http://www.vox.com/2016/3/7/11172550/drug-waste-pharma

Drug companies will earn $1.8 billion this year from cancer drugs that patients never take

Pharmaceutical companies will earn nearly $2 billion this year selling drugs that patients never take.

Updated by Sarah Kliff on March 7, 2016, 10:30 a.m. ET @sarahkliff sarah@vox.com

These are expensive cancer drugs that can cost upward of $13,000 per month. A new study suggests that the way drug companies package these intravenous drugs — in single-use vials that contain way more medication than an average patient needs — ends up wasting a lot of money.

"What manufacturers are doing is they're not right-sizing the vials to the dosages patients actually need," says study author Peter Bach, who is a physician at Memorial Sloan Kettering Cancer Center.

Cancer drugs are different from most other medications because they are delivered intravenously. Unlike pills that get dispensed out of a bottle, these are liquids or powders that will lose their potency if they sit on a shelf. Once opened, safety standards mandate that they must be used within six hours. After that, any leftovers have to go in the trash.

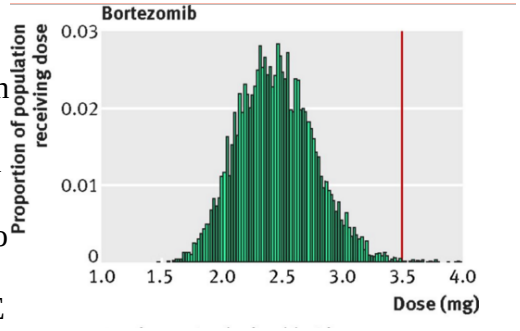
Bach and his co-authors argue in their new paper, published Monday in the *British Medical Journal*, that some drug companies sell too-large dosages that inevitably lead to waste. This creates income from medication that hospitals and patients will never actually use. That's bad for the health care system but good for the drugmakers who net more revenue.

One of the most striking examples of this oversizing is a drug called Velcade that treats multiple myeloma, a bone marrow cancer. Takeda Pharmaceutical, which makes Velcade, only sells the drug in 3.5 milligram vials in the United States (the company does manufacture 1 milligram vials abroad).

The amount of medication that patients need turns out to be significantly smaller than the single dosage size. Using data on the weight distributions of cancer patients, Bach and his colleagues estimate that the average Velcade dose is 2.2 milligrams.

The green bars below represent the estimated dosage of Velcade (also know by the name of its active compound, bortezomib) that American cancer patients need. The red line represents the current dosage that Velcade's manufacturer, Takeda, sells.

Each vial of Velcade contains 1.3 milligram more medication than the average cancer patient needs. This disparity between vial size and patient dosage means hospitals will waste about 27 to 30 percent of the Velcade they purchase. They'll spend $308 million on leftover Velcade that they never use.



I reached out to Takeda, the pharmaceutical company that manufactures Velcade, and spokesperson Amy Atwood told me the vial size was developed in coordination with the Food and Drug Administration.

"Takeda worked closely with the FDA to establish the VELCADE vial size of 3.5 mg to ensure that one vial of VELCADE would provide an adequate amount of the drug for a patient of almost any size," she wrote in an email.

But there is a solution that doesn't create nearly as much waste, and allows for accurate dosing.

A better way to package drugs — and save money

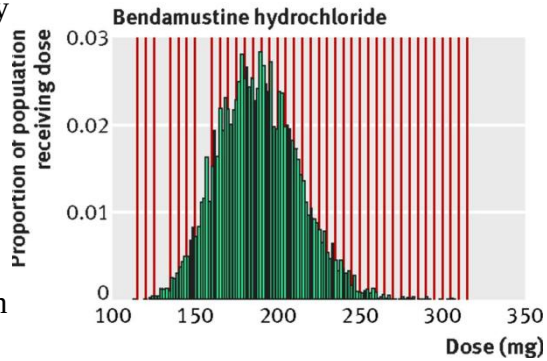
Bach argues that this much leftover medication is pricey and unnecessary. As a counterexample to Velcade, he points to Treanda, a leukemia drug manufactured by Teva Pharmaceuticals. Teva sells its drug in 25, 45, 100, and 180 milligram vials. This means that providers can essentially mix and match the different vials to more closely match the dosage their patients need.

You can see in this graph below how the different dosage combinations of Treanda (also known by the name of its active ingredient, bendamustine hydrochloride) overlay with the population of patients. The red bars show all the possible combinations of Treanda with those different-size vials.

This graph looks really different from the Velcade one; it shows that there are lots of dosage combinations. And that means less drug waste: Bach estimates about only 1 percent of all Treanda gets thrown out.

"When there are drugs where 30 percent are wasted and drugs with only 1 percent waste, its inconceivable that drug companies don't know about this," Bach says. "These are extremely sophisticated businesses. They know everything about the patients getting their drugs, and certainly have the capability to figure out what we've described in this paper."

There are, however, risks to combining dosages: Using more than one vial of medication does leave more space for math errors on the part of the provider. This is why the FDA generally encourages single vials that have enough medication to treat a patient.



If the FDA wanted to go further, it could more strictly regulate vial size — looking for dosages that are enough to treat the average patient but not so large that they lead to significant waste.

And this is something that PhRMA, the trade group for drug companies, did express some openness toward. "Manufacturers are committed to working with FDA and Congress ... to modify their products as we learn about the safety, efficacy and manufacturing of new medicines from the real world clinical setting," PhRMA spokesperson Allyson Funk said in a statement.

http://www.eurekalert.org/pub_releases/2016-03/ru-scc030716.php

Study: Cancer cells eat their neighbors' 'words'

Cancer cells capable of using information packets as energy source

HOUSTON - Cancer cells are well-known as voracious energy consumers, but even veteran cancer-metabolism researcher Deepak Nagrath was surprised by their latest exploit: Experiments in his lab at Rice University show that some cancer cells get 30-60 percent of their fuel from eating their neighbors' "words."

"Our original hypothesis was that cancer cells were modifying their metabolism based on communications they were receiving from cells in the microenvironment near the tumor," said Nagrath, assistant professor of chemical and biomolecular engineering at Rice and co-author of a new study describing the research in the open-access journal eLife. "None of us expected to find that they were converting the signals directly into energy."

The results were part of a four-year study by Nagrath, his students and collaborators at the University of Texas MD Anderson Cancer Center and other institutions about the role of exosomes in cancer metabolism. Exosomes are tiny packets of proteins, microRNA and nucleic acids that cells emit into their environment to both communicate with neighboring cells and influence their behavior. Nagrath, who directs Rice's Laboratory for Systems Biology of Human Diseases, found that some cancer cells are capable of using these information packets as a source of energy to fuel tumor growth.

Nagrath's team specializes in analyzing the unique metabolic profiles of various types of cancer.

His work is the latest in a series of discoveries about cancer metabolism that date to German chemist Otto Warburg's 1924 discovery that cancer cells produce far more energy from the metabolic process known as glycolysis than do normal cells. The Nobel Prize-winning discovery of the "Warburg effect" led scientists to believe, for decades, that all cancers were dependent on glycolysis. Nagrath's lab and others have shown in recent years that the truth is far more complex: Each type of cancer has a unique metabolic profile. Nagrath's work aims at better understanding those profiles and their role in cancer metastasis and drug resistance, and he ultimately hopes to use the knowledge to develop more effective cancer treatments.

In a May 2014 study, Nagrath and colleagues found that highly aggressive ovarian cancer cells were glutamine-dependent and that depriving the cells of external sources of glutamine -- as some experimental drugs do -- was an effective way to kill late-stage ovarian cancer cells in the lab. And a December 2014 study found that ovarian tumors coax adult stem cells into providing key metabolites they need to grow.

The exosome study began four years ago based upon a growing realization that exosomes might play a role in regulating cancer metabolism.

"A growing body of evidence suggests that exosomes can facilitate crosstalk between cancer cells and other types of cells that are nearby in the microenvironment that surrounds the tumor," said Hongyun Zhao, the first author of the eLife study. "Some studies suggested that exosomes harbored the potential to regulate cancer cell metabolism, but most research had focused on the exosomes that were produced and emitted by cancer cells themselves. We decided to look at the exosomes of stromal cells, a type of cell that is commonly found in the tumor microenvironment, and see if stromal exosomes were influencing the energy consumption of cancer cells."

Zhao's first experiments involved growing cultures of stromal cells, extracting their exosomes and exposing them to cancer cells, which were then monitored for metabolic changes. Nagrath said the tests suggested that the cancer was fueling itself by consuming amino acids directly from the exosomes, and a series of monthslong follow-up tests had to be conducted to rule out other possibilities.

"Our results show that not only do exosomes enhance the phenomenon of the 'Warburg effect' in tumors, but exosomes also contain 'off-the-shelf' metabolites within their cargo that cancer cells use directly in their metabolic processes," Zhao said.

Nagrath said some of Zhao's follow-up tests also suggest possible new treatment regimes. For example, in some tests, Zhao exposed cancer cell cultures to drugs that were known to block the uptake of exosomal signals. The tests, which showed that the cancer cell's metabolic activity dropped significantly, helped prove that the tumors were using the exosomes as fuel. The fact that four of the drugs used in the tests -- heparin, cytochalasin D, ethyl-isopropyl amiloride and choloroquine -- are already approved by the Food and Drug Administration for other uses suggests that they may also be useful as chemotherapeutic agents, Nagrath said.

"Disruption of the exosomal metabolic adaptation of cancer cells could provide a novel therapeutic avenue for exploitation," he said.

The research was supported by Rice's Ken Kennedy Institute for Information Technology via the John and Ann Doerr Fund for Computational Biomedicine.

Additional co-authors include Lifeng Yang, Joelle Baddour, Abhinav Achreja and Thavisha Tudawe, all of Rice; Vincent Bernard, Tyler Moss, Elena Seviour, Anthony San Lucas, Hector Alvarez, Sonal Gupta, Sourindra Maiti, Laurence Cooper, Prahlad Ram and Anirban Maitra, all of MD Anderson; Juan Marini of Baylor College of Medicine; and Donna Peehl of Stanford University.

A copy of the paper is available at: http://elifesciences.org/content/5/e10250v1

http://www.eurekalert.org/pub_releases/2016-03/nu-dpa030716.php

Dementia plaques attack language center of brain

Peering into brains of living persons with Alzheimer's language dementia offers insight into disease process and language loss

CHICAGO - The recent ability to peer into the brain of living individuals with a rare type of language dementia, primary progressive aphasia (PPA), provides important new insights into the beginning stages of this disease -- which results in language loss -- when it is caused by a buildup of a toxic protein found in Alzheimer's disease.

The research also offers additional insight into why this type of dementia causes people to lose the ability to express themselves and understand language.

Using a special imaging technique, Northwestern Medicine scientists have discovered the toxic build-up of amyloid protein is greater on the left side of the brain -- the site of language processing -- than on the right side in many individuals living with PPA.

Previously, amyloid accumulation in the brain could only be studied after an individual with Alzheimer's disease had died. This snapshot in time was after the disease had run its full course, and amyloid had spread throughout the entire brain. Now, a new technology called Amyloid PET Imaging allows researchers to study the build-up of the toxic amyloid during life.

