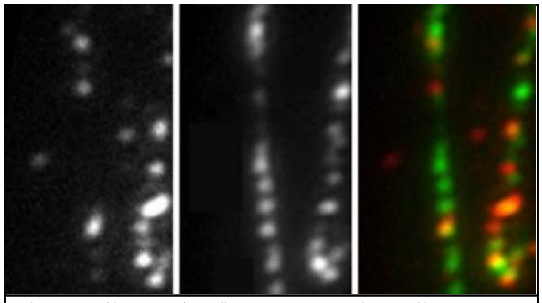
BBS proteins shown to run an export business that protects cilia

A protein complex mutated in human disease removes excess signaling molecules to prevent them from damaging cilia, say researchers from UMass Medical School. The study will be published in the December 28 issue of the Journal of Cell Biology (www.jcb.org).

Defective cilia cause a range of diseases including Bardet-Biedl syndrome (BBS), a rare, multi-tissue disorder linked to mutations in 12 different proteins. Seven of these form a complex called the BBSome, but the function of this protein assembly in cilia and flagella is unclear. In worms, the complex glues together the intraflagellar transport (IFT) machinery that assembles and maintains cilia by hauling cargo back and forth along the organelle's microtubules. But most mammalian cell types can still form cilia in the absence of BBS proteins, suggesting that the BBSome isn't essential for IFT.



The BBSome (red) removes signaling proteins from flagella by linking them to a subset of IFT particles (green).
Lechtreck, K.-F., et al. 2009. J. Cell Biol. doi:10.1083/jcb.200909183.

Lechtreck et al. turned to the green alga Chlamydomonas, and found that BBS proteins were only present on a subset of IFT particles in each of the alga's two flagella. Strains lacking components of the BBSome showed normal rates of IFT and proper flagellar structure, but couldn't steer away from bright light like wild-type cells could. Mutant flagella accumulated several signaling-related proteins, which the researchers think may disrupt the alga's response to light.

The researchers speculate that a similar buildup of disruptive proteins causes cilia dysfunction in BBS patients; the BBSome may remove excess signaling proteins from flagella by linking them to a subset of IFT particles undergoing retrograde transport out of the cilia. Author Karl Lechtreck says that the next step is to fluorescently tag the signaling proteins and compare their movements to BBS and IFT proteins.

Student sleuths using DNA reveal zoo of 95 species in NYC homes -- and new evidence of food fraud

Two New York City high school students exploring their homes using the latest high-tech DNA analysis techniques were astonished to discover a veritable zoo of 95 animal species surrounding them, in everything from fridges to furniture, from sidewalks to shipping boxes, and from feather dusters to floor corners.

Guided by DNA "barcoding" experts at The Rockefeller University and the American Museum of Natural History, Grade 12 students Brenda Tan and Matt Cost of Trinity School, Manhattan, also revealed a lot of apparent consumer fraud in progress, finding that the labels of 11 of 66 food products purchased at local markets misrepresented the actual contents.

The January edition of BioScience magazine will report on their "DNA House" project, detailed as well online at http://phe.rockefeller.edu/barcode/dnahouse.html.

Among other things, Tan and Cost also found an invasive species of insect in a box of grapefruit from Texas. And the duo might get to coin a Latin name for what could be a new species or subspecies of New York cockroach revealed by DNA barcoding.

The work builds on the 2008 "sushi-gate" findings of two other Trinity School students, Kate Stoeckle and Louisa Strauss, who found one-quarter of fish they bought at markets and restaurants in Manhattan were mislabeled. Some labels hid endangered fish species but most misrepresented cheap fish species like tilapia, sold as expensive species like tuna. Now second-year university students, Kate and Louisa will address the 2010 Annual Meeting of the American Association for the Advancement of Science.

Buyer beware - but how?

The new barcoding study by Tan and Cost uncovered additional examples and types of "mislabeled" food products:

* An expensive specialty "sheep's milk" cheese made in fact from cow's milk;
* "Venison" dog treats made of beef;
* "Sturgeon caviar" that was really Mississippi paddlefish;
* A delicacy called "dried shark," which proved to be freshwater Nile perch from Africa;
* A label of "frozen Yellow catfish" on Walking catfish, an invasive species;
* "Dried olidus" (smelt) that proved to be Japanese anchovy, an unrelated fish;
* "Caribbean red snapper" that turned out to be Malabar blood snapper, a fish from Southeast Asia.

While not publicly identifying the products or retailers involved, the students do offer opinions.

"You should get what you pay for," says Cost, 18. "We don't know where it occurs, but most of the mislabeling involves substitution of something less expensive or desirable, which suggests it's done for profit.

Also, mislabeling exposes people with an intolerance or allergy to certain foods, or misleads people with dietary restrictions. Many Hindus might be upset to discover that they had purchased a product labeled as 'sheep' that was in fact made from cows.

"Truth on labels -- especially when it comes to food -- needs to be beyond doubt absolutely. Fraudulent labeling has led to puffer fish poisoning cases in the US."

"Knowing the sources of foods for pets like cats and dogs is important too," adds Tan, 17. "And species identification can help protect the environment. Species that have protected status aren't supposed to be sold.

"But how are consumers supposed to protect themselves? Someday DNA barcoding may be a cool smartphone app. Until then, we think government agencies should start using these early versions of species identification tools to police the market, and the sooner the better."

"This report signals to food and health authorities worldwide how simple and easy it is today to check and certify the origins of products in the market, crack down on fraudsters, and protect both the health of consumers and depleted species," says Mark Stoeckle, a member of the adjunct faculty in the Program for the Human Environment at The Rockefeller University. "Several reports have appeared in the past year and a half about DNA barcode technology exposing mislabeled fish. Now Brenda and Matt have shown that many other food products are likewise misrepresented to buyers. We suspect it won't be long before we see the first criminal charges laid based on DNA barcoding evidence."

The U.S. Food and Drug Administration (FDA), which is responsible for ensuring the safety and accurate labeling of America's food supply, recently described the particular challenges posed by the many species of seafood and the high percentage of imported products, often processed to a point where traditional morphologic species determination is not possible.

"New methods that allow accurate and rapid species identifications are critical for both food borne illness investigations and for the prevention of deceptive practices, such as those where species are intentionally mislabeled to circumvent import restrictions or for resale as species of higher value," according to a November FDA paper.

DNA barcoding technology identifies and distinguishes known and unknown species quickly, cheaply, easily and accurately based on a snippet of genetic code. The agency is working with experts at various institutions to build a vouchered library of seafood species standards, which will include barcodes.

Other animals in the zoo at home

"We may think we live in a sterile, urban environment seemingly untouched by nature," says Cost. "We imagine objects are purified and cleansed in order to pass into our personal world with evidence of their original source all but erased. But DNA is amazingly resilient to damage through all the processing to which it is subjected. We got usable DNA from 151 of 217 of the items tested - including dried soup mix, dog biscuits, beef jerky, butter, a feather lying on the sidewalk, a dried bit of horse manure from Central Park, even a feather duster."

Other animals the students found they were living with include:

* Genetically distinct cockroaches that might be a new species or subspecies. The specimens collected looked to be ordinary American cockroaches (Periplaneta americana) but their DNA differed by about 4 percent from the reference sequence (differences within species are usually 1 percent or less).

"This might mean our specimens are a separate species or an isolated population within the species," says Tan.

* A strange-looking long-legged house centipede - an alien species that originated in Europe, and

* An Oriental latrine fly - an invasive species now in the southern United States. It was found inside a box of grapefruit shipped from Texas.

"The superintendent of the apartment building was surprised when we wanted to save rather than squash the cockroach," says Tan.

"Learning the species name was like finding a key that opened a new book," she adds. "It's exciting to learn still more after you know a species name. For example, 'dried shredded squid' turned out to be jumbo flying squid (Dosidicus gigas). We looked up jumbo flying squid and found it grows to 100 lbs, swims at depths up to 2,000 feet, travels in large schools containing hundreds of individuals, and hunts in cooperative packs like wolves. This gave us new thoughts about the oceans and about calamari salad!"

"There were a lot of surprises," adds Cost. "We tested 'buffalo mozzarella' cheese and found it is made from the milk of Water buffalos! We asked some adults who have ordered it on restaurant menus and they didn't know that."

DNA is resilient

The pair started the DNA House project in November 2008. Over the next four months the students became detectives, looking at the things in and around their homes through the lens of biological matter.

The students even collected a single strand of hair from eight classmates and "we were happy to report that they all came back as 100 percent human," says Tan.

A single bird feather was sufficient to yield a DNA sequence.

"New Yorkers think bird-droppings on the window sill are bad, but we saw an opportunity for science," she adds. "Strands of hair, dots of mold, and even our food became possible carriers of DNA. So after we realized that DNA was, indeed, omnipresent, an important question arose: How much abuse can this genetic material take before it becomes unintelligible or even unrecognizable?"

"Could we find decipherable DNA in a piece of cooked meat? A piece of cheese? A highly processed dog treat? What we found was astonishing. Few specific conditions proved able to destroy the DNA consistently."

Subjecting it to cold, drying, or chemicals seems to have little impact on DNA survival.

"Whether frozen, fermented, dried, or pickled, most of our specimens yielded DNA in a recognizable form," says Cost. "I did not used to think I was eating intact DNA when I was eating yogurt.

"DNA also survived the passage of time. For example, a fragment of deer antler yielded DNA even after eight years of sitting in a room with varying temperature and humidity."

The one exception of endurance was canned foods, processed at such high temperatures in the process that DNA broke into pieces, making contents identification often impossible.

Translating many samples into names

In total, the students sent 217 specimens to the American Museum of Natural History for analysis. Some 70 percent -- 151 -- contained readable DNA for the standard "barcode" region now used to identify animal species.

When the museum scientists reported a DNA sequence back to the students, they simply pasted it electronically, like a 650-letter word, into a search engine (http:///www.barcodinglife.org) that translates the species name almost instantly. The translation rests on a Rosetta Stone called BOLD.

The Barcode of Life Database (BOLD) is maintained by the Biodiversity Institute of Ontario at the University of Guelph, Canada, where DNA barcoding was pioneered. So far, scientists the world over have DNA barcoded over 750,000 individual specimens representing over 65,000 species. Their ultimate goal is a reference library of barcodes for all animals and plants on Earth.

Of the 95 different animal species identified by Brenda and Matt, 58 were vertebrates and 27 invertebrates. They placed the vertebrates and invertebrates on different branches of the evolutionary tree to see their genetic relationships (deer and cattle, for example).

