symptoms*. Photo by Thimmaraju Rudrappa**

The study is reported in the November issue of Plant Physiology and also is featured on the journal's cover. Rudrappa is the lead author of the research paper.

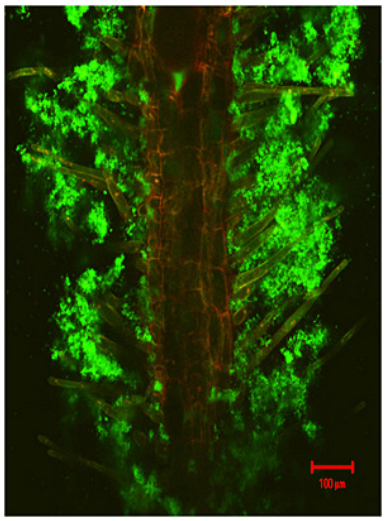
“Plants are a lot smarter than we give them credit for,” says Bais from his laboratory at the Delaware Biotechnology Institute.

“People think that plants, rooted in the ground, are just sitting ducks when it comes to attack by harmful fungi or bacteria, but we've found that plants have ways of seeking external help,” he notes.

In a series of laboratory experiments, the scientists infected the leaves of the small flowering plant Arabidopsis thaliana with a pathogenic bacterium, Pseudomonas syringae. Within a few days, the leaves of the infected plants began yellowing and showing other symptoms of disease.

This plant's roots were treated with the beneficial bacterium Bacillus subtilis. Photo by Thimmaraju Rudrappa

However, the infected plants whose roots had been inoculated with the beneficial microbe Bacillus subtilis were perfectly healthy.



Farmers often add B. subtilis to the soil to boost plant immunity. It forms a protective biofilm around plant roots and also has antimicrobial properties, according to Bais.

Using molecular biological tools, the scientists detected the transmission of a long-distance signal, a “call for help,” from the leaves to the roots in the plants that had Bacillus in the soil. The roots responded by secreting a carbon-rich chemical--malic acid.

All plants biosynthesize malic acid, Bais explains, but only under specific conditions and for a specific purpose--in this case, the chemical was actively secreted to attract Bacillus. Magnified images of the roots and leaves showed the ratcheted-up defense response provided by the beneficial microorganisms.

Czymmek captured the definitive proof using a state-of-the-art LSM 510 DUO laser scanning confocal microscope in UD's Bio-Imaging Center. UD is among only a few universities that own one of these million-dollar instruments.

***The green represents the beneficial bacterium Bacillus subtilis, which has formed a biofilm on the Arabidopsis root surface.* Photo by Thimmaraju Rudrappa**

"A plant is a challenge to image because at least half of it is below ground in the form of roots," Czymmek notes. "Here at UD, we use modern technologies including hydroponic growth systems with see-through chambers and sophisticated optical techniques that will enhance the image clarity when visualizing plants and the pathogens attacking them."

Bais and his colleagues are now working to determine what the aerial signal is from the infected leaf to the root using different pathogen-associated molecular markers (PAMPs).

The research not only sheds light on the remarkable signaling system in plants, but also is important to understand how invasive plants conquer new territory with the aid of plant microbes.

"Plants can't move from where they are, so the only way they can accrue good neighbors is through chemistry," Bais notes.

The research was funded by the National Science Foundation's Division of Integrative Organismal Systems, the University of Delaware Research Foundation and the Delaware Experimental Program to Stimulate Competitive Research (EPSCoR).

Scripps research team sheds light on immune system suppression

Work could aid development of new treatments for such conditions as HIV, measles, and tuberculosis

The work was reported in the October 16 issue of the journal Cell Host & Microbe.

The study described the suppression of this immune response in mice infected with lymphocytic choriomeningitis virus, pointing to potential new avenues for the development of drug treatments for immunosuppressive diseases in humans.

"It's the first demonstration that a virus causes suppression of the interferon response in vivo," says the paper's senior author Michael Oldstone, a Scripps Research professor and a pioneer in immune system studies. "This model explains how a secondary infection can be caused by a normal virus infection and this provides the guide for what to do and where to look in human diseases, which are of course more difficult."

Mammals have two main ways to fight off infections. Adaptive immune responses are those that involve the production of antibodies and T lymphocytes that attack specific infections. In contrast, innate immune responses are genetically encoded and are generally the same regardless of infection type. One key component of the innate immune system is interferon, which plays a range of roles including direct antiviral effects, activating innate natural killer cells and adaptive T lymphocytes, which destroy a wide range of infectious invaders.