"By understanding where these proteins accumulate first and over time, we can better understand the course of the disease and where to target treatment," said Emily Rogalski, the lead study investigator and research associate professor at Northwestern's Cognitive Neurology and Alzheimer's Disease Center (CNADC).

"It is important to determine what Alzheimer's looks like in PPA, because if it's caused by something else, there is no sense in giving a patient an Alzheimer's related drug, because it would be ineffective," Rogalski said.

The goal is to diagnose Alzheimer's disease during life in order to guide treatment and identify regions to target for future drug trials.

"This new technology is very exciting for Alzheimer's research," said Adam Martersteck, the first author and a graduate student in Northwestern's neuroscience program. "Not only can we tell if a person is likely or unlikely to have Alzheimer's disease causing their PPA, but we can see where it is in the brain. By understanding what the brain looks like in the beginning stages of Alzheimer's, we hope to be able to diagnose people earlier and with better accuracy."

This is the first study to examine and compare beta-amyloid buildup in the brain using the Amyvid amyloid PET imaging tracer between individuals with PPA and those with Alzheimer's memory dementia, the more common disease that causes memory problems. Both types of dementia (memory and language) can be caused by an accumulation of beta-amyloid, an abnormal toxic protein in the brain.

By using Amyloid PET Imaging, Northwestern scientists at CNADC showed the toxic amyloid protein was distributed differently in people that had the PPA language dementia versus the memory dementia in the early stages. Researchers found there was more amyloid in the left hemisphere parietal region of individuals with PPA compared to those with Alzheimer's memory dementia.

Scientists scanned 32 PPA patients, and 19 of them had high amounts of amyloid and were likely to have the Alzheimer's pathology. They were compared to 22 people who had the Alzheimer's memory dementia. Those with the memory dementia had the same amount of amyloid on the left and right side of the brain.

The study was published recently in the Annals of Neurology.

The paper is titled "Is in vivo Amyloid Distribution Asymmetric in Primary Progressive Aphasia?"

http://www.eurekalert.org/pub_releases/2016-03/du-tya030716.php

Trust your aha! moments, experiments show they're probably right

When a solution to a problem seems to have come to you out of thin air, it turns out you've more than likely been struck with the right idea, according to a new study.

A series of experiments conducted by a team of researchers determined that a person's sudden insights are often more accurate at solving problems than thinking them through analytically.

"Conscious, analytic thinking can sometimes be rushed or sloppy, leading to mistakes while solving a problem," said team member John Kounios, PhD, professor in Drexel University's College of Arts and Sciences and the co-author of the book "The Eureka Factor: Aha Moments, Creative Insight and the Brain." "However, insight is unconscious and automatic -- it can't be rushed. When the process runs to completion in its own time and all the dots are connected unconsciously, the solution pops into awareness as an Aha! moment. This means that when a really creative, breakthrough idea is needed, it's often best to wait for the insight rather than settling for an idea that resulted from analytical thinking."

Experiments with four different types of timed puzzles showed that those answers that occurred as sudden insights (also described as Aha! moments) were more likely to be correct. Moreover, people who tended to have more of these insights were also more likely to miss the deadline rather than provide an incorrect, but in-time, answer. Those who responded based on analytic thought (described as being an idea that is worked out consciously and deliberately) were more likely to provide an answer by the deadline, though these last-minute answers were often wrong.

Trust Yourself

Carola Salvi, PhD, of Northwestern University, was lead author on the paper "Insightful solutions are correct more often than analytic solutions" in the journal Thinking & Reasoning.

"The history of great discoveries is full of successful insight episodes, fostering a common belief that when people have an insightful thought, they are likely to be correct," Salvi explained. "However, this belief has never been tested and may be a fallacy based on the tendency to report only positive cases and neglect insights that did not work. Our study tests the hypothesis that the confidence people often have about their insights is justified."

Other co-authors on the paper with Salvi and Kounios were Mark Beeman (co-author of "The Eureka Factor" with Kounios), also of Northwestern, Edward Bowden, of the University of Wisconsin-Parkside, and Emanuela Bricolo, of Milano-Bicocca University in Italy.

Putting Insight to The Test

Each experiment making up the study used one group of distinct puzzles: one experiment used only linguistic puzzles, another used strictly visual ones, and two used puzzles with both linguistic and visual elements.

For example, one type of linguistic puzzle showed three different words: "Crab," "pine" and "sauce." The experiment participant was then asked to provide the word that could fit all of them to make a compound word, which was "apple," in this case. The visual puzzle provided a scrambled image and required the participant to say what object they thought the puzzle depicted.

Each experiment consisted of between 50 and 180 puzzles. Participants were given 15 or 16 seconds to respond after seeing a puzzle. As soon as the participant thought they solved the puzzle, they pressed a button and said their answer. Then they reported whether the solution came through insight or analytical thinking.

Overwhelmingly, responses derived from insight proved correct. In the linguistic puzzles, 94 percent of the responses classified as insight were correct, compared to 78 percent for the analytic thinking responses. For the visual puzzles, 78 percent of the responses were correct, versus 42 percent for the analytic responses.

Bad Guesses, Good Insights

When taking the timing into account, answers given during the last five seconds before the deadline had a lower probability of being correct. For the linguistic puzzles, 34 percent of the responses were wrong, compared to 10 percent of the responses being wrong for quicker answers; for the visual puzzles, 72 percent of the answers given during the last five seconds were wrong.

The majority of those late wrong answers were based on analytic thinking. In one of the experiments, the number of incorrect responses related to analytic thinking recorded in the last five seconds was more than double the number of incorrect responses recorded as insights.

Those numbers for the last five seconds pointed to some participants guessing at the puzzles' solutions. These participants were analytical thinkers.

"Deadlines create a subtle -- or not so subtle -- background feeling of anxiety," Kounios said. "Anxiety shifts one's thinking from insightful to analytic. Deadlines are helpful to keep people on task, but if creative ideas are needed, it's better to have a soft target date. A drop-dead deadline will get results, but they are less likely to be creative results."

Insightful thinkers tend not to guess. They don't give an answer until they have had an Aha! moment. "Because insight solutions are produced below the threshold of consciousness, it is not possible to monitor and adjust processing before the solution enters awareness," Salvi said.

Hmm vs. Aha!

Analytical thinking is best used for problems in which known strategies have been laid out for solutions, such as arithmetic, Kounios said. But for new problems without a set path for finding a solution, insight is often best. The new study shows that more weight should be placed on these sudden thoughts.

"This means that in all kinds of personal and professional situations, when a person has a genuine, sudden insight, then the idea has to be taken seriously," Kounios said. "It may not always be correct, but it can have a higher probability of being right than an idea that is methodically worked out."

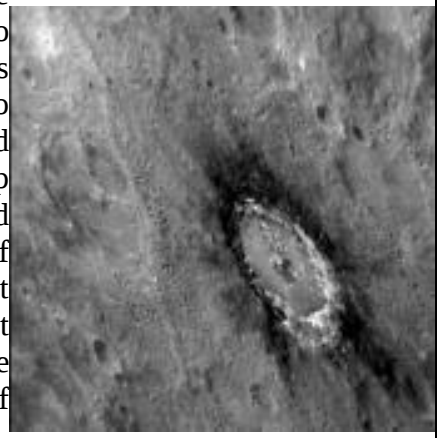
http://www.eurekalert.org/pub_releases/2016-03/ci-mm030316.php

Mercury's mysterious 'darkness' revealed

MESSENGER mission data confirm that a high abundance of carbon is present at Mercury's surface

Washington, D.C.- Scientists have long been puzzled about what makes Mercury's surface so dark. The innermost planet reflects much less sunlight than the Moon, a body on which surface darkness is controlled by the abundance of iron-rich minerals. These are known to be rare at Mercury's surface, so what is the "darkening agent" there?

About a year ago, scientists proposed that Mercury's darkness was due to carbon that gradually accumulated from the impact of comets that traveled into the inner Solar System. Now scientists, led by Patrick Peplowski of the Johns Hopkins University Applied Physics Laboratory, have used data from the MESSENGER mission* to confirm that a high abundance of carbon is present at Mercury's surface. However, they also have also found that, rather than being delivered by comets, the carbon most likely originated deep below the surface, in the form of a now-disrupted and buried ancient graphite-rich crust, some of which was later brought to the surface by impact processes after most of Mercury's current crust had formed. The results are published in the March 7, 2016, Advanced Online Publication of Nature Geoscience.



This oblique image of Basho shows the distinctive dark halo that encircles the crater. The halo is composed of so-called Low Reflectance Material (LRM), which was excavated from depth when the crater was formed. Basho is also renowned for its bright ray craters, which render the crater easily visible even from very far away.
NASA/Johns Hopkins University Applied Physics Laboratory/Carnegie Institution of Washington

Co-author and Deputy Principal Investigator of the MESSENGER mission, Carnegie's Larry Nittler, explained: "The previous proposal of comets delivering carbon to Mercury was based on modelling and simulation. Although we had prior suggestions that carbon may be the darkening agent, we had no direct evidence. We used MESSENGER's Neutron Spectrometer to spatially resolve the distribution of carbon and found that it is correlated with the darkest material on Mercury, and this material most likely originated deep in the crust. Moreover, we used both neutrons and X-rays to confirm that the dark material is not enriched in iron, in contrast to the Moon where iron-rich minerals darken the surface."

MESSENGER obtained its statistically robust data via many orbits on which the spacecraft passed lower than 60 miles (100 km) above the surface of the planet during its last year of operation. The data used to identify carbon included measurements taken just days before MESSENGER impacted Mercury in April 2015. Repeated Neutron Spectrometer measurements showed higher amounts of low-energy neutrons, a signature consistent with the presence of elevated carbon, coming from the surface when the spacecraft passed over concentrations of the darkest material. Estimating the amount of carbon present required combining the neutron measurements with other MESSENGER datasets, including X-ray measurements and reflectance spectra. Together, the data indicate that Mercury's surface rocks are made up of as much as a few weight percent graphitic carbon, much higher than on other planets. Graphite has the best fit to the reflectance spectra, at visible wavelengths, and the likely conditions that produced the material.

When Mercury was very young, much of the planet was likely so hot that there was a global "ocean" of molten magma. From laboratory experiments and modeling, scientists have suggested that as this magma ocean cooled, most minerals that solidified would sink. A notable exception is graphite, which would have been buoyant and floated to form the original crust of Mercury.

"The finding of abundant carbon on the surface suggests that we may be seeing remnants of Mercury's original ancient crust mixed into the volcanic rocks and impact ejecta that form the surface we see today. This result is a testament to the phenomenal success of the MESSENGER mission and adds to a long list of ways the innermost planet differs from its planetary neighbors and provides additional clues to the origin and early evolution of the inner Solar System," concluded Nittler.

**Authors on this paper are Patrick Peplowski, Rachel Klima, David Lawrence, Carolyn Ernst, Brett Denevi, Elizabeth Frank, John Goldsten, Scott Murchie, Larry Nittler and Sean Solomon. MESSENGER (MErcury Surface, Space ENvironment, GEochemistry, and Ranging) is a NASA-sponsored scientific investigation of the planet Mercury and the first space mission designed to orbit the planet closest to the Sun.*

http://www.eurekalert.org/pub_releases/2016-03/uotf-uo030316.php

'Person-on-a-chip': U of T engineers grow 3-D heart, liver tissues for better drug testing

Researchers at U of T Engineering have developed a new way of growing realistic human tissues outside the body.