Assisting the students were Stoeckle; Jesse Ausubel, director of Rockefeller's Program for the Human Environment and the Alfred P. Sloan Foundation; George Amato, Sergios Orestis-Kolokotronis, Matt Leslie and Cecilia Bartholomew at American Museum of Natural History; and Alison DiStefano, Jan Kang, and Frances Cary at Trinity School.

"High school students showed why DNA is the stuff of heredity: It's tough enough to survive in Manhattan," says Ausubel.

"I am delighted that Trinity continues to fulfill its mission to 'challenge the minds' and 'fire the imaginations' of our students while ensuring that they are engaging in 'the larger communities of city, nation, and world of which we are a part,'" says John C. Allman, Head of School at Trinity. "Their discoveries in the use of DNA testing demonstrate the creative thinking that will serve them well throughout their lives. Such work shows that students are not only the future, as is often said, but are the present as well. Congratulations to Brenda and Matt for their good work and thank you Drs. DiStefano, Kang, and Cary for being such wonderful Trinity teachers and mentors." *Tan and Cost plan to pursue biology and music respectively at university next fall.*

Drug-resistant urinary tract infections spreading worldwide

A sudden worldwide increase in an antibiotic-resistant bacterium is cause for concern, according to a review in f1000 Medicine Reports. Faculty of 1000 member Dr Johann Pitout, of the Department of Pathology and Laboratory Medicine, University of Calgary, urges the medical community to monitor the spread of a multi-drug resistant bacterium before it becomes necessary to use more powerful antibiotics as a first response.

Extended-spectrum β-lactamases (ESBLs) are bacterially-produced enzymes that confer resistance to penicillin-type antibiotics. ESBLs have been commonly linked to nosocomial infections, which are generally treated with intravenously-administered antibiotics such as the carbapenems.

However, in recent years there has been a drastic increase in community-acquired infections, caused by a single strain of ESBL-producing E. coli. Dr Pitout suggests that the rapid spread of this particular strain is due, at least in part, to international travel through high-risk areas such as the Indian subcontinent.

Using carbapenems as the first response to such infections increases the risk of inducing resistance to them in the community, nullifying some of our most powerful anti-bacterial strategies. Dr Pitout recommends that the medical community should use existing methods to identify infections caused by ESBL-producing bacteria, and empirically test the efficacy of other antibiotics in treating community-acquired infections.

Dr Pitout concludes, "If this emerging public health threat is ignored … the medical community may be forced to use the carbapenems as the first choice for the empirical treatment of serious [community-acquired UTIs]."

Notes to Editors

1. Dr Johann Pitout is a Faculty Member for f1000 Medicine, Infectious Diseases Section, and works at the Pathology and Laboratory Medicine, University of Calgary, Canada http://f1000medicine.com/member/5309018475971825

2. The full text of this article is available for subscribers at http://f1000medicine.com/reports/10.3410/M1-84/

Researchers find clues to why some continue to eat when full

DALLAS – The premise that hunger makes food look more appealing is a widely held belief – just ask those who cruise grocery store aisles on an empty stomach, only to go home with a full basket and an empty wallet.

Prior research studies have suggested that the so-called hunger hormone ghrelin, which the body produces when it's hungry, might act on the brain to trigger this behavior. New research in mice by UT Southwestern Medical Center scientists suggest that ghrelin might also work in the brain to make some people keep eating "pleasurable" foods when they're already full.

"What we show is that there may be situations where we are driven to seek out and eat very rewarding foods, even if we're full, for no other reason than our brain tells us to," said Dr. Jeffrey Zigman, assistant professor of internal medicine and psychiatry at UT Southwestern and co-senior author of the study appearing online and in a future edition of Biological Psychiatry.

Scientists previously have linked increased levels of ghrelin to intensifying the rewarding or pleasurable feelings one gets from cocaine or alcohol. Dr. Zigman said his team speculated that ghrelin might also increase specific rewarding aspects of eating.

Rewards, he said, generally can be defined as things that make us feel better.

"They give us sensory pleasure, and they motivate us to work to obtain them," he said. "They also help us reorganize our memory so that we remember how to get them."

Dr. Mario Perello, postdoctoral researcher in internal medicine and lead author of the current study, said the idea was to determine "why someone who is stuffed from lunch still eats – and wants to eat – that high-calorie dessert."

For this study, the researchers conducted two standard behavioral tests. In the first, they evaluated whether mice that were fully sated preferred a room where they had previously found high-fat food over one that had only offered regular bland chow. They found that when mice in this situation were administered ghrelin, they strongly preferred the room that had been paired with the high-fat diet. Mice without ghrelin showed no preference.

"We think the ghrelin prompted the mice to pursue the high-fat chow because they remembered how much they enjoyed it," Dr. Perello said. "It didn't matter that the room was now empty; they still associated it with something pleasurable."

The researchers also found that blocking the action of ghrelin, which is normally secreted into the bloodstream upon fasting or caloric restriction, prevented the mice from spending as much time in the room they associated with the high-fat food.

For the second test, the team observed how long mice would continue to poke their noses into a hole in order to receive a pellet of high-fat food. "The animals that didn't receive ghrelin gave up much sooner than the ones that did receive ghrelin," Dr. Zigman said.

Humans and mice share the same type of brain-cell connections and hormones, as well as similar architectures in the so-called "pleasure centers" of the brain. In addition, the behavior of the mice in this study is consistent with pleasure- or reward-seeking behavior seen in other animal studies of addiction, Dr. Zigman said.

The next step, Dr. Perello said, is to determine which neural circuits in the brain regulate ghrelin's actions.

Other UT Southwestern researchers involved in the study were Dr. Ichiro Sakata, postdoctoral researcher in internal medicine; Dr. Shari Birnbaum, assistant professor of psychiatry; Dr. Jen-Chieh Chuang, postdoctoral researcher in internal medicine; Sherri Osborne-Lawrence, senior research scientist; Sherry Rovinsky, research assistant in internal medicine; Jakub

Woloszyn, medical student; Dr. Masashi Yanagisawa, professor of molecular genetics and a Howard Hughes Medical Institute investigator; and Dr. Michael Lutter, co- senior author and assistant professor of psychiatry.
The work was supported by the National Institutes of Health, the Foundation for Prader-Willi Research, and the National Alliance for Research on Schizophrenia and Depression.

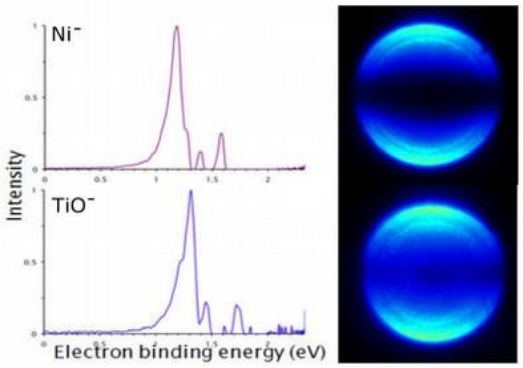
Superatoms mimic elements: Research gives new perspective on periodic table

Transforming lead into gold is an impossible feat, but a similar type of "alchemy" is not only possible, but cost-effective too. Three Penn State researchers have shown that certain combinations of elemental atoms have electronic signatures that mimic the electronic signatures of other elements. According to the team's leader A. Welford Castleman Jr., Eberly Distinguished Chair in Science and Evan Pugh Professor in the Departments of Chemistry and Physics, "the findings could lead to much cheaper materials for widespread applications such as new sources of energy, methods of pollution abatement, and catalysts on which industrial nations depend heavily for chemical processing."

The researchers also showed that the atoms that have been identified so far in these mimicry events can be predicted simply by looking at the periodic table. The team used advanced experimentation and theory to quantify these new and unexpected findings. "We're getting a whole new perspective of the periodic table," said Castleman. The team's findings will be published in the 28 December 2009 early on-line issue of the journal Proceedings of the National Academy of Sciences, and at a later date in the print edition of the journal.

Castleman and his team -- which includes Samuel Peppernick, a former Penn State graduate student who now is a postdoctoral researcher at the Pacific Northwest National Laboratory, and Dasitha Gunaratne, a Penn State graduate student -- used a technique, called photoelectron imaging spectroscopy, to examine similarities between titanium monoxide and nickel, zirconium monoxide and palladium, and tungsten carbide and platinum.

"Photoelectron spectroscopy measures the energy it takes to remove electrons from various electronic states of atoms or molecules, while simultaneously capturing snapshots of these electron-detachment events with a digital camera," said Castleman. "The method allows us to determine the binding energies of the electrons and also to observe directly the nature of the orbitals in which the electrons resided before they were detached. We found that the amount of energy required to remove electrons from a titanium-monoxide molecule the same as the amount of energy required to remove electrons from a nickel atom. The same is true for the systems zirconium monoxide and palladium and tungsten carbide and platinum. The key is that all of the pairs are composed of isoelectronic species, which are atoms with the same electron configuration." Castleman noted that, in this case, the term isoelectronic refers to the number electrons present in the outer shell of an atom or molecule.



The team used photoelectron imaging spectroscopy to examine similarities between a nickel atom and a titanium-monoxide molecule. Left: Graphical displays of energy peaks were similar between a nickel atom and a titanium-monoxide molecule. Right: Bright spots in the images, which correspond to the energy of the electrons emitted during their removal from the atoms' outer shells, appeared to be similar between a nickel atom (right, top) and a titanium-monoxide molecule (right, bottom). **Castleman lab, Penn State University**

The team looked at images of the photoelectron spectroscopy data. Bright spots in the images, which correspond to the energy of the electrons emitted during their removal from the atoms' outer shells, appeared to be similar between the pairs of species in the three systems studied. Likewise, graphical displays of energy peaks were similar between the pairs, and theoretical calculations also resulted in the pairs having matching energy levels.

Castleman explained that the molecules titanium monoxide, zirconium monoxide, and tungsten carbide are superatoms of nickel, palladium, and platinum, respectively. Superatoms are clusters of atoms that exhibit some property of elemental atoms. Former work in Castleman's lab has involved investigating the notion of superatoms. One of his previous experiments showed that a cluster of 13 aluminum atoms behaves like a single iodine atom. Adding a single electron to this aluminum-atom system results in the cluster behaving like a rare-gas atom. Further, he showed that a cluster of 14 aluminum atoms has a reactivity similar to an alkaline earth atom.