To better understand this system, the Scripps Research team, spearheaded by Elina Zuniga, formerly a postdoctoral fellow in the Oldstone lab who is now assistant professor at the University of California, San Diego, worked with mice infected with lymphocytic choriomeningitis virus, a model Oldstone describes as a Rosetta Stone for understanding viral pathogenesis and immune system recognition of foreign substances like microbes and viruses. The researchers found that the virus suppressed the mouse immune system by interacting with immune cells known as plamacytoid dendritic cells, which are key producers of one of two critical groups of interferons, known as type I.

When plasmacytoid dendritic cells come in contact with viruses and other foreign invaders, they bind with them via membrane proteins known as toll-like receptors. Under normal conditions, this binding triggers massive production of type I interferon that then triggers other immune responses.

But the lymphocytic choriomeningits virus, and presumably other immunosupressor viruses like measles and HIV, disable this system. This then compromises other reactions, most critically activation of the natural killers that would otherwise destroy the virus-infected cells, as well as other invaders.

The researchers showed that once in this infected condition, a secondary opportunistic agent, in this case the herpes virus murine cytomegalovirus, which the mice could have otherwise fought off, grew unchecked. Remarkably, opportunistic infections with herpes viruses are frequently observed in patients infected with HIV and the mechanism described in this study could well be one of the underlying causes.

One critical aspect of the group's findings is that while the initial lymphotcytic choriomeningitis virus effectively blocked interferon production, it did not kill the dendritic cells, instead allowing them to function as long-term hosts. This allows such viruses to persist, causing persistent immunosuppression.

"I think the implications are that many of the diseases we don't know the causes for, be they behavioral, mental, cardiovascular, or endocrine, may well be caused by viruses that persist without destroying the differentiated cells they infect, alter their functions, and by this means alter homeostasis and cause disease," says Oldstone. "Examples would be viruses that persistently infect neurons and cause problems in learning and behavior, viruses that infect oligodendrocytes and cause demyelination, and viruses that infect endocrine cells and alter their production of hormones. There may be some differences, but most certainly there are a lot of commonalities."

Oldstone says that knowing such basic details about how a virus can suppress the mouse immune system could well aid the development of new treatments for the many immunosuppressive conditions such as HIV and measles that plague humans. "I think that our study opens up an avenue for people who work in those human diseases to translate our findings," says Oldstone.

For now, Oldstone's group is focused on identifying the signals and molecules involved in the lymphocytic choriomeningitis virus's crippling of the dendritic cells' interferon production.

In addition to Oldstone and Zuniga, the authors of the study, titled "Persistent virus infection inhibits type I interferon production by plasmacytoid dendritic cells to facilitate opportunistic infections," are Li-Ying Liou, and Marilyn Mendoza, from The Scripps Research Institute, and Lauren Mack, who is a master's of science student at the Zuniga laboratory at UCSD. This work was funded by grants from the National Institutes of Health and a Pew Foundation Latin American Fellowship that supported Zuniga during her time at Scripps Research.

Physical decline caused by slow decay of brain's myelin

It's more than just achy joints and arthritis, researchers say

During this year's baseball playoffs, Chicago White Sox outfielder Ken Griffey Jr., 38, threw a picture-perfect strike from center field to home plate to stop an opposing player from scoring. The White Sox ultimately won the game by a single run and clinched the division title.

Had Griffey been 40, it could be argued, he might not have made the throw in time. That's because in middle age, we begin to lose myelin — the fatty sheath of "insulation" that coats our nerve axons and allows for fast signaling bursts in our brains.

Reporting in the online version of the journal Neurobiology of Aging, Dr. George Bartzokis, professor of psychiatry at the UCLA Semel Institute for Neuroscience and Human Behavior at UCLA, and his colleagues compared how quickly a group of males ranging in age from 23 to 80 could perform a motor task and then correlated their performances to their brains' myelin integrity. The researchers found a striking correlation between the speed of the task and the integrity of myelination over the range of ages. Put another way, after middle age, we start to lose the battle to repair the myelin in our brain, and our motor and cognitive functions begin a long, slow downhill slide.

The myelination of brain circuits follows an inverted U-shaped trajectory, peaking in middle age. Bartzokis and others have long argued that brain aging may be primarily related to the process of myelin breakdown.

"Studies have shown us that as we age, myelin breakdown and repair is continually occurring over the brain's entire 'neural network,'" said Bartzokis, who is also a member of UCLA's Ahmanson–Lovelace Brain Mapping Center and the UCLA Laboratory of Neuro Imaging. "But in older age, we begin losing the repair battle. That means the average performance of the networks gradually declines with age at an accelerating rate."

The researchers proposed that cognitive, sensory and motor processing speeds are all highly related to this decline. To test their hypothesis, they used one of the simplest and best understood tests of central nervous system processing speed: how fast an individual can tap their index finger.

It's well known that the speed of a movement increases with the frequency of neuronal action potential (AP) bursts in the brain. AP is an electrical discharge that travels over the axons connecting nerves, whether it's Ken Griffey Jr.'s brain ordering his arm to throw or the brain telling a finger to tap. Fast movements require high-frequency AP bursts that depend on excellent myelin integrity over the entire axon network involved in controlling that movement.