Their "person-on-a-chip" technology, called AngioChip, is a powerful platform for discovering and testing new drugs, and could eventually be used to repair or replace damaged organs.

Professor Milica Radisic (IBBME, ChemE), graduate student Boyang Zhang and the rest of the team are among those research groups around the world racing to find ways to grow human tissues in the lab, under conditions that mimic a real person's body. They have developed unique methods for manufacturing small, intricate scaffolds for individual cells to grow on. These artificial environments produce cells and tissues that resemble the real thing more closely than those grown lying flat in a petri dish.

The team's recent creations have included BiowireTM -- an innovative method of growing heart cells around a silk suture -- as well as a scaffold for heart cells that snaps together like sheets of Velcro™. But AngioChip takes tissue engineering to a whole new level. "It's a fully three-dimensional structure complete with internal blood vessels," says Radisic. "It behaves just like vasculature, and around it there is a lattice for other cells to attach and grow." The work is published today in the journal Nature Materials.

Zhang built the scaffold out of POMaC, a polymer that is both biodegradable and biocompatible. The scaffold is built out of a series of thin layers, stamped with a pattern of channels that are each about 50 to 100 micrometres wide. The layers, which resemble the computer microchips, are then stacked into a 3D structure of synthetic blood vessels. As each layer is added, UV light is used to cross-link the polymer and bond it to the layer below.

When the structure is finished, it is bathed in a liquid containing living cells. The cells quickly attach to the inside and outside of the channels and begin growing just as they would in the human body.

"Previously, people could only do this using devices that squish the cells between sheets of silicone and glass," says Radisic. "You needed several pumps and vacuum lines to run just one chip. Our system runs in a normal cell culture dish, and there are no pumps; we use pressure heads to perfuse media through the vasculature. The wells are open, so you can easily access the tissue."

Using the platform, the team has built model versions of both heart and liver tissues that function like the real thing. "Our liver actually produced urea and metabolized drugs," says Radisic. They can connect the blood vessels of the two artificial organs, thereby modelling not just the organs themselves, but the interactions between them. They've even injected white blood cells into the vessels and watched as they squeezed through gaps in the vessel wall to reach the tissue on the other side, just as they do in the human body.

AngioChip has great potential in the field of pharmaceutical testing. Current drug-testing methods, such as animal testing and controlled clinical trials, are costly and fraught with ethical concerns. Testing on lab-grown human tissues would provide a realistic model at a fraction of the cost, but this area of research is still in its infancy. "In the last few years, it has become possible to order cultures of human cells for testing, but they're grown on a plate, a two-dimensional environment," says Radisic. "They don't capture all the functional hallmarks of a real heart muscle, for example."

A more realistic platform like AngioChip could enable drug companies to detect dangerous side effects and interactions between organ compartments long before their products reach the market, saving countless lives. It could also be used to understand and validate the effectiveness of current drugs and even to screen libraries of chemical compounds to discover new drugs. Through TARA Biosystems Inc., a spin-off company co-founded by Radisic, the team is already working on commercializing the technology.

In future, Radisic envisions her lab-grown tissues being implanted into the body to repair organs damaged by disease. Because the cells used to seed the platform can come from anyone, the new tissues could be genetically identical to the intended host, reducing the risk of organ rejection. Even in its current form, the team has shown that the AngioChip can be implanted into a living animal, its artificial blood vessels connected to a real circulatory system. The polymer scaffolding itself simply biodegrades after several months.

The team still has much work to do. Each AngioChip is currently made by hand; if the platform is to be used industrially, the team will need to develop high-throughput manufacturing methods to create many copies at once. Still, the potential is obvious. "It really is multifunctional, and solves many problems in the tissue engineering space," says Radisic. "It's truly next-generation."

http://www.eurekalert.org/pub_releases/2016-03/cwru-atb030716.php

A toxic byproduct of hemoglobin could provide treatments for Creutzfeldt-Jakob disease

Brain's normal prion protein is upregulated in damaged tissue following stroke and protects the tissue from further damage

Scientists at Case Western Reserve University School of Medicine have identified a novel mechanism that could be used to protect the brain from damage due to stroke and a variety of neurodegenerative conditions, including sporadic Creutzfeldt-Jakob disease, Alzheimer's disease, and Parkinson's disease.

Neena Singh, MD, PhD, a professor of pathology at the school, has spent much of her career studying the role of metals such as iron, copper, and zinc in the pathology of neurodegenerative diseases. She has previously reported that some of these metals are regulated by the brain's normal prion protein, called PrPC. Her goal is to identify common pathogenic processes in neurodegenerative diseases that could lead to the development of a new generation of treatments.

In her latest study, published in The Journal of Alzheimer's Disease, Singh and post-doctoral research fellow Ajai K. Tripathi, PhD, studied a byproduct of hemoglobin called hemin that is released from red blood cells during stroke and is toxic to neurons. Other scientists have reported that PrPC is upregulated in damaged tissue following stroke, and protects the tissue from further damage.

It was this finding that got Singh and her group interested in how PrPC protects neurons from hemin-induced toxicity. In a series of elegant experiments, Singh

said they found that hemin binds to PrPC on many diverse cell lines. What was surprising was that the interaction between hemin and PrPC actually up-regulated hemoglobin synthesis in hematopoietic and neuronal cells. "Neuronal hemoglobin may be endowed with similar biological functions that are found in red cells, and is likely to improve neuronal survival by supporting their metabolism," explained Singh.

In addition, hemin and PrPC form a complex, resulting in the removal of hemin and reducing the amount of PrPC available for conversion to the PrP-scrapie form. The latter is responsible for scrapie in sheep and goats and Creutzfeldt-Jakob disease in humans. Treatment with hemin has been shown to delay the onset of scrapie in experimental models. This study suggests that in addition to reducing the generation of PrP-scrapie, hemin protects neurons by inducing hemoglobin synthesis. "The hemin-PrPC interaction therefore reveals a unique function of PrPC that is likely to impact the therapeutic management of cerebral hemorrhage and CJD."

This synergy may play a role in other brain diseases as well. Dr. Singh said that altered levels of neuronal hemoglobin have been reported in multiple sclerosis, Alzheimer's disease, Parkinson's disease, and dementia with Lewy bodies. "We think that manipulation of neuronal hemoglobin may provide an effective method of improving neuronal survival," said Dr. Singh. "Further studies are necessary to explore viable options that take advantage of PrPC and hemin in this process."

http://bit.ly/1LRi8as

Urine from premature babies could repair damaged kidneys

If you're looking for stem cells, urine luck…

Urine from premature babies could provide a rich supply of stem cells for medical treatments or for rebooting worn-out kidneys for transplantation.

Stem cells are the cellular putty from which all tissues in our body are made. They can be hard to come by though. Embryos provide a great source of stem cells that can change into a whole manner of tissues, but they involve the destruction of an embryo.

Over the years, researchers have found other sources of stem cells at a slightly later stage of development that can develop into specific cell types. For example, a type of stem cell destined to become kidney cells can be isolated from adult urine. But babies born early might provide a better source, says Elena Levtchenko at the Catholic University of Leuven (KUL), Belgium.

She and her colleagues collected urine samples from premature babies born at between 31 and 36 weeks. The team then searched for cells with specific markers that flagged them as stem cells. The team developed these stem cells into a range of types of kidney cell by changing the nutrients in which they were bathed. "They act like kidney cells, and do what kidney cells are supposed to do," says Levtchenko. There were also plenty of stem cells to be found – many more than the team collected from adult urine, says Levtchenko. The urine of premature babies is much more likely to provide a source of enough stem cells to be used in any potential therapies, she says. This could be because a fetus's kidneys continue to develop right up to birth, so premature babies' kidneys are still developing.

As good as new

The premature babies' stem cells seem to be able to protect other cells from damage. When the team applied cisplatin – a toxic cancer drug – to adult kidney cells, all of the cells died. But when the team added stem cells to the mix, they found that although some kidney cells died, others regenerated and survived.

The team is testing their urine-derived stem cells on human organs that are too old or damaged to be used for transplantation. The aim is to regenerate damaged kidney tissue, pepping-up worn out organs.

Levtchenko will next test whether the cells have the same protective effect in living animals, and eventually people. In theory, the cells could be used to rescue kidney cells that are damaged as a result of disease, she says. If treatments work, it might make sense to bank stem cells from premature babies' urine for future use, she says.

Journal reference: Journal of the American Society of Nephrology, *DOI: 10.1681/asn.2015060664*

http://www.eurekalert.org/pub_releases/2016-03/asa-pit030816.php

People in their 60s uniquely benefit from giving advice despite fewer chances to offer it

A new study reveals that individuals in their 60s who give advice to a broad range of people tend to see their lives as especially meaningful.

WASHINGTON, DC - At the same time, this happens to be the age when opportunities for dispensing advice become increasingly scarce.

According to the study, which appears in the March issue of Social Psychology Quarterly, individuals in their 60s who report giving advice to a wide variety of people -- to family members, friends, neighbors, and strangers -- see their lives as highly meaningful, while adults in that age group who dispense advice to fewer types of people are much less likely to report high life meaning.

"This association between advice giving and life meaning is not evident for other age groups," said Markus H. Schafer, an assistant professor of sociology at the University of Toronto and the lead author of the study. "Overall, we interpret these findings to suggest that the developmental demands of late midlife -- particularly the desire to contribute to others' welfare and the fear of feeling 'stagnant' -- fit poorly with the social and demographic realties for this segment of

the life course. Just when giving advice seems to be most important, opportunities for doing so seem to wane."

Titled, "The Age-Graded Nature of Advice: Distributional Patterns and Implications for Life Meaning," the study relies on a nationally representative sample of 2,583 U.S. adults who were 18 and above when they were surveyed in 2006.

Schafer and his co-author Laura Upenieks, a doctoral candidate in sociology at the University of Toronto, found that 21 percent of people in their 60s and 27 percent of people 70 or older reported giving advice to no one in the previous year. By comparison, only about 10 percent of people in their 20s (this group also included 18 and 19-year-olds), 30s, 40s, and 50s said they gave no advice in the past year.

"Conventional age norms suggest that the ideal mentor or advice-giver is someone who has a lot of life experience," Schafer said. "However, compared to their younger counterparts, older adults occupy fewer social roles, are less socially active, and interact with a more restricted range of people. So, while the average 65-year-old may well have more wisdom than the average 30-year-old, demographic and social structure factors seem to provide the latter with more opportunity for actually dispensing advice."

Some scholars have argued that the essence of mattering -- the idea that one is meaningful and consequential to other people -- is most under threat during late-middle age when many people retire and enter the "empty nest" phase of life, according to Schafer.

"The mattering perspective helps explain why it is this period of the life span, in particular, when it is important for people to feel like they can still have influence on others through actions such as giving advice," Schafer said.