Now, Castleman's new research takes the superatom idea to a new level and provides a sound quantitative foundation for the concept of superatoms. "It looks like we can predict which combinations of elemental atoms mimic other elemental atoms," he said. "For example, by looking at the periodic table, you can predict that titanium monoxide will be a superatom of nickel. Simply start at titanium, which has four outer-shell electrons,

and move six elements to the right, because atomic oxygen possesses six outer-shell electrons. The element you end up on is nickel, whose 10 outer-shell electrons make it isoelectronic with the 10 outer-shell electron molecule resulting from the combination of titanium and oxygen. We thought this finding must be a curious coincidence, so we tried it with other atoms and we found that a pattern emerged."

Castleman said that he doesn't know if the pattern will occur across the entire periodic table or if it will be confined to only a part of it. Right now, he and his team are working through the transition-metal atoms. In the future, they plan to take the research a step further to investigate whether or not the superatoms are chemically similar to their respective single atoms. "Platinum is used in nearly all catalytic converters in automobiles, but it is very expensive," said Castleman. "In contrast, tungsten carbide, which mimics platinum, is cheap.

A significant amount of money can be saved if catalytic-converter manufacturers are able to use tungsten carbide instead of platinum. Likewise, palladium is used in certain combustion processes, yet it is mimicked by zirconium monoxide, which is less expensive by a factor of 500. Our new findings are exciting from both a scientific as well as a practical point of view."

This research was funded by the Air Force Office of Scientific Research.

Schizophrenia mouse model should improve understanding and treatment of the disorder

AUGUSTA, Ga. – Scientists have created what appears to be a schizophrenic mouse by reducing the inhibition of brain cells involved in complex reasoning and decisions about appropriate social behavior.

Findings by Medical College of Georgia scientists, published Dec. 28 in PNAS, elucidate the critical balance between excitation and inhibition of these cells that appears to go awry in schizophrenia. They also provide the first animal model for studying the disabling psychiatric disorder that affects about 1 percent of the population.

"We believe the mouse, which exhibits some of the same aberrant behavior as patients with this disorder, will help identify better therapies," said Dr. Lin Mei, a developmental neurobiologist who directs MCG's Institute of Molecular Medicine and Genetics. "We are doing testing to see if antipsychotic drugs already on the market are effective in treating the mouse."

MCG scientists made the mouse by deleting a candidate gene for schizophrenia, ErbB4, from interneurons, which are brain cells that help shower larger decision-making neurons, called pyramidal cells, with inhibition.

In their earlier work, they identified how ErbB4 and another candidate gene, neuregulin-1, work together to balance the activity of these pyramidal cells. They reported in Neuron in May 2007 that the two help keep a healthy balance between excitation and inhibition by increasing release of GABA, a major inhibitory neurotransmitter in the inhibitory synapses of the brain's prefrontal cortex. Seven years earlier, they showed the two also put a damper on excitatory synapses, communication points between neurons where the neurotransmitter glutamate excites cells to action.

To further test these findings, this time they altered the natural check and balance in cells directly involved with supplying pyramidal neurons with the inhibitor GABA. They did this by knocking out the ErbB4 gene in nearby chandelier and basket interneurons that supply GABA to pyramidal cells. "If we take out ErbB4 in these two interneurons, the neuregulin should have no effect because it can't promote GABA," Dr. Mei, Georgia Research Alliance Eminent Scholar in Neuroscience, said.

His postulation played out in the behavior of the mouse, who exhibited schizophrenia-like behavior including increased movement and impaired short-term memory. The scientists are still gathering data on the manic aspect of schizophrenia in their mice.

For example, both the normal and knockout mice learned they would find a food pellet in each arm of an eight-armed chamber but that if they went to the same arm for seconds, there were none. But the knockouts took longer to learn and finish the task. Knockouts also spent a lot more time sniffing and snooping around and revisiting empty arms.

In another test, knockouts couldn't – or wouldn't - make the connection that a relatively low noise would be followed by a slightly louder one. When they treated the knockouts with diazepam, an anti-anxiety medication, they responded similarly to the normal mice: the first sound prepared them for the second.

Dr. Mei suspects that if he could look at the chandelier and basket interneurons in the prefrontal cortex of schizophrenics, he would also find something wrong with their usual role of sensing the need for the inhibitor GABA and supplying it to the pyramidal cells. "In schizophrenia, the baseline of the excitatory neurotransmitter is probably high," he said.

The research was funded by the National Institutes of Health and the National Alliance for Research on Schizophrenia and Depression, for which he is a distinguished investigator.

Co-authors include MCG scientists Drs. Wen-Cheng Xiong, Alvin Terry and Almira Vazdarjanova and postdoctoral fellows Drs. Lei Wen, Yi-Sheng Lu and Xin-Hong Zhu.

Chlorophylls effective against aflatoxin

CORVALLIS, Ore. – A new study has found that chlorophyll and its derivative chlorophyllin are effective in limiting the absorption of aflatoxin in humans. Aflatoxin is produced by a fungus that is a contaminant of grains including corn, peanuts and soybeans; it is known to cause liver cancer – and can work in concert with other health concerns, such as hepatitis.

Levels of aflatoxin are carefully regulated in the United States, but are often found in the food supplies of developing nations, especially those with poor storage facilities.

OSU scientist George Bailey, a distinguished professor of environmental and molecular toxicology, pioneered studies of aflatoxin in China, where he found that in one region, one out of every 10 adults died from liver cancer.

But what has the science world particularly intrigued with this follow-up study is the methodology used by the researchers - a new "Phase 0" approach that safely tests low levels of carcinogens in human volunteers to measure the total aflatoxin exposure and to determine the effect of dietary chlorophylls on reducing this exposure.

Results of the study were just published in the journal Cancer Prevention Research.

Bailey and several other researchers, including lead author Carole Jubert, were part of the recent study. The journal also included a perspective written by a pair of Johns Hopkins researchers – Thomas Kensler and John Groopman – who praise the methodology and suggest that these Phase 0 "microdosing" studies should be expanded.

They wrote: "…microdosing studies with carcinogens have the potential to provide important insights into chemopreventive interventions and to enhance the overall clinical development and safety evaluation of preventive agents."

The Phase 0 study "…may open the door for all kinds of new research," said Jubert, a former researcher in Bailey's lab at OSU's Linus Pauling Institute. Jubert now works for Life Microsystems, an OSU spinoff company that hopes to continue work with natural products grown in Oregon, including pure chlorophylls.

"The technology is not particularly difficult," she added. "It's just a novel approach to evaluate toxin exposure in humans."

In their study, Jubert and her colleagues gave very low doses of aflatoxin labeled with carbon-14 isotopes as a tracer to four human volunteers. They then gave the volunteers the same doses of aflatoxin along with doses of either chlorophyll or chlorophyllin, which previously had been shown to reduce carcinogen bioavailability in trout and rats.

Using an accelerator mass spectrometer, they measured the rate of aflatoxin bioavailability. This technique is extremely sensitive, the researchers say, allowing measurement of minute amounts of any labeled compound. Their research revealed rapid absorption of aflatoxin, which was significantly limited after the chlorophyll and chlorophyllin treatments.

"The beauty of this kind of 'Phase 0' study is the use of ultra-sensitive technology and 'microdoses' of environmental carcinogens to study toxicokinetics within the human body," said John Mata, an OSU pharmacologist and second author on the study. "These measurements can be important because they allow us to better design future studies to understand the effects of dietary constituents on cancer risk.

"In this case, clearly the results merit further study," Mata added. "We showed that aflatoxin is absorbed quite rapidly and that chlorophyll and chlorophyllin have an ameliorating effect, preventing the toxin from getting into the bloodstream. Further studies can more precisely explore the interactions, as well as dosage levels."

Jubert and Mata also have tested the feasibility of using similar technology on human exposure to other toxins, including smokers who ingest carcinogens through cigarette smoke.

Mata, a professor in OSU's College of Veterinary Medicine, is a pharmacologist who previously worked in the drug industry. He said Phase 1 studies are designed to see if a compound is safe; Phase 2 expands the scope of the project, and Phase 3 looks at the compounds' efficacy. Phase 0 represents a new concept – a way to measure the kinetics of a drug by using extremely small doses that pose little risk to the volunteers.

In this case, the amount of radiation given the human volunteers was equal to that you would encounter from a one-hour airplane ride; the level of aflatoxin administered was 1/30th the amount the Food and Drug Administration allows in a peanut butter sandwich.

Findings

Carpe Diem? Maybe Tomorrow

By JOHN TIERNEY

Viktor Koen

For once, social scientists have discovered a flaw in the human psyche that will not be tedious to correct. You may not even need a support group. You could try on your own by starting with this simple New Year's resolution: Have fun ... now!

Then you just need the strength to cash in your gift certificates, drink that special bottle of wine, redeem your frequent flier miles and take that vacation you always promised yourself. If your resolve weakens, do not succumb to guilt or shame. Acknowledge what you are: a recovering procrastinator of pleasure.

It sounds odd, but this is actually a widespread form of procrastination — just ask the airlines and other marketers who save billions of dollars annually from gift certificates that expire unredeemed. Or the poets who have kept turning out exhortations to seize the day and gather rosebuds.

But it has taken awhile for psychologists and behavioral economists to analyze this condition. Now they have begun to explore the strange impulse to put off until tomorrow what could be enjoyed today.

Why, for instance, is it so hard to find time to visit landmarks in your own backyard? People who have moved to Chicago, Dallas and London get to fewer local landmarks during their entire first year than the typical tourist visits during a two-week stay, according to a study conducted by Suzanne B. Shu and Ayelet Gneezy, who are professors of marketing at the University of California, Los Angeles, and the University of California, San Diego, respectively. The Chicagoans in the study had visited more landmarks in other cities than in their own, and even their relatively small amount of local sightseeing was done mainly in the course of entertaining out-of-towners. Otherwise, the only time Chicagoans rushed to see the local landmarks was just before they were about to move to another city, when that deadline inspired sudden passions for taking architectural tours and going to the zoo.

When there is no immediate deadline, we're liable to put off going to the zoo this weekend because we assume that we will be less busy next weekend - or the weekend after that, or next summer. This is the same sort of thinking that causes us to put the gift certificate in the drawer because we expect to have more time for shopping in the future.