In the study, each of the 72 participants had a magnetic resonance imaging (MRI) scan that measured the myelin integrity in the vulnerable wiring of their brain's frontal lobes. The maximum finger-tapping speed (the number of taps over a period of 10 seconds) was measured just before the MRI measure was obtained.

The results supported what the researcher had suspected, that finger-tapping speed and myelin integrity measurements were correlated and "had lifespan trajectories that were virtually indistinguishable," according to Bartzokis. And yes, they both peaked at 39 years of age and declined with an accelerating trajectory thereafter.

Bartzokis said these observations are consistent with the hypothesis that "maximum motor speeds depend upon high frequency AP bursts that, in turn, depend on the myelin integrity of the neural networks involved in the task."

"Beginning in middle age," he said, "the process of age-related myelin breakdown slowly erodes myelin's ability to support the very highest frequency AP bursts. That may well be why, besides achy joints and arthritis, even the fittest athletes retire and all older people move slower than they did when they were younger."

"The results are pretty striking," Bartzokis said. "The nearly identical trajectory across the lifespan for both measures of myelin integrity and fine motor speed supports the notion that myelin health underlies maximum AP burst frequency."

Significantly, the research suggests that the myelin breakdown process should also reduce all other brain functions for which performance speed is dependent on higher AP frequencies, including memory; it also supports the suggestion that myelin breakdown is a biological process of aging underlying the erosion of physical skills and cognitive decline, including the onset of such age-driven disorders as Alzheimer's disease.

There is, however, some good news, according to Bartzokis.

"Since in healthy individuals brain myelin breakdown begins to occur in middle age, there is a decades-long period during which therapeutic interventions could alter the course of brain aging and possibly delay age-driven degenerative brain disorders such as Alzheimer's," he said. "Non-invasive, serial evaluations of myelin integrity could be used to monitor the effects of new and current treatments that may slow the process of myelin breakdown as early as midlife."

Other authors of the study included Po H. Lu, Kathleen Tingus, Mario F. Mendez, Aurore Richard, Douglas G. Peters, Bolanle Oluwadara, Katherine A. Barrall, J. Paul Finn, Pablo Villablanca, Paul M. Thompson, and Jim Mintz. The authors report no conflict of interest.

The study was supported by the National Institutes of Health, the RCS Alzheimer's Foundation, Sidell-Kagan Foundation; and the U.S. Department of Veterans Affairs.

Prehistoric drug kit is evidence of Stoned Age

Jonathan Leake, Science Editor

Stone Age humans could well have deserved the name. Scientists have found the drug paraphernalia used by prehistoric humans to cook up herbal mixtures to get themselves high.

Scientists have long suspected that humans have an ancient history of drug use but much of the evidence has been indirect, ranging from the bizarre images found in prehistoric cave art to the discovery of hemp seeds in excavations.

Now, however, researchers have found equipment used to prepare hallucinogenic drugs for sniffing, and dated them back to South American tribes.

Quetta Kaye, of University College London, and Scott Fitz-patrick, an archeologist from North Carolina State University, found the ceramic bowls, plus tubes used to inhale drug fumes or powders, on the Caribbean island of Carriacou.

The bowls appear to have originated in South America between 100BC and 400BC and were then carried the 400 miles to the islands. One implication is that drug use may have been widespread for thousands of years before this time.

Kaye's research, published in the Journal of Archaeological Science, said: "The objects tested for this study are ceramic inhaling bowls that were likely used for the ingestion of hallucinogenic substances."

The use of such paraphernalia for inhaling drugs is well-known but the age was a surprise. What is less clear is exactly which drugs would have been used. Cannabis was not found in the Caribbean then.

There were, however, alternatives. Kaye believes one of the most likely was cohoba, a hallucinogen made from the beans of a mimosa species.

Archeological investigations in Mexico and Texas have found indirect evidence that as far back as 5,000 years ago humans were extracting mind-expanding drugs from mescal beans and peyote cacti, while opiates can be obtained from species such as poppies.

Fungi may also have been used. Moulds, including the powerfully hallucinogenic ergot found on rotting vegetation, were common in caves. Fungi like the fly agaric toadstool or psilocybin mushroom were also widespread.

Richard Davenport-Hines, a former history lecturer at the London School of Economics and author of The Pursuit of Oblivion, a global history of narcotics, believes humans have been using drugs for thousands of years.

"Drug use became widespread in many early agriculture-based societies simply because it was the only way people could cope with spending long hours working in the fields, often in horrible conditions like baking sun," he said.

Many archeologists believe religion and spiritual beliefs must also have played a part, with drugs being used to induce spiritual or trance-like states.