In terms of the study's implications, Schafer said, "The results should prompt reflection on the social fabric of American communities and how late-middle age adults fit into the picture. Our findings underscore the importance of giving older adults occasions to share their wisdom and life experiences. Schools, churches, civic organizations, and other community groups could consider how to facilitate intergenerational mentorship experiences and to creatively enable more older adults to be advice-givers."

http://www.eurekalert.org/pub_releases/2016-03/ps-gta030816.php

Green tea and iron, bad combination

Consuming green tea along with dietary iron may actually lessen green tea's benefits

Green tea is touted for its many health benefits as a powerful antioxidant, but experiments in a laboratory mouse model of inflammatory bowel disease suggest that consuming green tea along with dietary iron may actually lessen green tea's benefits.

"If you drink green tea after an iron-rich meal, the main compound in the tea will bind to the iron," said Matam Vijay-Kumar, assistant professor of nutritional sciences, Penn State. "When that occurs, the green tea loses its potential as an antioxidant. In order to get the benefits of green tea, it may be best to not consume it with iron-rich foods." Iron-rich foods include red meat and dark leafy greens, such as kale and spinach. According to Vijay-Kumar, the same results also apply to iron supplements.

Vijay-Kumar and colleagues found that EGCG -- the main compound in green tea -- potently inhibits myeloperoxidase, a pro-inflammatory enzyme released by white blood cells during inflammation. Inactivation of myeloperoxidase by EGCG may be beneficial in mitigating IBD flare-ups. But when EGCG and iron are consumed simultaneously, iron-bound EGCG loses its ability to inhibit myeloperoxidase.

Adding to this complexity, they found that EGCG can also be inactivated by a host protein, which is highly abundant in inflammatory conditions. The researchers published their findings in the American Journal of Pathology.

IBD is characterized by chronic inflammation of the digestive tract, which results in bloody diarrhea, pain, fatigue, weight loss and other symptoms including iron deficiency/anemia. It is common for IBD patients to be prescribed iron supplements. In this scenario, the intake of green tea and iron supplements at the same time would be counterproductive as both nutrients would bind and cancel each other out.

"It is important that IBD patients who take both iron supplements and green tea know how one nutrient affects the other," Vijay-Kumar said. "The information from the study could be helpful for both people who enjoy green tea and drink it for its general benefits, as well as people who use it specifically to treat illnesses and conditions."

"The benefit of green tea depends on the bioavailability of its active components," said Beng San Yeoh, graduate student in immunology and infectious diseases and first author of the study. "It is not only a matter of what we eat, but also when we eat and what else we eat with it."

Other researchers on the project include Rodrigo Aguilera Olvera, Vishal Singh and Xia Xiao, Department of Nutritional Sciences; Mary J. Kennett, Department of Veterinary and Biomedical Sciences; and Joshua D. Lambert, Department of Food Science, all at Penn State; and Bina Joe, Department of Physiology and Pharmacology, The University of Toledo College of Medicine and Life Sciences.

The National Institutes of Health (NIH) funded this study.

http://www.eurekalert.org/pub_releases/2016-03/uoz-bcc030816.php

Bird communication: Chirping with syntax

Japanese great tits communicate according to syntactic rules

Language is one of the defining characteristics of human beings: It enables us to generate unlimited meanings from a finite number of phonetic elements. Using syntactic rules, humans are able to combine words to form phrases and sentences, and thus ascribe meaning to various things and activities.

Research on communication systems suggests that non-human primates and birds, too, have evolved the ability to assign meaning to arbitrary vocal elements. But until now, the evolution of syntax has been considered unique to human language.

Warning signal plus mating call means "flock together"

Evolutionary biologists at The Graduate University for Advanced Studies in Japan, the Uppsala University in Sweden and the University of Zurich are now challenging this view.

For the first time, these researchers have demonstrated that Japanese great tits (Parus minor) have developed syntactic rules. These small birds are known for their large vocal repertoire, and the team discovered that they use a variety of calls and combinations of calls to interact with one another in specific situations.

The combination of sounds such as the "ABC calls", for instance, means "watch out!". The great tits use them when a sparrowhawk or another predator is nearby -- a potentially dangerous situation. By contrast, "D calls" mean "come over here," a call the birds use after discovering a new source of food or when wanting their partner to come to the nest.

Tits frequently combine these two calls into ABC-D calls when, for instance, the birds encounter predators and join forces to deter them. When hearing a recording of these calls played in the natural order of ABC-D, the birds are alarmed and flock together. When, however, the call ordering is artificially reversed to D-ABC, the birds do not respond.

Generating meaning by combining limited vocabulary

The researchers have therefore drawn the conclusion that syntax is not unique to human language: It has also evolved independently in birds. "The results lead to a better understanding of the underlying factors in the evolution of syntax. Because the tits combine different calls, they are able to create new meaning with their limited vocabulary. That allows them to trigger different behavioral reactions and coordinate complex social interactions," says Dr. Michael Griesser, at the Institute of Anthropology at the University of Zurich.

He believes these factors may well have contributed to the development of language in humans.

http://www.eurekalert.org/pub_releases/2016-03/ki-sll030816.php

Surprisingly long learning curve for surgeons operating on oesophageal cancer

Surgeons operating on oesophageal cancer must have performed 60 operations to gain experience to avoid adversely affecting long-term survival of the patients

According to a major Swedish cohort study from researchers at Karolinska Institutet in Sweden and Imperial College London, a surgeon who operates on oesophageal cancer must have performed 60 operations to prevent any lack of experience adversely affecting the long-term survival of the patients. The finding, which is published in the Journal of Clinical Oncology, has potential significance for clinical practice.

While it is well known that patient survival after oesophagectomy is related to the surgeon's experience of the procedure, no figure has been put on how many operations are needed for the surgeon to attain the competence needed for achieving optimal results as regards patient survival. The new study is the first to examine the surgeon's learning curve in relation to short and long-term fatality rates.

"What the study shows us is that a surgeon needs to perform 15 operations to obtain stable results as regards survival during the first months following the operation, and a full 60 before he or she achieves optimal results on long-term survival," says the chief investigator Jesper Lagergren at Karolinska Institutet's Department of Molecular Medicine and Surgery, and also affiliated to the Division of Cancer Studies at King's College London.

"What surprised me was that the learning curve for optimising the long-term prognosis for tumour relapse was so long and the effect so pronounced."

Jesper Lagergren's research team has in collaboration with colleagues at Imperial College London examined a Swedish cohort of 1,821 patients operated on for oesophageal cancer in Sweden between 1987 and 2010 by 139 different surgeons. Using data on which surgeons performed which operations, the researchers studied their learning curves and found that even though the surgeons were experienced with other procedures when starting to perform oesophagectomies, the turning point for their learning curves for a stable 5-year fatality rate was at 60 operations.

The form of surgery studied is relatively uncommon with some 150 such operations performed a year in Sweden. The new finding indicates that it is worth concentrating oesophageal cancer operations to a small number of surgeons with a particular interest in this kind of surgery. "Our results can guide clinical practice and indicate that a properly organised mentorship and training programme should

be introduced for oesophageal cancer surgery," adds Professor Lagergren, who is himself an oesophageal cancer surgeon. "Surgeons who start operating on oesophageal cancer should perform many operations together with a more experienced oesophageal cancer surgeon before they begin to operate independently."

The study was financed with grants from the Swedish Research Council and the Swedish Cancer Society.

Publication: 'Surgical Proficiency Gain and Survival Following Esophagectomy for Cancer', Sheraz R. Markar, Hugh Mackenzie, Pernilla Lagergren, George B. Hanna, Jesper Lagergren, Journal of Clinical Oncology, online March 7, 2016.

http://bit.ly/1U7Z3TW

Zika virus disease renamed to reflect range of impacts on fetus

The fetal disease caused by Zika virus could soon have a new name: Zika virus congenital syndrome.

The name was proposed by the team who confirmed that the virus causes damage beyond microcephaly – the first fetal condition to be linked to the virus.

Karin Nielsen-Saines at the University of California, Los Angeles, and her colleagues performed ultrasound scans on pregnant women in Rio de Janeiro, Brazil. Among the 42 Zika-infected women in the study, 12 were carrying fetuses with severe abnormalities, including absence or withering of brain structures, tissue death, restricted growth and, in one case, microcephaly.

Two otherwise healthy babies were stillborn following infection late in pregnancy. There were no health problems seen in fetuses from 16 uninfected women. “As we noticed such a spectrum of abnormalities, it’s fair to say this is a constellation of findings, which defines a congenital syndrome,” says Nielsen-Saines.

Because impacts of Zika infection were seen whatever stage of pregnancy it occurred at, Nielsen-Saines advises women to try and avoid infection throughout. She says the impacts are consistent with earlier studies showing that the virus appears to preferentially infect fetal brain tissue and the placenta.

Nevertheless, it is encouraging that 70 per cent of the infected women had healthy fetuses, although it is not clear why they were unaffected.

“We don’t yet have any information to speculate on why,” says Nielsen-Saines. “It could be that they had less viral load, they had protective antibodies, or the placenta stopped the virus reaching the fetus.” “We’ve been seeing growing evidence of the association between Zika and congenital central nervous system malformations, not just microcephaly, since the first cases were picked up,” says Wim Van Bortel, senior expert on vector-borne diseases at the European Centre for Disease Prevention and Control in Solna, Sweden.

New England Journal of Medicine, DOI: 10.1056/NEJMoa1602412

http://bit.ly/1RFxKKL

Zika Virus: Microcephaly May Be 'Tip of the Iceberg' for Infant Problems

Pregnant women infected with Zika virus at risk for not only having a child with microcephaly, but also having a fetus with other serious health issues

Rachael Rettner and Karen Rowan

Pregnant women who become infected with Zika virus may be at risk for not only having a child with microcephaly, but also having a fetus with other serious health issues, including problems with the nervous system and even fetal death, according to a new study from Brazil.

The study — which provides some of the strongest evidence that Zika virus causes microcephaly — found that nearly one-third of women who had Zika infections during their pregnancy had an ultrasound that showed fetal abnormalities. These abnormalities included problems with growth, such as microcephaly (meaning an abnormally small head); problems with the placenta; and lesions in the brain or spine.

"Zika definitely causes the problems. We think microcephaly is only the tip of the iceberg," said study co-author Dr. Karin Nielsen-Saines, a professor of clinical pediatrics at the David Geffen School of Medicine at UCLA.

Infants and fetuses in the study showed a variety of problems, including calcification (or hardening) of brain tissues, problems with the amniotic fluid and an abnormally small body size. There were two stillbirths in the study. Usually, viral infections don't cause only one problem, and because of the array of problems now linked with Zika, the researchers suggest using the term congenitial Zika virus syndrome, Nielsen-Saines said. The new study provided a stronger type of evidence than previous studies of the effects of Zika during pregnancy because it was prospective, meaning that women who went to the clinic in Brazil were tested for Zika and were then followed over time (regardless of whether they tested positive for the virus).

In addition, the researchers tested the women for Zika by looking for the virus's genetic material — which is more reliable than looking for antibodies, or proteins produced by the immune system in response to a Zika infection, Nielsen-Saines said.

The new study is "what people have been waiting for," in terms of the type of evidence needed to prove that Zika infection in pregnancy causes microcephaly, said Dr. Amesh Adalja, an infectious disease specialist and a senior associate at the University of Pittsburgh Medical Center's Center for Health Security, who was not involved in the study. That's because the researchers compared pregnant

women infected with the Zika virus with pregnant women who were not infected with Zika virus and lived in the same area — a so-called "case control" study.