We're trying to do a cost-benefit analysis of the time lost versus the pleasure or money to be gained, but we're not accurate in our estimates of "resource slack," as it is termed by Gal Zauberman and John G. Lynch. These behavioral economists found that when people were asked to anticipate how much extra money and time they would have in the future, they realistically assumed that money would be tight, but they expected free time to magically materialize.

Hence you're more likely to agree to a commitment next year, like giving a speech, that you would turn down if asked to find time for it in the next month. This produces what researchers call the "Yes ... Damn!" effect: when the speech comes due next year, you bitterly discover you're still as busy as ever.

Dr. Shu and Dr. Gneezy demonstrated another effect of this fallacy by giving people gift certificates good for movie tickets and French pastries. Some got certificates that expired within two to three weeks; others got certificates good for six to eight weeks.

The people who received the long-term certificates were more confident than the others that they would redeem the gifts — a logical enough assumption, given all the extra time they had. But they just kept putting it off, and ultimately they were more likely to let the gift go unredeemed than the people who had received the short-term certificates.

Once you start procrastinating pleasure, it can become a self-perpetuating process if you fixate on some imagined nirvana. The longer you wait to open that prize bottle of wine, the more special the occasion has to be.

If you're determined to get the absolute maximum out of those frequent flier miles, you can end up wasting them, as Dr. Shu found in an experiment offering people a chance to use discount coupons in the course of buying a series of plane tickets. Once the subjects were told that they might have a chance at a free flight worth $1,000, they scorned lesser awards and hung on to their coupons so long that in the end they had to use them for much cheaper flights.

"People can become overly focused on an ideal," Dr. Shu said. "Even if they know it's unlikely, they get so focused on the perfect scenario that they block everything else. Or they anticipate that they'll kick themselves

later if they take second-best option and then see the best one is still available. But they don't realize that regret can go the other way. They'll end up with something worse and regret not taking the second-best one."

But even if you know about all this research, how can you apply these lessons? How can you avoid the temptation to postpone pleasure? (You can offer suggestions at nytimes.com/tierneylab.) One immediate strategy, Dr. Shu said, is to cash in quickly any gift certificate you received this holiday season. "The biggest danger is that it will be forgotten and expire," she said. "One of the best presents you can give back to the giver is to use it quickly and then tell them how much you enjoyed it. The regret from not using it will be bigger than the regret from using it on a nonperfect occasion, for you and especially for the person who gave it."

Another tactic is to give yourself deadlines. Cash in the miles by summer, even if you can't get a round-the-world trip out of them. Instead of waiting for a special occasion to indulge yourself, create one. Dr. Shu approvingly cites the pioneering therapeutic work of Dorothy J. Gaiter and John Brecher, who for the past decade used their Wall Street Journal column on wine to proclaim the last Saturday of February to be "Open That Bottle Night."

But you don't even have to wait until Feb. 27. Remember the advice offered in the movie "Sideways" to Miles, who has been holding on to a '61 Cheval Blanc so long that it is in danger of going bad. When Miles says he is waiting for a special occasion, his friend Maya puts matters in perspective:

"The day you open a '61 Cheval Blanc, that's the special occasion."

Scientists Start a Genomic Catalog of Earth's Abundant Microbes

By CARL ZIMMER

If you want to appreciate the diversity of life on earth, you will need a microscope.

There are about 5,400 species of mammals on the planet, but just a spoonful of soil may contain twice as many species of microbes. They can dwell in habitats where so-called higher life forms like us would quickly die, including acid-drenched mines and Antarctic deserts. By one rough estimate, there may be, all told, 150 million species of microbes.

"Microbes represent the vast majority of organisms on earth," said Hans-Peter Klenk, a microbiologist for the German Collection of Micro-organisms and Cell Cultures, a government microbiology research center.

Yet scientists still know very little about our microbial planet. The genomes of only about 1,000 species of microbes have been sequenced. That leaves 99.99999 percent to go. Making matters worse, the genomes scientists have sequenced so far are clustered together in groups of closely related species, leaving vast stretches of the microbial tree of life virtually unexplored. It would be as if all we knew about the animal kingdom were based entirely on a stuffed ferret and a pickled tarantula.

To shed light on this enormous stretch of biological darkness, the Joint Genome Institute at the Energy Department has started what it calls a "genomic encyclopedia." It is filling the encyclopedia with the genomes of microbes from remote reaches of the tree of life.

In the Dec. 24 issue of Nature, Dr. Klenk and his colleagues present their first analysis of the encyclopedia, based on the first 56 species they have sequenced. Using this new evolution-based approach, the scientists have discovered many kinds of genes, some of which may prove a boon to the biotechnology industry.

"The encyclopedia is guaranteed to yield new things," said Norman Pace, a University of Colorado microbiologist who was not involved in the study. "We humans haven't even scratched the surface of natural microbial diversity."

When scientists first began to pick microbes for genome sequencing in the 1990s, they favored species they had been studying for years, like E. coli. As the technology improved and costs fell, they moved from these microbial lab rats to species that were important to humans for one reason or another, like those causing diseases.

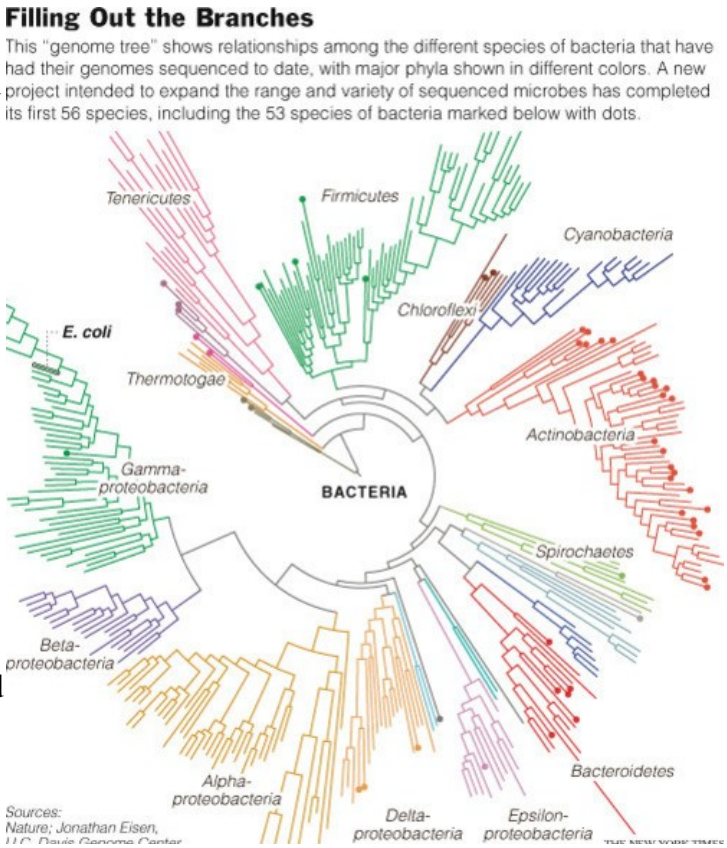
It gradually became clear that this approach neglected most of the diversity of microbes. A number of microbiologists began to argue that a broader survey of the microbial world would bring many new insights. Comparing a gene in many different species can often help scientists figure out what a gene does in the first place, for example. "It's been blatantly obvious that this should be done," said Jonathan Eisen, an evolutionary biologist at the University of California, Davis, and the lead author of the Nature paper.

Taking advantage of the falling cost of DNA sequencing, Dr. Eisen, Dr. Klenk and their colleagues at the Joint Genome Institute established the Genomic Encyclopedia of Bacteria and Archaea. (Bacteria and Archaea are two of the major branches of the tree of life. The third branch contains eukaryotes, which includes animals, fungi, plants and protozoa.) The scientists selected 200 species to analyze. Dr. Klenk and his colleagues in Germany plucked the microbes from their collection and reared them in huge numbers, split open the cells and isolated long fragments of DNA from them.

Once the scientists had sequenced 56 genomes, they decided to see whether their approach was paying off. For part of their analysis, they tallied up how many new genes they had found: tens of thousands. But more importantly, they found 1,768 new gene families - sets of genes that share a common ancestor. “We didn’t remotely expect it to be this striking,” Dr. Eisen said.

Dr. Eisen expects that many of these new genes will lead to important research. One gene, from a microbe that lives in salt flats, encodes an enzyme that can cut up cellulose in the presence of lots of salt. This type of enzyme might be useful for extracting biofuels from plants. “The biotech industry loves these things,” he said.

The encyclopedia is also upending some basic rules of biology. All eukaryotes, ourselves included, have Lego-like skeletons in our cells made from a molecule called actin. “We have this rule that actin is in eukaryotes,” Dr. Eisen said, “and it’s not in bacteria and archaea.” Now he and his colleagues have found a gene for actin in a species of marine bacteria. “It’s wildly cool,” he said.



Dr. Eisen suspects that the actin gene was ferried from eukaryotes to the bacteria long ago. Now the bacteria may inject actin into eukaryotes to disrupt their cells.

The genomic encyclopedia includes not only the raw data on genes, but also predictions about what those genes are actually for. To see if those predictions are right will require a lot more time and labor. The joint genome institute has set up an “Adopt a Genome Program” to enlist the help of college students. Undergraduate microbiology students can pick a species from the encyclopedia and analyze its biology. “We need them,” Dr. Eisen said.

Students at Davidson College in North Carolina have already published a paper on the salt-flat microbe with the cellulose enzyme.

In years to come, Dr. Eisen and his colleagues hope to have many genomes for students to analyze. They are continuing to select species, and they hope, in a few years, to have 1,500 in the encyclopedia.

“We’ve made a dent,” Dr. Eisen said, “but it’s a small dent.”

Music therapy for tinnitus hope

Individually designed music therapy may help reduce the noise levels experienced by people who suffer from tinnitus, say German researchers.

They altered participants' favourite music to remove notes which matched the frequency of the ringing in their ears. After a year of listening to the modified music, individuals reported a drop in the loudness of their tinnitus. The researchers said the "inexpensive" treatment could be used alongside other techniques to relieve the condition.

It is thought that around 1-3% of the population have chronic ringing in their ears which is significant enough to reduce their overall quality of life. Writing in the Proceedings of the National Academy of Sciences, the researchers said although the cause of tinnitus remains unknown, it has been shown that the part of the brain that processes sounds is frequently disrupted in people with the condition.

The theory behind the new technique is that removing the spectrum of noise associated with tinnitus from the music reduces activity in the brain relating to that frequency, alleviating the condition.