"This is the closest we've gotten to [proving] causation," Adalja said. Although more studies are still needed to solidify the link, "for all intents and purposes, this justifies the concern raised early on," that at least a proportion of the microcephaly cases in Brazil were caused by Zika virus, Adalja said.

The Zika virus is currently spreading rapidly in Central and South America. Health officials became concerned about a link between the virus and microcephaly after there was a dramatic rise in cases of this birth defect in Brazil last year.

The study involved 88 pregnant women in Rio de Janeiro who were tested for Zika virus because they had recently developed a rash — one of the symptoms of the infection. Of these women, 72 tested positive for Zika virus, and they were at various stages of pregnancy — anywhere from five to 38 weeks pregnant.

The researchers performed ultrasounds on 42 women who had a Zika infection and 16 women who did not have a Zika infection. (A number of women in the study who tested positive for Zika did not agree to have ultrasounds, Nielsen-Saines said and, in some of those cases, were due to women not wanting to know whether the fetuses they were carrying potentially had health problems.)

About 30 percent of the Zika-infected women showed a fetal abnormality on their ultrasound, compared to none of the women without a Zika infection. The Zika-infected women were all previously healthy and did not have other risk factors for adverse pregnancy outcomes, the researchers said.

Five of the Zika-infected women (12 percent) had fetuses with microcephaly, but in most of these cases, the fetus also had a condition called intrauterine growth restriction, meaning the whole fetus, and not just the head, was abnormally small.

Seven women (16 percent) had fetuses with lesions on the brain or spinal cord, or other central nervous system problems, and seven women appeared to have placental insufficiency, when the placenta doesn't work as it should so that the fetus does not receive a sufficient amount of oxygen and other nutrients.

Two women infected with Zika had stillbirths at 36 and 38 weeks of pregnancy, respectively. In previous studies, there was some speculation that Zika infections may be more damaging if they strike earlier in pregnancy. But in the new findings, the both stillbirths happened in women who were infected late in their pregnancies, Nielsen-Saines said. And in another case, a baby had to be "urgently delivered" from a woman with a later Zika infection, because the baby would have died otherwise, she said.

None of those three cases involved microcephaly or other problems with the central nervous system, but rather these cases had other problems such as placenta or amniotic fluid abnormalities, she said. There "may be a high risk of fetal demise with infections in the last trimester," she said.

The finding that nearly 30 percent of Zika-infected women had an abnormality on their ultrasound is "worrisome," the researchers said. They noted that the rate of fetal death in women with Zika was 4.8 percent, which is about twice the rate of fetal death among women infected with HIV living in the same area.

However, Adalja said that because the new study was small and in a single area, more studies are needed before researchers know the true rate of Zika-related pregnancy complications. In addition, there were 30 women in the study who were infected with Zika but did not have an ultrasound. It will be important for future studies to perform ultrasounds on all Zika-infected women in order to generalize the findings, Adalja said.

In Brazil, fears about Zika are running very high, Nielsen-Saines said. "People are very worried; there is a lot of fear and concern," she said. Some pregnant women who become infected with the virus are coming to doctors and requesting to have their labor induced right away – some in the third trimester, but also some still in their second trimester -- in hopes of minimizing the damage to their fetus, she said.

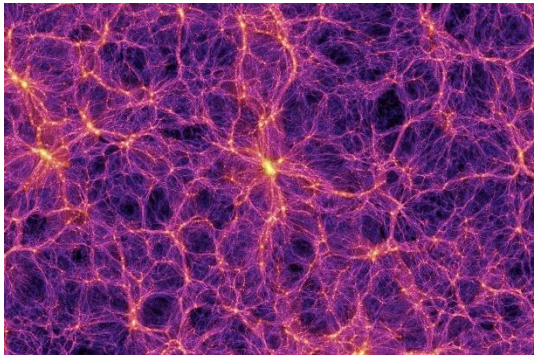
The study is published today (March 4) in The New England Journal of Medicine.

http://bit.ly/1MdIiit

Billion-light-year galactic wall may be largest object in cosmos

Astronomers peering into the distant universe have discovered the BOSS Great Wall, a vast superstructure of 830 galaxies that is a billion light years across

Here's the latest reminder that space is really, really big. At a cool billion light years across, a distant complex of galaxy superclusters may be the largest structure yet found in the cosmos.



Individual galaxies like our own Milky Way are bound together by gravity into clusters, and these clusters clump into superclusters. These can in turn link together into long lines of galaxies called walls. On the grandest scales, the universe resembles a cosmic web of matter surrounding empty voids – and these walls are the thickest threads.

The universe is a web of giant clusters of matter surrounding empty voids **Volker Springel/Max Planck Institute For Astrophysics/SPL**

In the nearby universe, we know of the Sloan Great Wall, and in 2014, the Milky Way was found to be part of a supercluster system called Laniakea. Both are enormous. But the newly spotted BOSS Great Wall, with a total mass perhaps

10,000 times as great as the Milky Way, is two-thirds bigger again than either of them.

Heidi Lietzen of the Canary Islands Institute of Astrophysics and her team found it by looking for clumped-together galaxies in a vast area between 4.5 and 6.4 billion light years away. In all that space, one dense, giant system stood out.

"It was so much bigger than anything else in this volume," Lietzen says. The BOSS Great Wall contains 830 galaxies we can see and probably many more that are too far away and faint to be observed by survey telescopes.

Like other galaxy walls, this one's size is a little subjective.

"I don't entirely understand why they are connecting all of these features together to call them a single structure," says Allison Coil of the University of California in San Diego. "There are clearly kinks and bends in this structure that don't exist, for example, in the Sloan Great Wall."

Brent Tully of the University of Hawaii, who discovered the Laniakea cluster, says that deciding what constitutes a single structure depends on your definition.

A denser region of galaxies is traditional, he says, and indeed the new wall contains five times as many galaxies as an average patch of sky. But tracking whether the galaxies are moving together – impossible, given how far away they are – might give a different answer.

Galaxy superclusters also have competition for the "biggest known object" crown. Some distant light sources like quasars or gamma ray bursts seem to be clustered together in certain regions of the sky. If they are truly connected, they belong to structures so large that current cosmological theories can't explain them.

But many astronomers aren't sure that these objects really belong together, as they lack a physical mechanism to link them. Instead, they prefer to look for huge linkages of galaxies that sit on the cosmic web. In that arena, the new-found BOSS Great Wall is king.

Journal reference: arxiv.org/abs/1602.08498, to appear in Astronomy & Astrophysics

http://bit.ly/1peG9hq

Bacteria Can Convey Electrical Messages the Same Way Neurons Do

Electrical signaling was previously thought to occur only in multicellular organisms

By Diana Kwon on March 1, 2016

Bacteria may be ancient organisms, but don't call them primitive. Despite being unicellular, they can behave collectively—sharing nutrients with neighbors, moving in concert with others and even committing suicide for the greater good of their colony. Molecules that travel from cell to cell enable such group behavior in a signaling process called quorum sensing. Now new evidence reveals that bacteria may have another way to "talk" to one another: communication via electrical signaling—a mechanism previously thought to occur only in multicellular organisms.

In 2010 molecular biologist Gürol Süel, now at the University of California, San Diego, set out to understand how a soil bacterium called Bacillus subtilis could grow into massive communities of more than a million cells and still thrive. He and his colleagues found that once the colony reaches a critical size, bacteria on the periphery stop reproducing to leave core cells with a sufficient nutrient supply. But that observation led to the question of how the edge cells receive word to cease dividing. In a recent follow-up study, Süel discovered that the intercellular signals in this case were in fact electrical. The messages travel via ion channels, proteins on a cell's surface that control the flow of charged particles—in this case, potassium ions—into and out of a cell. The opening and closing of these channels can change the charges of neighboring cells, inducing them to release such particles and thereby relaying electrical signals from one cell to the next. "We've known that bacteria had ion channels and people have assigned them different functions, but only in the context of the single cell," Süel says. "Now we're seeing that they're also being used to coordinate behavior over millions of cells." The study appears in the journal Nature.

Electrical signaling of this type is also how neurons in our brain pass along information. This and other findings are therefore prompting scientists to reevaluate their assumptions about single-celled life. "Bacteria have been thought of as limited because they are not multicellular," says Steve Lockless, a biologist at Texas A&M University who was not involved in the study. But as unicellular organisms increasingly offer evidence of multifaceted behaviors, that may not be the case for much longer.

http://www.eurekalert.org/pub_releases/2016-03/aaft-cra030716.php

Compounds restore antibiotics' efficacy against MRSA

Antibiotics rendered useless by MRSA may get a second life

Japanese translation here

Antibiotics rendered useless by the notorious methicillin-resistant Staphylococcus aureus, (MRSA) may get a second life, thanks to compounds that can restore the bug's susceptibility to antibiotics, according to a new study in mice. The compounds have no antimicrobial activity on their own, but become lethal when combined with existing antibiotics, offering a potential combination strategy against MRSA. MRSA poses a major public health crisis worldwide and is the second leading cause of death from drug-resistant bacterial infections in the U.S. The bacteria have grown resistant to the entire class of β-lactam antibiotics, which includes penicillin and methicillin, creating an urgent need to develop new drugs

or, alternatively, boost the efficacy of existing ones. Here, Sang Ho Lee and colleagues conducted a drug screen for inhibitors of wall teichoic acid, a major structural component of the bacterial cell wall that is thought to buffer MRSA against the antimicrobial effects of β-lactams.

The researchers identified two synthetic compounds, which they named tarocin A and tarocin B, that block an enzyme that kickstarts wall teichoic acid production. In culture, the compounds on their own had no effect on MRSA growth, but when paired with β-lactams, killed various clinical strains of MRSA. Whereas mice succumbed to MRSA infection when treated with either tarocin or β-lactam alone, animals treated with both drugs showed markedly reduced infection and improved survival. The researchers say that with further development, tarocins may offer a new class of adjuvants for reviving β-lactam antibiotics' efficacy against MRSA.

http://www.eurekalert.org/pub_releases/2016-03/uon-rbm030916.php

Researchers build molecule that could significantly reduce brain damage in stroke victims

By suppressing stroke-related enzyme, molecule found to reduce brain damage by as much as 66 percent

Research teams separated by 14 hours and 9,000 miles have collaborated to advance prospective treatment for the world's second-leading cause of death.

University of Nebraska-Lincoln chemists partnered with medical researchers from the National University of Singapore to develop a molecule that can inhibit an enzyme linked with the onset of stroke.

Most strokes occur when a disruption of blood flow prevents oxygen and glucose from reaching brain tissue, ultimately killing neurons and other cells. The team found that its molecule, known as 6S, reduced the death of brain tissue by as much as 66 percent when administered to the cerebrum of a rat that had recently suffered a stroke.

It also appeared to reduce the inflammation that typically accompanies stroke, which the World Health Organization has estimated kills more than 6 million people annually.

"The fact that this inhibitor remained effective when given as post-stroke treatment ... is encouraging, as this is the norm in the treatment of acute stroke," the researchers reported in a March 9 study published by the journal ACS Central Science.

The inhibitor works by binding to cystathionine beta-synthase, or CBS - an enzyme that normally helps regulate cellular function but can also trigger production of toxic levels of hydrogen sulfide in the brain. Though hydrogen sulfide is an important signaling molecule at normal concentrations, stroke patients exhibit elevated concentrations believed to initiate the brain damage they often suffer.

Chemist David Berkowitz and his UNL colleagues modeled their inhibitor on a naturally occurring molecule produced by the CBS enzyme, tailoring the molecule's structure to improve its performance. By swapping out functional groups of atoms known as amines with hydrazines, the team ultimately increased the inhibitor's binding time from less than a second to hours.

"We wanted a compound that would bind well, specifically to this enzyme," said Berkowitz, a Willa Cather Professor of chemistry. "But we also wanted one that could be synthesized easily. Those are two very different considerations."

Berkowitz and his colleagues achieved the latter goal, in part, by plucking out the molecule's carbon-sulfur bond and replacing it with a double bond. Slicing that double bond gave the researchers two identical halves of the molecule. With the assistance of a Nobel Prize-winning technique called cross-metathesis, the team was then able to "synthesize two halves of the molecule for the price of one," Berkowitz said.

To test the effectiveness of the 6S molecule in treating stroke, Berkowitz and fellow UNL chemist Christopher McCune reached out to Peter Wong, professor of pharmacology at the National University of Singapore.

"We started researching this and came upon Peter's work pretty quickly," Berkowitz said. "We saw that he was one of the protagonists, one of the guys who is on the leading edge of understanding how (hydrogen sulfide) signaling works."

Though the research teams have never actually met in person, Berkowitz said videoconferencing and a steady stream of emails have helped overcome the barriers of time and distance. In the process, he said, each team has developed a profound appreciation for the other's work.

"Peter ended up latching onto the chemistry more than we did, and we ended up latching onto the biology," Berkowitz said. "It's actually been really fun. These are two kinds of science that are pretty far apart, and that's probably the most exciting thing about this: the interdisciplinary nature."

Because the 6S inhibitor has demonstrated its effects in cell cultures and the brain tissue of rats, Berkowitz cautioned that it represents just an initial step toward developing a stroke-treating drug for humans. However, he said the proof-of-principle experiments effectively illustrate the concept's promise.

Berkowitz also expressed optimism that the synthesis method detailed in the study could streamline the more general production of enzyme-targeting inhibitors.

"We started out with a very fundamental-science perspective on understanding the chemistry of this whole class of vitamin B6-dependent enzymes," he said. "We're in a good place now, because that science has allowed us to make these inhibitors

and many others. We're now working on several enzymes that may represent important targets for translation of the basic inhibitor chemistry into truly therapeutic goals."

Berkowitz, McCune and Wong co-authored the ACS Central Science study with Matthew Beio, UNL graduate student in chemistry; Weijun Shen, who earned a doctorate at UNL; Woo Jin Chung, a former UNL postdoctoral researcher; Laura Szczesniak, graduate student at SUNY Upstate Medical University; the National University of Singapore's Su Jing Chang and Shu Qing Koh; and the National Neuroscience Institute's Chou Chai.

http://www.eurekalert.org/pub_releases/2016-03/oup-opf030916.php

UP publishes free article collection about Fukushima Daiichi nuclear power plant disaster

March 11, 2016 marks five years since the Fukushima Daiichi nuclear power plant disaster.

In the last five years, researchers all over the world have been conducting substantial studies to find out the effect on the environment, human bodies, and our society. In honour of their great work, Oxford University Press (OUP) has made 30 research articles about the accident from nine journals freely available to read online for a year.

The virtual issue can be found here:

- ***Five years after Fukushima Daiichi nuclear power plant accident -- What has been the impact on the environment, human bodies, and society?***

http://www.oxfordjournals.org/our_journals/jrr/fukushima_article_collection.html

Example articles:

- ***Dependence of radiation dose on the behavioral patterns among school children: a retrospective analysis 18 to 20 months following the 2011 Fukushima nuclear incident in Japan*** ***http://jrr.oxfordjournals.org/content/57/1/1.full***
- ***Quantification of the increase in thyroid cancer prevalence in Fukushima after the nuclear disaster in 2011--a potential overdiagnosis?***

http://jjco.oxfordjournals.org/content/46/3/284.full

- ***Comparison of the accident process, radioactivity release and ground contamination between Chernobyl and Fukushima-1***

http://jrr.oxfordjournals.org/content/56/suppl_1/i56.full

http://www.bbc.com/news/health-35762713

'Stunning' operation regenerates eye's lens

A pioneering procedure to regenerate the eye has successfully treated children with cataracts in China.

By James Gallagher Health editor, BBC News website

More than half of all cases of blindness are caused by cataracts - the clouding of the eye's lens. An implanted lens is normally needed to restore sight, but the operation described in Nature activated stem cells in the eye to grow a new one.

Experts describe the breakthrough as one of the finest achievements in regenerative medicine.

The lens sits just behind the pupil and focuses light on to the retina. About 20 million people are blind because of cataracts, which become more common with age - although some children are born with them. Conventional treatment uses ultrasound to soften and break up the lens, which is then flushed out. An artificial intraocular lens must then be implanted back into the eye, but this can result in complications, particularly in children. The technique developed by scientists at the Sun Yat-sen University and the University of California, San Diego removes the cloudy cataract from inside the lens via a tiny incision.

Crucially it leaves the outer surface - called the lens capsule - intact. This structure is lined with lens epithelial stem cells, which normally repair damage.

The scientists hoped that preserving them would regenerate the lens. The team reported that tests on rabbits and monkeys were successful, so the approach was trialled in 12 children. Within eight months the regenerated lens was back to the same size as normal.

Dr Kang Zhang, one of the researchers, told the BBC News website: "This is the first time an entire lens has been regenerated. The children were operated on in China and they continue to be doing very well with normal vision." It also showed a dramatically lower complication rate "by almost every measure, supporting the superiority of the treatment".

However, he says larger trials are needed before it should become the standard treatment for patients.

The procedure was tried in children because their lens epithelial stem cells are more youthful and more able to regenerate than in older patients. Yet the overwhelming majority of cataracts are in the elderly. Dr Zhang says tests have already started on older pairs of eyes and says the early research "looks very encouraging".

Commenting on the findings, Prof Robin Ali from the UCL Institute of Ophthalmology, said the work was "stunning". He told the BBC News website: "This new approach offers greatly improved prospects for the treatment of paediatric cataracts as it results in regeneration of a normal lens that grows naturally." He said getting similar results in adults "is likely to be more difficult to achieve" but could "have a major impact". "It might be superior to the artificial lenses that are currently implanted, as the natural lenses should be able to accommodate looking at different distances more effectively," he added.

Dr Dusko Ilic, a reader in stem cell science at King's College London, said: "The study is one of the finest achievements in the field of regenerative medicine until now. "It is science at its best."

Far-reaching

Dr Zhang believes that targeting stem cells already sitting in the eye could have "great potential" for treating a wide range of diseases from macular degeneration to glaucoma.

A separate study by Osaka University in Japan and Cardiff University, used stem cells to mirror the development of the eye. They were able to produce a range of specialised eye tissues including those that make the cornea, conjunctiva, lens and retina. The findings, also published in Nature, showed the lab-grown tissues could restore sight to rabbits with corneal blindness.

One of the researchers, Prof Andrew Quantock, said: "Our work not only holds potential for developing cells for treatment of other areas of the eye, but could set the stage for future human clinical trials of anterior eye transplantation to restore visual function."

http://nyti.ms/22d0nX6

New Procedure Allows Kidney Transplants From Any Donor

Successful alteration of patients' immune systems allows them to accept kidneys from incompatible donors

By GINA KOLATA MARCH 9, 2016

Clint Smith, at home in New Orleans, had a procedure that altered his immune system to allow his body to accept a kidney from an incompatible donor. It "changed my life," he said. **William Widmer for The New York Times**

In the anguishing wait for a new kidney, tens of thousands of patients on waiting lists may never find a match because their immune systems will reject almost any transplanted organ. Now, in a large national study that experts are calling revolutionary, researchers have found a way to get them the desperately needed procedure.

In the new study, published Wednesday in The New England Journal of Medicine, doctors successfully altered patients' immune systems to allow them to accept kidneys from incompatible donors. Significantly more of those patients were still alive after eight years than patients who had remained on waiting lists or received a kidney transplanted from a deceased donor.

The method, known as desensitization, "has the potential to save many lives," said Dr. Jeffery Berns, a kidney specialist at the University of Pennsylvania's Perelman School of Medicine and the president of the National Kidney Foundation.

It could slash the wait times for thousands of people and for some, like Clint Smith, a 56-year-old lawyer in New Orleans, mean the difference between receiving a transplant and spending the rest of their lives on dialysis.

The procedure, Mr. Smith said, "changed my life."

Researchers estimate about half of the 100,000 people in the United States on waiting lists for a kidney transplant have antibodies that will attack a transplanted organ, and about 20 percent are so sensitive that finding a compatible organ is all but impossible. In addition, said Dr. Dorry Segev, the lead author of the new study and a transplant surgeon at the Johns Hopkins University School of Medicine, an unknown number of people with kidney failure simply give up on the waiting lists after learning that their bodies would reject just about any organ. Instead, they resign themselves to dialysis, a difficult and draining procedure that can pretty much take over a person's life.

Desensitization involves first filtering the antibodies out of a patient's blood. The patient is then given an infusion of other antibodies to provide some protection while the immune system regenerates its own antibodies. For some reason — exactly why is not known — the person's regenerated antibodies are less likely to attack the new organ, Dr. Segev said. But if the person's regenerated natural antibodies are still a concern, the patient is treated with drugs that destroy any white blood cells that might make antibodies that would attack the new kidney.

The process is expensive, costing $30,000, and uses drugs not approved for this purpose. The transplant costs about $100,000. But kidney specialists argue that desensitization is cheaper in the long run than dialysis, which costs $70,000 a year for life.

Although by far the biggest use of desensitization would be for kidney transplants, the process might be suitable for living-donor transplants of livers and lungs, researchers said. The liver is less sensitive to antibodies so there is less need for desensitization, "but it's certainly possible if there are known incompatibilities," Dr. Segev said. With lungs, he said, desensitization "is theoretically possible," although he said he was not aware of anyone doing it yet.

In the new study, 1,025 patients at 22 medical centers who had an incompatible donor were compared to an equal number of patients who remained on waiting lists for an organ or who had an organ from a deceased but compatible donor. After eight years, 76.5 percent of those who received an incompatible kidney were still alive, compared with 62.9 percent who remained on the waiting list or received a deceased donor kidney and 43.9 percent who remained on the waiting list but never got a transplant.

The desensitization procedure takes time — for some patients as long as two weeks — and is performed before the transplant operation, so patients must have a

living donor. It is not known how many have someone willing to donate a kidney, but doctors say they often see situations in which a relative or even a friend is willing to donate but is incompatible.

"Often patients are told that their living donor is incompatible, so they are stuck on waiting lists," for a deceased donor, Dr. Segev said.

In recent years, an option called a kidney exchange has helped some in this situation. Patients who have incompatible living donors can swap donors with someone whose donor may be compatible with them. Often, there are chains of patient-donor pairs leading to a compatible organ swap.