Therapy

The 39 patients who took part in the study all had chronic tinnitus for an average of five years but had no other hearing problems. They were split into three groups and were offered either the modified music therapy, a dummy version of music therapy or usual treatment.

Participants listened to the music for an average of 12 hours a week and by the end of the study, those who had been given the tailored music reported a significant drop in the level of the ringing they heard compared with those listening to the dummy version.

Study leader Dr Christo Pantev, from Westphalian Wilhelms University in Munster, said the approach specifically targeted the part of the brain responsible for tinnitus.

"The notched music approach can be considered as enjoyable, low cost, and presumably causal treatment that is capable of specifically reducing tinnitus loudness.

"It could significantly complement widely-used and rather indirect psychological treatment strategies."

Dr Ralph Holmes, director of biomedical research at deaf and hard of hearing charity, RNID, said he would look in detail at the findings. "While we find it encouraging there is new investment in treatment for tinnitus, we know there is no proven 'cure'. This seems to be similar to tinnitus retraining therapy which is one of the most common ways of managing the condition."

In New Way to Edit DNA, Hope for Treating Disease

By NICHOLAS WADE

Only one man seems to have ever been cured of AIDS, a patient who also had leukemia. To treat the leukemia, he received a bone marrow transplant in Berlin from a donor who, as luck would have it, was naturally immune to the AIDS virus.

If that natural mutation could be mimicked in human blood cells, patients could be endowed with immunity to the deadly virus. But there is no effective way of making precise alterations in human DNA.

That may be about to change, if a powerful new technique for editing the genetic text proves to be safe and effective. At the University of Pennsylvania, Dr. Carl June and colleagues have used the technique to disrupt a gene in patients' T cells, the type attacked by the AIDS virus. They have then infused those cells back into the body. A clinical trial is now under way to see if the treated cells will reconstitute a patient's immune system and defeat the virus.

The technique, which depends on natural agents called zinc fingers, may revive the lagging fortunes of gene therapy because it overcomes the inability to insert new genes at a chosen site. Other researchers plan to use the zinc finger technique to provide genetic treatments for diseases like bubble-boy disease, hemophilia and sickle-cell anemia.

In principle, the zinc finger approach should work on almost any site on any chromosome of any plant or animal. If so, it would provide a general method for generating new crop plants, treating many human diseases, and even making inheritable changes in human sperm or eggs, should such interventions ever be regarded as ethically justifiable.

Zinc fingers are essential components of proteins used by living cells to turn genes on and off. Their name derives from the atom of zinc that holds two loops of protein together to form a "finger." Because the fingers recognize specific sequences of DNA, they guide the control proteins to the exact site where their target gene begins.

After many years of development, biologists have learned how to modify nature's DNA recognition system into a general system for manipulating genes. Each natural zinc finger recognizes a set of three letters, or bases, on the DNA molecule. By stringing three or four fingers together, researchers can generate artificial proteins that match a particular site.

The new system has been developed by a small biotech company, Sangamo BioSciences of Richmond, Calif., and, to some degree separately, by academic researchers who belong to the Zinc Finger Consortium.

Sangamo was founded in 1995 by Edward O. Lanphier II, a former executive with a gene therapy company. Reading an article by Aaron Klug, the British crystallographer who discovered the zinc finger design, he saw the technique's potential for genetic manipulation. He bought a company Dr. Klug had founded and worked with him and researchers like Carl O. Pabo to improve the technique and develop combinations of zinc fingers to match any sequence of DNA letters.

"We now have a full alphabet of zinc fingers," Mr. Lanphier said, "but when we started the company it was like typing a novel with two fingers."

Zinc finger proteins have many potential uses. One is to link them to agents that turn on or turn off the gene at the site recognized by the fingers. More powerfully, the zinc fingers can be deployed as a word processing system for cutting and pasting genetic text. Two sets of zinc fingers are attached to a protein that cuts the DNA in between the two sites matched by the fingers. The cell quickly repairs the break but sometimes in a way that disrupts the gene. This is the approach used in destroying the gene for the receptor used by the AIDS virus to gain entry to white blood cells.

Or, if DNA for a new gene is inserted into a cell at the same time as the zinc fingers that scissor the DNA, the new gene will be incorporated by the cell's repair system into the DNA at the break site. Most gene therapy techniques use a virus to carry new genes into a cell but cannot direct the virus to insert genes at a specific site.

"I think it's a broadly applicable technology which has already allowed experiments that would not have been possible before," said J. Keith Joung, a biologist who designs zinc finger proteins at the Massachusetts General Hospital.

Daniel F. Voytas, a plant geneticist at the University of Minnesota, said the zinc finger technique would allow breeders to change the oil composition of any plant, the types of carbohydrates produced or the way carbon dioxide is captured. “We can go in and make any change we want to any plant species,” Dr. Voytas said.

Zinc fingers can also be used for “trait stacking,” the positioning of several beneficial genes at a single site. This avoids heavy regulatory costs because genetically altered plants must be tested for safety for each site that is modified.

The zinc finger technology has taken many years to prepare because of the difficulty of designing the fingers and also of preventing them from cutting the genome in the wrong places. Only a handful of laboratories are currently using the technique, but proponents expect to see rapid growth.

The Zinc Finger Consortium, founded by Dr. Joung and Dr. Voytas, makes the method available free, and researchers need only pay for materials. But there are some 200 steps in Dr. Joung’s recipe for making zinc fingers, and it takes time and dedication to do them all correctly.

The alternative is to buy zinc fingers. Sangamo has a commanding patent position and has licensed Sigma-Aldrich, a large life science company in St. Louis, to make zinc finger proteins for researchers. Sigma-Aldrich’s charge for a zinc finger protein that cuts the genome at the site of your choice is $39,000, with a discount for academic researchers. Zinc fingers that cut well-known human genes cost $12,000. Sigma-Aldrich has used the technology to generate rats with genetic defects that mimic human disease. A schizophrenic rat can be had for $100.

David Smoller, president of Sigma-Aldrich’s biotechnology unit, licensed the technology from Sangamo in 2006 when he felt the company had proved it worked. “This technology is just amazing,” Dr. Smoller said. “It’s a game changer.”

Sangamo has licensed the use of zinc fingers to Dow Agrosciences for creating new crop plants, and has reserved medical uses for itself. It has four Phase 2 clinical trials in progress, including treatments for diabetic neuropathy and amyotrophic lateral sclerosis. In an ambitious effort to cure AIDS, Sangamo and the University of Pennsylvania started a clinical trial in February.

The AIDS virus enters the T cells of the immune system by latching on to a receptor called CCR5, but about 10 percent of Europeans have a mutation that disables the CCR5 gene. People who inherit two disabled copies of the gene do not have CCR5 on the surface of their T cells, so the AIDS virus has nothing to grab. These people are highly resistant to H.I.V.

In the zinc finger approach, the patient’s T cells are removed, and zinc finger scissors are used to disable the CCR5 gene. The treated cells are allowed to multiply, then reinjected into the patient. In experiments with mice, the treated cells turned out to have a strong natural advantage over the untreated ones, since those are under constant attack by the AIDS virus.

Whether or not zinc fingers will make gene therapy practical remains to be seen. “It’s a little too early to know since clinical trials are in their early stages,” said Dr. Katherine A. High, a hemophilia expert at the University of Pennsylvania.

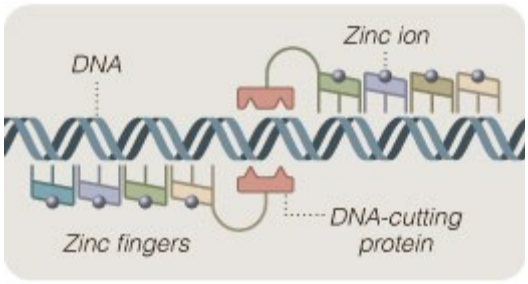
Dr. Matthew H. Porteus, a pediatric geneticist at the University of Texas, said, “I think it has the potential to solve a lot of the problems that have plagued the gene therapy field.” But Dr. Porteus noted that even the most carefully designed zinc fingers seemed to do some snipping away from their target site, a potentially serious safety problem.

Zinc fingers could be the gift that stem cell researchers have been waiting for. Stem cells taken from a patient may need to be genetically corrected before use, but until now there had been no way of doing so.

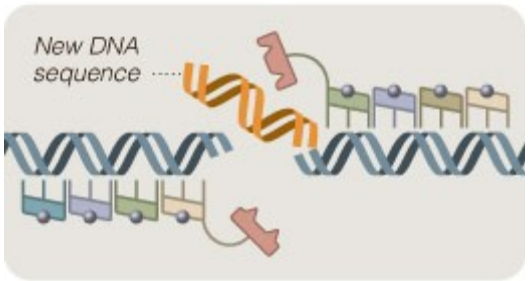
Dr. Rudolf Jaenisch, a stem cell expert at the Whitehead Institute in Cambridge, Mass., reported in August that he had successfully singled out three genes in induced embryonic stem cells with the help of zinc finger scissors designed by Sangamo. “This is a really important tool for human embryonic stem cells,” Dr. Jaenisch said. The technology has not yet reached perfection. Some of the zinc fingers Sangamo provided “worked beautifully,” he said, but some did not.

Cut and Paste

Biologists are developing a powerful technique for making precise modifications to DNA.



ZINC FINGERS are naturally occuring proteins, each built around a single ion of zinc. Each zinc finger recognizes a set of three letters of DNA, and several can be chained together to match a particular site on the genome.



ALTERING DNA Zinc fingers can be linked to other proteins that do useful work, like activating a gene or cutting a specific DNA sequence. The cell quickly repairs the break, but if DNA for a new gene is inserted into the cell it may be incorporated into the repair.

Source: Nature

THE NEW YORK TIMES

Zinc fingers may also make technically possible a morally fraught procedure that has been merely a theoretical possibility - the alteration of the human germ line, meaning the egg or sperm cells. Genetic changes made in current gene therapy are to body cells, and they would die with the individual. But changes made to the germ line would be inherited. Many ethicists and others say this is a bridge that should not be crossed, since altering the germ line, even if justifiable for medical reasons, would lower the barrier to other kinds of change.

Several scientists were reluctant to discuss the issue, or dismissed it by saying that even zinc fingers did not meet the error-free standards that would be required for germ-line engineering. But zinc finger scissors are so efficient that only 5 to 10 embryos need be treated to get one with the desired result. This could make it practical to alter the germ line.