That process can be successful, said Dr. Krista L. Lentine, the medical director of the living donation program at the Saint Louis Center for Transplantation, but patients often still cannot find a compatible organ because they have antibodies that would reject almost every kidney. In those cases, "desensitization may be the only realistic option for receiving a transplant," said Dr. Lentine, who was not involved with the study.

Dr. Jeffrey Campsen, a transplant surgeon at the University of Utah Health Sciences Center who also was not a study investigator, said his group focused on exchanges and had been fairly successful. But he also comes across patients whose donors do not want to participate. "There is a hurdle if the donor and patient have an emotional bond," he said.

The new data showing the success of desensitization "lets people get behind it," Dr. Campsen said, adding, "I do think it is something we would consider."

Mr. Smith, the New Orleans patient who went through desensitization, had progressive kidney disease that slowly scarred his kidneys until, in 2004, they stopped functioning. His sister-in-law, Allison Sutton, donated a kidney to him, and he had a transplant, but after six and a half years, it failed. He went on dialysis, spending four days a week hooked up to dialysis machines for hours. It was keeping him alive, he told his friends, but it was not a life.

Then a nurse suggested that he ask Johns Hopkins about its desensitization study. "I was like, whatever I could do," he said. He discovered that he qualified for the study. But he needed a donor.

One day, his wife, Sheryl Smith, was talking on the phone to a college friend, Angela Watkins, who lives in Augusta, Ga., and mentioned that Mr. Smith was praying for a donor. Mrs. Watkins's husband, David Watkins, a judge in state court, had been friends with Mr. Smith in college and the two wives, also college friends, had kept in touch over the years.

Mrs. Watkins told her husband about the conversation, and they asked themselves if they should offer to donate.

"We talked and researched and prayed," Judge Watkins said. Finally, he said, they came to a conclusion. "We have a moral obligation to at least see if we would qualify." And he thought that he should be the one to go first. If he did not qualify, his wife could be tested.

Mr. Smith warned his old friend that donating was an enormous undertaking. "He said, 'You can't grasp what you are doing.' I heard him but it didn't register," Judge Watkins said. "I told him, 'I have something you need, so what's the big deal?' "

Of course, it was a big deal. Although Judge Watkins had prepared by getting himself in top physical shape, it still took about six months to recover from the operation.

That was four years ago, and Mr. Smith's new kidney is still functioning and he is back to his active life, forever grateful to his friend.

"Every night," he says, "during my nightly prayers with my wife, I thank God for bringing David and Allison to me and for giving me the gift of life.

"But for David giving me this gift, I would still be in that dialysis chair."

http://www.eurekalert.org/pub_releases/2016-03/ru-ehh030916.php

Early human habitat, recreated for first time, shows life was no picnic

Pioneering Rutgers scientist helps reconstruct an ancient East African landscape where human ancestors lived 1.8 million years ago

Scientists have pieced together an early human habitat for the first time, and life was no picnic 1.8 million years ago.

Our human ancestors, who looked like a cross between apes and modern humans, had access to food, water and shady shelter at a site in Olduvai Gorge, Tanzania. They even had lots of stone tools with sharp edges, said Gail M. Ashley, a professor in the Rutgers Department of Earth and Planetary Sciences in the School of Arts and Sciences.

This is an artist's rendition of an early human habitat in East Africa 1.8 million years ago. **M.Lopez-Herrera via The Olduvai Paleoanthropology and Paleoecology Project and Enrique Baquedano.**

But "it was tough living," she said. "It was a very stressful life because they were in continual competition with carnivores for their food."

During years of work, Ashley and other researchers carefully reconstructed an early human landscape on a fine scale, using plant and other evidence collected at the sprawling site. Their pioneering work was published recently in the Proceedings of the National Academy of Sciences.

The landscape reconstruction will help paleoanthropologists develop ideas and models on what early humans were like, how they lived, how they got their food (especially protein), what they ate and drank and their behavior, Ashley said.

Famous paleoanthropologist Mary Leakey discovered the site in 1959 and uncovered thousands of animal bones and stone tools. Through exhaustive excavations in the last decade, Ashley, other scientists and students collected numerous soil samples and studied them via carbon isotope analysis.

The landscape, it turned out, had a freshwater spring, wetlands and woodland as well as grasslands.

"We were able to map out what the plants were on the landscape with respect to where the humans and their stone tools were found," Ashley said. "That's never been done before. Mapping was done by analyzing the soils in one geological bed, and in that bed there were bones of two different hominin species."

The two species of hominins, or early humans, are Paranthropus boisei - robust and pretty small-brained - and Homo habilis, a lighter-boned species. Homo habilis had a bigger brain and was more in sync with our human evolutionary tree, according to Ashley. Both species were about 4.5 to 5.5 feet tall, and their lifespan was likely about 30 to 40 years.

Through their research, the scientists learned that the shady woodland had palm and acacia trees. They don't think the hominins camped there. But based on the high concentration of bones, the primates probably obtained carcasses elsewhere and ate the meat in the woods for safety, Ashley said.

In a surprising twist, a layer of volcanic ash covered the site's surface, nicely preserving the bones and organic matter, said Ashley, who has conducted research in the area since 1994.

"Think about it as a Pompeii-like event where you had a volcanic eruption," she said, noting that a volcano is about 10 miles from the site. The eruption "spewed out a lot of ash that completely blanketed the landscape."

On the site, scientists found thousands of bones from animals such as giraffes, elephants and wildebeests, swift runners in the antelope family. The hominins may have killed the animals for their meat or scavenged leftover meat. Competing carnivores included lions, leopards and hyenas, which also posed a threat to hominin safety, according to Ashley.

Paleoanthropologists "have started to have some ideas about whether hominins were actively hunting animals for meat sources or whether they were perhaps scavenging leftover meat sources that had been killed by say a lion or a hyena," she said.

"The subject of eating meat is an important question defining current research on hominins," she said. "We know that the increase in the size of the brain, just the evolution of humans, is probably tied to more protein." The hominins' food also may have included wetland ferns for protein and crustaceans, snails and slugs.

Scientists think the hominins likely used the site for a long time, perhaps tens or hundreds of years, Ashley said.

"We don't think they were living there," she said. "We think they were taking advantage of the freshwater source that was nearby."

The study was conducted by Ashley; Clayton R. Magill of the Geological Institute in Zurich, Switzerland; Manuel Domínguez-Rodrigo of Complutense University in Madrid, Spain; and Katherine H. Freeman of Pennsylvania State University.

http://www.eurekalert.org/pub_releases/2016-03/uops-wuk031016.php

Widely used kidney cancer drugs can't stop recurrence

Sunitinib or sorafenib after surgery should not be pursued, Abramson cancer center researcher says

PHILADELPHIA -- Two widely used targeted therapy drugs approved by the FDA for the treatment of metastatic kidney cancer--sorafenib and sunitinib--are no more effective than a placebo in preventing return of the disease to increase life spans of patients suffering from advanced kidney cancer after surgery, according to a new multi-institutional study in the *Lancet* led by a researcher at the Abramson Cancer Center (ACC) of the University of Pennsylvania.

Naomi B. Haas, MD, an associate professor in the division of Hematology/Oncology at the Perelman School of Medicine and director of the Prostate and Kidney Cancer Program at the ACC, and her colleagues in the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN), treated 1,943 patients in the United States and Canada with one year of sorafenib, sunitinib, or a placebo drug after surgery to remove their kidney tumors. The study found no difference in median years of disease-free survival in the adjuvant setting (post-surgery): 5.8 years for sunitinib; 6.1 years for sorafenib; and 6.6 years for placebos.

Although the study did not establish a role for the drugs in the adjuvant setting, it has provided a definitive answer about their use that will help prevent any associated costs and toxic effects.

Preliminary results of this randomized, double-blind phase III trial, known as ASSURE, were presented last year during the American Society of Clinical Oncology 2015 Genitourinary Cancers Symposium.

The study involved patients and researchers from 226 centers, including Massachusetts General Hospital and the Dana Farber Cancer Institute. Robert Uzzo, MD, chair of Surgery, and Yu Ning Wong, MD, an associate professor of Medicine, at Fox Chase Cancer Center -- Temple Health in Philadelphia, served as co-authors.

While surgery is typically the best initial treatment for renal tumors, surgical resection alone is not enough to prevent return of the disease in many patients. Adjuvant therapies (applied after initial treatment with the goal of suppressing secondary tumor formation) are often needed to improve survival.

Sunitinib and sorafenib are examples of adjuvant therapies known as kinase inhibitors. Kinases are proteins on or near the surface of cells; they help cancer grow and survive. Kinase inhibitors block the growth of kinases and associated blood vessels which nourish cancers. Sorafenib and sunitinib, which are taken in pill form on a daily basis, are thought to block different kinases.

Both drugs have been shown to be effective when kidney cancer has spread to other parts of the body. Could they also be effective in preventing recurrence of the disease?

"The current standard of care for these patients is close observation," Haas said. "Unfortunately, we found that the use of sunitinib or sorafenib in this setting did not reduce the incidence of recurrence as compared to placebo. Fortunately, the use of these drugs in this setting did not appear to make the outcome of patients receiving them any worse."

The findings closely mirror those of adjuvant trials in other tumors, such as breast and metastatic colorectal cancers, in which the benefits of bevacizumab in metastatic disease were not seen in the adjuvant setting.

This study, designed and conducted by ECOG-ACRIN, is the first and largest trial on the effectiveness of these two kinase inhibitors in patients whose kidney tumors have been completely removed and who are at high risk for recurrence. Haas said that there are other ongoing adjuvant trials investigating different lengths of therapy with sunitinib and sorafenib, as well as different kinase inhibitors. The results of these investigations are not yet available and could have different results than the Penn study.

"It is important to support these trials so we learn how to better treat kidney cancer in the adjuvant setting," she said.

In the early years of the trial, about a third of patients stopped treatment because they found the side effects, such as hypertension and fatigue, of the medications too hard to tolerate.

Patients in the study also contributed blood and urine samples as a part of their participation. Ongoing analyses of these samples may shed light on who might still benefit or not benefit from sunitinib and sorafenib in the treatment of kidney cancer in the adjuvant setting or point to other therapies that target specific pathways or tap into the immune system.

Haas and her colleagues collected the samples at the beginning of treatment and subsequent to recurrence of the cancer in patients who suffered a relapse -- and continue to do so more than five years after the formal conclusion of the study.

"This will afford opportunities to uncover molecular clues and other information that could help explain why some patients had a recurrence of their cancer or a spreading elsewhere and others did not," Haas said.

There are also plans for a perioperative trial with an immune checkpoint inhibitor with this group of patients set to open in the near future.

ECOG-ACRIN Cancer Research Group is a membership-based scientific organization that focuses on cancer research involving adults who have or are at risk of developing cancer. It is comprised of nearly 1100 member institutions, including Penn Medicine.

This study was funded by Public Health Service Grants to the ECOG-ACRIN Cancer Research Group, Pfizer and Bayer.

http://www.eurekalert.org/pub_releases/2016-03/aaft-tpb030716.php

The plastic-eating bacteria breakdown

Researchers have identified a species of bacteria that uses just two enzymes to break down plastic.