Since the germ lines of rats and zebra fish have already been altered with zinc finger scissors, “in principle there is no reason why a similar strategy could not be used to modify the human germ line,” Dr. Porteus said. The kind of disease that might be better treated in the germ line, if ethically acceptable, is cystic fibrosis, which affects many different tissues.

The disease could be corrected in unfertilized eggs, using the zinc finger technique, Dr. Porteus said. But he added, “I don’t think our society is ready for someone to propose this.”

Guideline: Widely used device for pain therapy not recommended for chronic low back pain

ST. PAUL, Minn. – A new guideline issued by the American Academy of Neurology finds that transcutaneous electric nerve stimulation (TENS), a widely used pain therapy involving a portable device, is not recommended to treat chronic low-back pain□pain that has persisted for three months or longer□because research shows it is not effective. The guideline is published in the December 30, 2009, online issue of Neurology®, the medical journal of the American Academy of Neurology.

The guideline determined that TENS can be effective in treating diabetic nerve pain, also called diabetic neuropathy, but more and better research is needed to compare TENS to other treatments for this type of pain.

Research on TENS for chronic low-back pain has produced conflicting results. For the guideline, the authors reviewed all of the evidence for low-back pain lasting three months or longer. Acute low-back pain was not studied. The studies to date show that TENS does not help with chronic low-back pain.

All but one of the studies excluded people with known causes of low-back pain, such as a pinched nerve, severe scoliosis (curving of the spine), severe spondylolisthesis (displacement of a backbone or vertebra) or obesity. In the one study that looked at low-back pain associated with known conditions, TENS was not shown to be effective. The only specific neurologic cause of chronic low-back pain where TENS was studied was multiple sclerosis, and TENS was not shown to help.

"The strongest evidence showed that there is no benefit for people using TENS for chronic low-back pain," said guideline author Richard M. Dubinsky, MD, MPH, of Kansas University Medical Center in Kansas City and a Fellow of the American Academy of Neurology. "Doctors should use clinical judgment regarding TENS use for chronic low-back pain. People who are currently using TENS for their low-back pain should discuss these findings with their doctors."

Dubinsky stated further that good evidence showed that TENS can be effective in treating diabetic nerve pain.

With TENS, a portable, pocket-sized unit applies a mild electrical current to the nerves through electrodes. TENS has been used for pain relief in various disorders for years. Researchers do not know how TENS may provide relief for pain. One theory is that nerves can only carry one signal at a time. The TENS stimulation may confuse the brain and block the real pain signal from getting through.

Back pain—both acute and chronic—is the second most common neurologic ailment in the United States, according to the National Institute of Neurological Disorders and Stroke, and is the most common cause of job-related disability. About 60 percent of people with diabetes will develop neuropathy.

Body's own veins are superior material for aortic grafts

DALLAS – A vascular surgical technique pioneered at UT Southwestern Medical Center and designed to replace infected aortic grafts with the body’s own veins has proved more durable and less prone to new infection than similar procedures using synthetic and cadaver grafts.

Aortic graft infections are one of the most serious complications in patients undergoing aortic grafting procedures for peripheral arterial disease (PAD) and aortic aneurysms. PAD reduces blood circulation in the pelvis and lower extremities, and aortic aneurysms result in a weakening of the aortic wall that can cause lethal rupture of the aorta, the largest artery in the body. Patients with PAD and aortic aneurysms often require surgery, and aortic grafting procedures using synthetic grafts are typically the first line of treatment.

For patients with PAD, the procedure restores blood circulation to the legs, and for patients with aneurysm, it replaces the weakened aortic wall and prevents rupture. Synthetic grafts made of Dacron, a polyester material, are placed in the aorta and femoral arteries in the abdomen and groin, which feed blood to the legs. But in about 1 percent to 2 percent of these patients, the grafts become infected – a complication that causes amputation and death if left untreated.

Dr. G. Patrick Clagett, chief of vascular surgery at UT Southwestern, pioneered a technique called the neo-aortoiliac system (NAIS) that repairs these aortic-graft infections. The procedure involves removing the infected graft and replacing it with sections of femoral-popliteal veins harvested from the patient's thighs, rather than another synthetic graft or vessels harvested from human cadavers.

In a recent study published in the Journal of Vascular Surgery, Dr. Clagett and his team reported on 187 patients at UT Southwestern treated for aortic graft infections who underwent the NAIS procedure from 1990 to 2006. It is the largest group of such patients ever studied, and the researchers found that the incidence of re-infection was lower and the procedure resulted in superior durability with much lower long-term amputation rates when compared with other operations to treat this condition.

"This operation has gained favor worldwide in the treatment of this devastating condition," said Dr. Clagett. "Since performing the first operation here in the 1990s, we have accumulated data over the years and have found this procedure to be far superior in overall patient outcomes."

Simply replacing the old Dacron graft with a new synthetic graft can result in devastating infection of the new one, said Dr. Clagett, who is immediate past president of the Society for Vascular Surgery. His team and others also have found that the new synthetic or cadaver grafts tend to develop clots and new blockages.

"When we use the patient's own tissue to construct a new graft, it provides an advantage because they are less likely to form clots within the graft and less likely to develop new blockages," Dr. Clagett said. "Patients also need fewer subsequent procedures, a common problem with the other treatments for this complication."

He added that patients who have the NAIS procedure don't need to be on lifelong antibiotic therapy. Because the aortic reconstruction is fashioned with the patient's own tissue, there is no foreign material that is prone to re-infection.

Other UT Southwestern researchers who contributed to the study included Dr. J. Gregory Modrall, associate professor of surgery; Dr. R. James Valentine, professor of surgery; and Jennie Hocking, assistant professor of physician assistant studies. Dr. Ahsan Ali, a former vascular surgery fellow at UT Southwestern now at the University of Arkansas, was the lead author of the study. Visit http://www.utsouthwestern.org/heartlungvascular to learn more about UT Southwestern's clinical services for heart, lung and vascular diseases and conditions.

Short-term school closures may worsen flu pandemics, Pitt study finds

PITTSBURGH, – Closing schools for less than two weeks during a flu pandemic may increase infection rates and prolong an epidemic, say University of Pittsburgh researchers in a study published ahead-of-print and online in the Journal of Public Health Management and Practice. The findings, developed from a series of computer simulations based on U.S. census data, indicate that schools may need to be closed for at least eight weeks in order to significantly decrease the spread of infection.

The value of school closures has been debated as a possible strategy to stem or slow the current H1N1 influenza pandemic. Indeed, hundreds of schools across the country have been closed at different periods during 2009 for fear the virus would spread more quickly if they stayed open.

"Although closing schools may seem like a reasonable way to slow the spread of flu, we found that it was not effective unless sustained for at least eight weeks after implementation," said study lead author, Bruce Lee, M.D., M.B.A., assistant professor or medicine, epidemiology and biomedical informatics, University of Pittsburgh. Closing schools quickly at the start of an outbreak was much less important than keeping them closed continually throughout the epidemic, he added.

According to study authors, short-duration school closures can increase transmission rates by returning susceptible students back to school in the middle of an epidemic when they are most vulnerable to infection.

The study also found that identifying sick students individually and keeping them from attending school had minimal impact on an epidemic. In addition, there were no significant differences between individual school closures and system-wide closures in mitigating an epidemic.

The study was based on an agent-based computer simulation model of Allegheny County, Pa., that represented the county's population, school systems, workplaces, households and communities. Simulations were based on the movement of residents each weekday from their households to designated workplaces or schools, and included 1.2 million people—200,000 of whom were school-aged children. The study also included more than 500,000 households and nearly 300 schools.

Co-authors of the study include Shawn T. Brown, Ph.D., Pittsburgh Supercomputing Center; Philip Cooley, M.S., William Wheaton, M.A., and Diane Wagener, Ph.D., RTI International; Ronald Voorhees, M.D., M.P.H., Allegheny County Health Department; and Maggie Potter, J.D., Samuel Stebbins, M.D., M. P.H., John Grefenstette, Ph.D., Shanta Zimmer, M.D., Richard Zimmerman, M.D., M.P.H., Tina-Marie Assi, M.P.H., Rachel Bailey, M.P.H., and Donald S. Burke, M.D., University of Pittsburgh.

The study is part of the University of Pittsburgh Models of Infectious Disease Agents Study (MIDAS) funded by the National Institutes of Health.

Russia 'plans to stop asteroid'

The head of Russia's federal space agency has said it will work to divert an asteroid which will make several passes near the Earth from 2029.

Anatoly Perminov told the Voice of Russia radio service that the agency's science council would hold a closed meeting to discuss the issue. Any eventual plan is likely to be an international collaboration, he said.

The US space agency said in October that there is a one-in-250,000 chance of Apophis hitting Earth in 2036.

That announcement was a significant reduction in the probability of an impact, based on previous calculations that put the chances at about one-in-45,000. The asteroid is estimated to pass within about 30,000 km of the Earth in 2029.

Mr Perminov, who is the chief of Roscosmos, gave little detail of any plans that the agency has, but was quoted by Interfax news agency as saying that the solution would not entail the use of nuclear weapons.

Other schemes that have been put forth in the past for diverting asteroids from collision courses include spacecraft that nudge the space rocks out of their trajectory through force, or diverting them with "solar sails" that use the wind of particles ejected from the Sun.

"People's lives are at stake," Mr Perminov reportedly told the radio service Golos Rossii (Voice of Russia).

"We should pay several hundred million dollars and build a system that would allow us to prevent a collision, rather than sit and wait for it to happen and kill hundreds of thousands of people."

Devil cancer source 'identified'

By Mark Kinver Science and environment reporter, BBC News

Researchers believe they have identified the source of fatal tumours that threaten to wipe out the wild population of Tasmanian devils.

Since the mid-1990s, Tasmanian devil numbers have crashed

Writing in Science, an international team of scientists suggest cells that protect nerves are the likely origin of devil facial tumour disease (DFTD).

The disease is a transmissible cancer that is spread by physical contact, and quickly kills the animals.

DFTD has caused the devil population to collapse by 60% in the past decade.

"To look more closely at the tumours' origin, we sequenced the genes that are expressed in this devil cancer and compared them with other genes that are expressed in other devil tissues," explained lead author Elizabeth Murchison, from the Australian National University in Canberra.

She told the Science podcast the team's findings delivered surprising results.

"We found that the tumours expressed genes that were normally only expressed by Schwann cells, which are cells that are found in the peripheral nervous system that protect nerves."

'Genetically distinct'

The researchers sampled 25 different tumours from all over Tasmania, the only place on the planet where the world's largest carnivorous marsupials are found.

They found that the growths were genetically distinct from their hosts, but were identical to one another.

Dr Murchison, who is also a researcher at Cold Spring Harbor Laboratory, US, said the teams findings had a number of positive outcomes: "Most importantly, this has led to the development of a diagnostic test for the disease.

"Devils are susceptible to a number of different types of cancer. Just like humans, they can get breast cancer, leukaemia, etc - especially in their old age.

"Sometimes it can be difficult to tell the difference between these types of cancer and the transmissible disease.

"Now that we know that these very specific Schwann genes are expressed in the cancer, we can use these genes as diagnostic markers."

DFTD was first described in the mid-1990s, when devils with large facial tumours were photographed in north-eastern Tasmania.

By the end of 2008, the disease - which kills infected animals within nine weeks - had been confirmed at 64 locations, covering more than 60% of the Australian island state's mainland.

Experts warn that without intervention, the disease could wipe out the wild population of the world's largest carnivorous marsupial within decades.

Dr Murchison hoped identifying the catalogue of genes associated with DFTD would lead to the development of vaccines, or possibly therapies.

"As yet, unfortunately, there is nothing we can do to help the devils that have the disease," she said.

"This devil facial cancer is very unusual as it is an infection cancer; it is a little bit like an organ transplant," she said.

"In an organ transplant, you have an organ that is transplanted into an unrelated individual. In the case of the devil cancer, you have a cancer that is transplanted into another unrelated devil through biting.

"One of the big questions about this cancer is why it is not being rejected or being recognised as a foreign graft.

"If we could understand that... we could perhaps use this data to develop a vaccine that could help the devils' immune system reject the cancer before it takes hold."

DEVILS IN DETAIL

Scientific name: Sarcophilus harrisii
Devils were given their common name
by early settlers, who were haunted by "demonic growls"
Largest living carnivorous marsupial
Now only found in Tasmania
Can live up to five years in wild
Weight: male 10-12kg; female 6-8kg
They favour habitats where they can shelter by day and scavenge by night

Using modern sequencing techniques to study ancient modern humans

DNA that is left in the remains of long-dead plants, animals, or humans allows a direct look into the history of evolution. So far, studies of this kind on ancestral members of our own species have been hampered by scientists' inability to distinguish the ancient DNA from modern-day human DNA contamination. Now, research by Svante Pääbo from The Max-Planck Institute for Evolutionary Anthropology in Leipzig, published online on December 31st in Current Biology — a Cell Press publication — overcomes this hurdle and shows how it is possible to directly analyze DNA from a member of our own species who lived around 30,000 years ago.

DNA — the hereditary material contained in the nuclei and mitochondria of all body cells — is a hardy molecule and can persist, conditions permitting, for several tens of thousands of years. Such ancient DNA provides scientists with unique possibilities to directly glimpse into the genetic make-up of organisms that have long since vanished from the Earth. Using ancient DNA extracted from bones, the biology of extinct animals, such as mammoths, as well as of ancient humans, such as the Neanderthals, has been successfully studied in recent years.

The ancient DNA approach could not be easily applied to ancient members of our own species. This is because the ancient DNA fragments are multiplied with special molecular probes that target certain DNA sequences. These probes, however, cannot distinguish whether the DNA they recognize comes from the ancient human sample or was introduced much later, for instance by the archaeologists who handled the bones. Thus, conclusions about the genetic make-up of ancient humans of our own species were fraught with uncertainty.

Using the remains of humans that lived in Russia about 30,000 years ago, Pääbo and his colleagues now make use of the latest DNA sequencing (i.e., reading the sequence of bases that make up the DNA strands) techniques to overcome this problem. These techniques, known as "second-generation sequencing," enable the researchers to "read" directly from ancient DNA molecules, without having to use probes to multiply the DNA. Moreover, they can read from very short sequence fragments that are typical of DNA ancient remains because over time the DNA strands tend to break up. By contrast, DNA that is younger and only recently came in contact with the sample would consist of much longer fragments. This and other features, such as the chemical damage incurred by ancient as opposed to modern DNA, effectively enabled the researchers to distinguish between genuine ancient DNA molecules and modern contamination. "We can now do what I thought was impossible just a year ago – determine reliable DNA sequences from modern humans - but this is still possible only from very well-preserved specimens," says Pääbo.

The application of this technology to the remains of members of our own species that lived tens of thousands of years ago now opens a possibility to address questions about the evolution and prehistory of our own species that were not possible with previous methods, for instance whether the humans living in Europe 30,000 years ago are the direct ancestors of present-day Europeans or whether they were later replaced by immigrants that brought new technology such as farming with them.

The authors include Johannes Krause, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany; Adrian Briggs, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany; Matrin Kircher, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany; Tomislav Maricic, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany; Nicolas Zwyns, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany; Anatoli Derevianko, Russian Academy of Sciences, Novosibirsk, Russia; Svante Paabo, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany.

Scripps Florida scientists show 'lifeless' prions capable of evolutionary change and adaptation

Research may point to more effective therapeutic targets for deadly prion diseases

Jupiter, Fl – Scientists from The Scripps Research Institute have determined for the first time that prions, bits of infectious protein devoid of DNA or RNA that can cause fatal neurodegenerative disease, are capable of Darwinian evolution.

The study from Scripps Florida in Jupiter shows that prions can develop large numbers of mutations at the protein level and, through natural selection, these mutations can eventually bring about such evolutionary adaptations as drug resistance, a phenomenon previously known to occur only in bacteria and viruses. These breakthrough findings also suggest that the normal prion protein – which occurs naturally in human cells – may prove to be a more effective therapeutic target than its abnormal toxic relation.

The study was published in the December 31, 2009 issue of the journal Science Express, an advance, online edition of the prestigious journal Science.

"On the face of it, you have exactly the same process of mutation and adaptive change in prions as you see in viruses," said Charles Weissmann, M.D., Ph.D., the head of Scripps Florida's Department of Infectology, who led the study. "This means that this pattern of Darwinian evolution appears to be universally active. In viruses, mutation is linked to changes in nucleic acid sequence that leads to resistance. Now, this adaptability has moved one level down – to prions and protein folding – and it's clear that you do not need nucleic acid for the process of evolution."

Infectious prions (short for proteinaceous infectious particles) are associated with some 20 different diseases in humans and animals, including mad cow disease and a rare human form, Creutzfeldt-Jakob disease. All these diseases are untreatable and eventually fatal. Prions, which are composed solely of protein, are classified by distinct strains, originally characterized by their incubation time and the disease they cause. Prions have the ability to reproduce, despite the fact that they contain no nucleic acid genome.

Mammalian cells normally produce cellular prion protein or PrPC. During infection, abnormal or misfolded protein – known as PrPSc – converts the normal host prion protein into its toxic form by changing its conformation or shape. The end-stage consists of large assemblies (polymers) of these misfolded proteins, which cause massive tissue and cell damage.

"It was generally thought that once cellular prion protein was converted into the abnormal form, there was no further change," Weissmann said. "But there have been hints that something was happening. When you transmit prions from sheep to mice, they become more virulent over time. Now we know that the abnormal prions replicate, and create variants, perhaps at a low level initially. But once they are transferred to a new host, natural selection will eventually choose the more virulent and aggressive variants."

Drug Resistance

In the first part of the study, Weissmann and his colleagues transferred prion populations from infected brain cells to culture cells. When transplanted, cell-adapted prions developed and out-competed their brain-adapted counterparts, confirming prions' ability to adapt to new surroundings, a hallmark of Darwinian evolution. When returned to brain, brain-adapted prions again took over the population.

To confirm the findings and to explore the issue of evolution of drug resistance, Weissmann and his colleagues used the drug swainsonine or swa, which is found in plants and fungi, and has been shown to inhibit certain prion strains. In cultures where the drug was present, the team found that a drug-resistant sub-strain of prion evolved to become predominant. When the drug was withdrawn, the sub-strain that was susceptible to swainsonine again grew to become the major component of the population.

Weissmann notes that the findings have implications for the development of therapeutic targets for prion disease. Instead of developing drugs to target abnormal proteins, it could be more efficient to try to limit the supply of normally produced prions – in essence, reducing the amount of fuel being fed into the fire. Weissmann and his colleagues have shown some 15 years ago that genetically engineered mice devoid of the normal prion protein develop and function quite normally (and are resistant to prion disease!).

"It will likely be very difficult to inhibit the production of a specific natural protein pharmacologically," Weissmann said, "You may end up interfering with some other critical physiological process, but nonetheless,

finding a way to inhibit the production of normal prion protein is a project currently being pursued in collaboration with Scripps Florida Professor Corinne Lasmezas in our department."

Quasi-Species

Another implication of the findings, according to the study, is that drug-resistant variants either exist in the prion population at a low level prior to exposure or are generated during exposure to the drug. Indeed, the researchers found some prions secreted by infected cells were resistant to the drug before exposure, but only at levels less than one percent.

The scientists show that prion variants constantly arise in a particular population. These variants, or "mutants", are believed to differ in the way the prion protein is folded. As a consequence, prion populations are, in fact, comprised of multiple sub-strains.

This, Weissmann noted, is reminiscent of something he helped define some 30 years ago – the evolutionary concept of quasi-species. The idea was first conceived by Manfred Eigen, a German biophysicist who won the Nobel Prize in Chemistry in 1967. Basically stated, a quasi-species is a complex, self-perpetuating population of diverse and related entities that act as a whole. It was Weissmann, however, who provided the first confirmation of the theory through the study of a particular bacteriophage – a virus that infects bacteria – while he was director of the Institut für Molekularbiologie in Zürich, Switzerland.

"The proof of the quasi-species concept is a discovery we made over 30 years ago," he said. "We found that an RNA virus population, which was thought to have only one sequence, was constantly creating mutations and eliminating the unfavorable ones. In these quasi-populations, much like we have now found in prions, you begin with a single particle, but it becomes very heterogeneous as it grows into a larger population."

There are some unknown dynamics at work in the prion population that leads to this increased heterogeneity, Weissmann added, that still need to be explored.

"It's amusing that something we did 30 years has come back to us," he said. "But we know that mutation and natural selection occur in living organisms and now we know that they also occur in a non-living organism. I suppose anything that can't do that wouldn't stand much of a chance of survival."

The joint first authors of the Science study, "Darwinian Evolution of Prions in Cell Culture," are Jiali Li and Shawn Browning of The Scripps Research Institute. Other authors include Sukhvir P. Mahal and Anja M. Oelschlegel also of The Scripps Research Institute. Weissmann notes that after the manuscript was accepted by Science, an article by Ghaemmanghami et al. appeared in PLoS Pathogens that described emergence of prions resistant to a completely different drug, quinacrine, providing additional support to the Scripps Research team's conclusions.

The Scripps Research study was supported by a grant from the National Institutes of Health and by a generous donation to the Weissmann laboratory from the Alafi Family Foundation.

Earlier bedtimes may help protect adolescents against depression and suicidal thoughts

Westchester, Ill. — A study in the Jan. 1 issue of the journal Sleep found that adolescents with bedtimes that were set earlier by parents were significantly less likely to suffer from depression and to think about committing suicide, suggesting that earlier bedtimes could have a protective effect by lengthening sleep duration and increasing the likelihood of getting enough sleep.

Results show that adolescents with parental set bedtimes of midnight or later were 24 percent more likely to suffer from depression (odds ratio = 1.24) and 20 percent more likely to have suicidal ideation (OR=1.20) than adolescents with parental set bedtimes of 10 p.m. or earlier. This association was appreciably attenuated by self-reported sleep duration and the perception of getting enough sleep. Adolescents who reported that they usually sleep for five or fewer hours per night were 71 percent more likely to suffer from depression (OR=1.71) and 48 percent more likely to think about committing suicide (OR=1.48) than those who reported getting eight hours of nightly sleep. Participants who reported that they "usually get enough sleep" were significantly less likely to suffer from depression (OR=0.35) and suicidal ideation (OR=0.71).

Lead author James E. Gangwisch, PhD, assistant professor at Columbia University Medical Center in New York, N.Y., said that the results strengthen the argument that short sleep duration could play a role in the etiology of depression.

"Our results are consistent with the theory that inadequate sleep is a risk factor for depression, working with other risk and protective factors through multiple possible causal pathways to the development of this mood disorder," said Gangwisch. "Adequate quality sleep could therefore be a preventative measure against depression and a treatment for depression."

Data were collected from 15,659 adolescents and their parents who had participated in the National Longitudinal Study of Adolescent Health (Add Health), a school-based, nationally representative, probability-based sample of U.S. students in grades seven to 12 in 1994 to 1996. Seven percent of participants (1,050) were found to have depression using the Centers for Epidemiologic Study-Depression Scale, and 13 percent (2,038)

reported that they seriously thought about committing suicide during the past 12 months. Depression and suicidal ideation were associated with later parental set bedtime, shorter sleep duration, self-perception of not getting enough sleep, female sex, older age and lower self-perception of how much parents care.

Fifty-four percent of parents reported that their adolescent had to go to bed by 10 p.m. or earlier on weeknights, 21 percent reported setting a bedtime of 11 p.m., and 25 percent reported setting a bedtime of midnight or later. Caucasians were more likely than adolescents of other racial/ethnic groups to have a parental set bedtime of 11 p.m. Nearly 70 percent of adolescents reported going to bed at a time that complied with the weeknight bedtime that was set by their parents. Adolescents reported going to bed only about five minutes later on average than their parental set bedtime.

The average adolescent-reported sleep duration was seven hours and 53 minutes, which contrasted sharply with the nine or more hours of nightly sleep that the AASM recommends for adolescents. Participants with a parental set bedtime of 10 p.m. or earlier reported that they usually slept for an average of eight hours and 10 minutes, which was 33 minutes more than adolescents with a bedtime of 11 p.m. (seven hours, 37 minutes) and 40 minutes more than those with a bedtime of midnight or later (seven hours, 30 minutes). With the exception of sleep durations of 10 hours or more per night, higher average self-reported sleep durations were associated with progressively earlier average bedtimes.

The authors reported that there are a number of potential mechanisms by which chronic partial sleep deprivation could contribute to depression and suicidal ideation. A lack of sleep may affect the modulation of emotional brain responses to aversive stimuli; produce moodiness that hinders the ability to cope with daily stresses and impairs relationships with peers and adults; and affect judgment, concentration and impulse control.

They also suggested that behavioral interventions that involve educating adolescents and their parents about healthier sleep hygiene practices and helping them modify maladaptive sleep habits could sever as primary preventative measures against depression and suicidal ideation.

An abstract of this study (#1064) was presented in Seattle, Wash., on June 9, 2009, at SLEEP 2009, the 23rd Annual Meeting of the Associated Professional Sleep Societies LLC (APSS).

For a copy of the study, "Earlier Parental Set Bedtimes as a Protective Factor Against Depression and Suicidal Ideation," or to arrange an interview with an AASM spokesperson, please contact Kelly Wagner, AASM public relations coordinator, at (708) 492-0930, ext. 9331, or kwagner@aasmnet.org.

Italian scientists' 'wood to bone' medical breakthrough

Scientists in Italy have discovered a way of making artificial replacement bones out of wood.

Early trials on sheep have showed encouraging results.

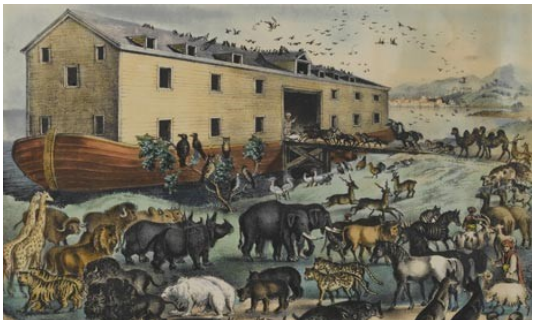
The team behind the programme hopes the new bones will soon be available for patients whose own bones have been damaged by accident or disease.

Duncan Kennedy reports.

Relic reveals Noah's ark was circular

Newly translated tablet gives building instructions Amateur historian's find was almost overlooked

Maev Kennedy



That they processed aboard the enormous floating wildlife collection two-by-two is well known. Less familiar, however, is the possibility that the animals Noah shepherded on to his ark then went round and round inside.

According to newly translated instructions inscribed in ancient Babylonian on a clay tablet telling the story of the ark, the vessel that saved one virtuous man, his family and the animals from god's watery wrath was not the pointy-prowed craft of popular imagination but rather a giant circular reed raft.

A 19th-century illustration by Currier & Ives shows the traditional vision of Noah's ark. Photograph: Brooklyn Museum/Corbis

The now battered tablet, aged about 3,700 years, was found somewhere in the Middle East by Leonard Simmons, a largely self-educated Londoner who indulged his passion for history while serving in the RAF from 1945 to 1948.

The relic was passed to his son Douglas, who took it to one of the few people in the world who could read it as easily as the back of a cornflakes box; he gave it to Irving Finkel, a British Museum expert, who translated its 60 lines of neat cuneiform script.

There are dozens of ancient tablets that have been found which describe the flood story but Finkel says this one is the first to describe the vessel's shape.

"In all the images ever made people assumed the ark was, in effect, an ocean-going boat, with a pointed stem and stern for riding the waves – so that is how they portrayed it," said Finkel. "But the ark didn't have to go anywhere, it just had to float, and the instructions are for a type of craft which they knew very well. It's still sometimes used in Iran and Iraq today, a type of round coracle which they would have known exactly how to use to transport animals across a river or floods."

Finkel's research throws light on the familiar Mesopotamian story, which became the account in Genesis, in the Old Testament, of Noah and the ark that saved his menagerie from the waters which drowned every other living thing on earth.

In his translation, the god who has decided to spare one just man speaks to Atram-Hasis, a Sumerian king who lived before the flood and who is the Noah figure in earlier versions of the ark story. "Wall, wall! Reed wall, reed wall! Atram-Hasis, pay heed to my advice, that you may live forever! Destroy your house, build a boat; despise possessions And save life! Draw out the boat that you will built with a circular design; Let its length and breadth be the same."

The tablet goes on to command the use of plaited palm fibre, waterproofed with bitumen, before the construction of cabins for the people and wild animals.

It ends with the dramatic command of Atram-Hasis to the unfortunate boat builder whom he leaves behind to meet his fate, about sealing up the door once everyone else is safely inside: "When I shall have gone into the boat, Caulk the frame of the door!"

Fortunes were spent in the 19th century by biblical archaeology enthusiasts in hunts for evidence of Noah's flood. The Mesopotamian flood myth was incorporated into the great poetic epic Gilgamesh, and Finkel, curator of the recent British Museum exhibition on ancient Babylon, believes that it was during the Babylonian captivity that the exiled Jews learned the story, brought it home with them, and incorporated it into the Old Testament.

Despite its unique status, Simmons' tablet – which has been dated to around 1,700 BC and is only a few centuries younger than the oldest known account – was very nearly overlooked.

"When my dad eventually came home, he shipped a whole tea chest of this kind of stuff home – seals, tablets, bits of pottery," said Douglas. "He would have picked them up in bazaars, or when people knew he was interested in this sort of thing, they would have brought them to him and earned a few bob."

Simmons senior became a scenery worker at the BBC, but kept up his love of history, and was very disappointed when academics dismissed treasures of his as commonplace and worthless. His son took the tablet to a British Museum open day, where Finkel "took one look at it and nearly fell off his chair" with excitement.

"It is the most extraordinary thing," Simmons said of the tablet. "You hold it in your hand, and you instantly get a feeling that you are directly connected to a very ancient past – and it gives you a shiver down your spine."

Raiders of the lost ark

The human fascination with the flood and the whereabouts of the ark shows few signs of subsiding.

The story has travelled down the centuries from the ancient Babylonians and continues to fascinate in the 21st century. Countless expeditions have travelled to Mount Ararat in Turkey, where Noah's ark is said to have come to rest, but scientific proof of its existence has yet to be found.

Recent efforts to find it have been led by creationists, who are keen to exhibit it as evidence of the literal truth of the Bible.

"If the flood of Noah indeed wiped out the entire human race and its civilization, as the Bible teaches, then the ark constitutes the one remaining major link to the pre-flood world," says John D Morris of the Institute for Creation Research. "No significant artefact could ever be of greater antiquity or importance."

In the Victorian era some became obsessed with the ark story. George Smith – the lowly British museum assistant who, in 1872, deciphered the Flood Tablet which is inscribed with the Assyrian version of the Noah's ark tale – could apparently not contain his excitement at his discovery.

According to the museum's archives: "He jumped up and rushed about the room in a great state of excitement and to the astonishment of those present began to undress himself."