Poly(ethylene terephthalate), or PET, is a type of polymer used in plastic that is highly resistant to biodegradation. About 56 million tons of PET was produced worldwide in 2013 alone, and the accumulation of PET in ecosystems around the globe is increasingly problematic. To date, very few species of fungi - but no bacteria - have been found to break down PET. Here, Yoshida et al. collected 250 samples of PET debris and screened for bacterial candidates that depend on PET film as a primary source of carbon for growth. They identified a novel bacterium, which they named Ideonella sakaiensis 201-F6, which could nearly completely degrade a thin film of PET after six weeks at a temperature of 30° Celsius. Further investigation identified an enzyme, ISF6_4831, which works with water to break down PET into an intermediate substance, which is then further broken down by a second enzyme, ISF6_0224. These two enzymes alone can break down PET into its simpler building blocks. Remarkably, these enzymes seem to be highly unique in their function compared to the closest related known enzymes of other bacteria, raising questions of how these plastic-eating bacteria evolved. A Perspective by Uwe Bornscheuer describes these findings in greater detail.

http://www.eurekalert.org/pub_releases/2016-03/kcl-lbg030916.php

Link between gum disease and cognitive decline in Alzheimer's

A new study jointly led by King's College London and the University of Southampton has found a link between gum disease and greater rates of cognitive decline in people with early stages of Alzheimer's Disease.

Periodontitis or gum disease is common in older people and may become more common in Alzheimer's disease because of a reduced ability to take care of oral hygiene as the disease progresses. Higher levels of antibodies to periodontal bacteria are associated with an increase in levels of inflammatory molecules elsewhere in the body, which in turn has been linked to greater rates of cognitive decline in Alzheimer's disease in previous studies.

The latest study, published in the journal PLOS ONE, set out to determine whether periodontitis or gum disease is associated with increased dementia severity and subsequent greater progression of cognitive decline in people with Alzheimer's disease.

In the observational study, 59 participants with mild to moderate Alzheimer's Disease were cognitively assessed and a blood sample was taken to measure inflammatory markers in their blood. Participants' dental health was assessed by a dental hygienist who was blind to cognitive outcomes. The majority of participants (52) were followed-up at six months when all assessments were repeated.

The presence of gum disease at baseline was associated with a six-fold increase in the rate of cognitive decline in participants over the six-month follow-up period of the study. Periodontitis at baseline was also associated with a relative increase in the pro-inflammatory state over the six-month follow-up period. The authors conclude that gum disease is associated with an increase in cognitive decline in Alzheimer's Disease, possibly via mechanisms linked to the body's inflammatory response.

Limitations of the study included the small number of participants; the authors advise that the study should be replicated ideally with a larger cohort. The precise mechanisms by which gum disease may be linked to cognitive decline are not fully clear and other factors might also play a part in the decline seen in participants' cognition alongside their oral health.

However, growing evidence from a number of studies links the body's inflammatory response to increased rates of cognitive decline, suggesting that it would be worth exploring whether the treatment of gum disease might also benefit the treatment of dementia and Alzheimer's Disease.

Professor Clive Holmes, senior author from the University of Southampton, says: "These are very interesting results which build on previous work we have done that shows that chronic inflammatory conditions have a detrimental effect on disease progression in people with Alzheimer's disease. Our study was small and lasted for six months so further trials need to be carried out to develop these results. However, if there is a direct relationship between periodontitis and cognitive decline, as this current study suggests, then treatment of gum disease might be a possible treatment option for Alzheimer's."

Dr Mark Ide, first author from the Dental Institute at King's College London says: "Gum disease is widespread in the UK and US, and in older age groups is thought to be a major cause of tooth loss. In the UK in 2009, around 80% of adults over 55 had evidence of gum disease, whilst 40% of adults aged over 65-74 (and 60% of those aged over 75) had less than 21 of their original 32 teeth, with half of them reporting gum disease before they lost teeth.

"A number of studies have shown that having few teeth, possibly as a consequence of earlier gum disease, is associated with a greater risk of developing dementia. We also believe, based on various research findings, that the presence of teeth with active gum disease results in higher body-wide levels of the sorts of inflammatory molecules which have also been associated with an elevated risk of other outcomes such as cognitive decline or cardiovascular disease. Research has suggested that effective gum treatment can reduce the levels of these molecules closer to that seen in a healthy state.

"Previous studies have also shown that patients with Alzheimer's Disease have poorer dental health than others of similar age and that the more severe the dementia the worse the dental health, most likely reflecting greater difficulties with taking care of oneself as dementia becomes more severe."

http://www.medscape.com/viewarticle/859942

Zika Questions From Medscape Readers: The CDC Responds

Questions and concerns posed by Medscape readers and answered by CDC

Denise Jamieson, MD, MPH

Editor's Note:

Medscape works with the Zika team at the Centers for Disease Control and Prevention (CDC) so that we can bring our readers the very latest information on identifying and treating Zika virus. The following are questions and concerns posed by Medscape readers and answered by CDC. You will find all of our Zika-related information in the Zika Virus Resource Center.

What Is the Prevalence of Microcephaly in Regions and Countries Affected by the Zika Virus?

It is difficult to monitor microcephaly in populations because the term is defined and used inconsistently. It may not be possible to diagnose microcephaly until late

in the second or early in the third trimester of pregnancy. Sometimes, microcephaly is not diagnosed until after birth.

Birth defect programs in each country may collect prevalence data in different ways. The outbreak of Zika virus infection in Brazil occurred earlier than in many other countries.

It is possible that other countries will start to see microcephaly or other adverse pregnancy outcomes later as the Zika virus outbreak evolves, additional pregnant women in areas with Zika virus transmission receive prenatal care and testing, and pregnant women deliver. These factors may affect estimates of prevalence and explain some of the differences in estimates between countries.

What Is the Long-term Risk of Zika Virus for Pregnant Women, Infants, and Children?

Zika virus can pass from a pregnant woman to her fetus during pregnancy. We do not know how often this occurs. We do not know the likelihood of a fetus developing birth defects if the mother is infected with Zika while she is pregnant. Currently, there is no evidence to suggest that Zika virus, after it is cleared from the pregnant woman's blood, poses a risk for birth defects in future pregnancies.

Information on long-term outcomes among infants and children with acute Zika virus disease is limited.

Most children infected with Zika virus are asymptomatic or have mild illness, similar to the findings seen in adults with Zika virus infection. (For more on children and Zika virus, see "Zika for Pediatricians: Critical Update."

When Are Pregnant Women Most at Risk for Fetal Effects?

We do not know when pregnant women are most at risk for fetal effects. Pregnant women can be infected with Zika virus at any time of their pregnancy. Zika virus can be passed from a mother to her fetus during pregnancy. CDC is investigating the link between Zika and microcephaly.

(For more information, see "Advising Pregnant Women About Zika: The Latest Guidance From CDC."

Does Zika Immunity Result After an Infection?

If Zika behaves like similar infections, once you have been infected with Zika virus, you are likely to be protected from future infections.

Are There Other Possibilities That Might Explain the Increase in Microcephaly Cases in Brazil?

Microcephaly can happen for many reasons, including genetics, maternal infections, and exposure to toxins during pregnancy. Results of recent epidemiologic and laboratory studies performed in Brazil strongly suggest but don't yet prove a link between Zika virus infection during pregnancy and microcephaly.

You may have heard recent media reports suggesting that a pesticide called pyriproxyfen might be linked with microcephaly. These media reports stem from a single publication authored by an Argentine physicians' organization, which claims that the use of pyriproxyfen in drinking water in Brazil is responsible for the country's increase in microcephaly cases.

Pyriproxyfen is a registered pesticide in Brazil and other countries and has been used for decades.

A team of scientists from the World Health Organization (WHO) recently reviewed data on the toxicology of pyriproxyfen, one of 12 larvicides that WHO recommends to reduce mosquito populations.

It found no evidence that the larvicide affects the course of pregnancy or the development of a fetus. The US Environmental Protection Agency and EU investigators reached a similar conclusion when they carried out a separate review of the product.

CDC is working closely with international partners to study infants with microcephaly to better understand what role various factors, including Zika virus, may play in this birth defect.

Have There Been Any Reports of Airborne Transmission of Zika Virus?

There have been no documented cases of airborne transmission of Zika virus. Zika virus, like other flaviviruses, such as dengue and chikungunya, is spread primarily through the bite of an infected mosquito.

What Is the Zika Virus Incubation Period?

Although the exact incubation period of Zika virus has yet to be determined, evidence from case reports and experience from related flavivirus infections indicate that the incubation period is probably 3 days to 2 weeks.

How Long Does Zika Virus Infectivity Last?

Zika virus usually remains in the blood of an infected person for about a week. We do not know how long Zika virus is present in the semen of men who have been infected.

Evidence suggests that Zika virus can be detected in the semen longer than in the blood. One report found the virus in semen at least 2 months after illness, but this was not a test for live virus; therefore, we do not know if the semen was infectious. Another report found live virus in the semen at least 2 weeks after illness onset. In both of these cases, no follow-up testing was done to determine when Zika virus was no longer present in the semen.

At this time, we do not know how long after exposure Zika virus can be sexually transmitted from a male partner.

Public Information from the CDC and Medscape

http://www.eurekalert.org/pub_releases/2016-03/uos-riq031016.php

Retirement is good for your health

Study finds that retirement leads to positive lifestyle changes

A landmark study led by University of Sydney has found that people become more active, sleep better and reduce their sitting time when they retire.

Published in the Journal of Preventative Medicine, the study followed the lifestyle behaviours of 25,000 older Australians including physical activity, diet, sedentary behaviour, alcohol use and sleep patterns.

"Our research revealed that retirement was associated with positive lifestyle changes," said lead researcher Dr Melody Ding, Senior Research Fellow at the University's School of Public Health.

"Compared with people who were still working, retirees had increased physically activity levels, reduced sitting time, were less likely to smoke, and had healthier sleep patterns.

"A major life change like retirement creates a great window of opportunity to make positive lifestyle changes - it's a chance to get rid of bad routines and engineer new, healthier behaviours." she said.

The data revealed that retirees:

Increased physical activity by 93 minutes a week
Decreased sedentary time by 67 minutes per day
Increased sleep by 11 minutes per day
50 per cent of female smokers stopped smoking

The differences were significant even after adjusting for factors such as age, sex, urban/rural residence, marital status and education. There was no significant association found between retirement and alcohol use or fruit and vegetable consumption.

Dr Ding said retirement gave people more time to pursue healthier lifestyles.

"The lifestyle changes were most pronounced in people who retire after working full-time. When people are working and commuting, it eats a lot of time out of their day. When they retire, they have time to be physically active and sleep more," she said.

"In terms of sedentary time, the largest reduction in sitting time occurred in people who lived in urban areas and had higher educational levels.

Dr Ding's mother's experience of retirement was a trigger for the study.

"My mother still lives in China and they have mandatory retirement for women at age 55. When she turned 55 she was really anxious about stopping work -- she felt like she was not as valuable. So I thought I'd like to find some positive information about retirement."

"She now spends her days enjoying so many hobbies, she can't remember how she had time to work."

Retired bank manager Des (89 years) said: "I have more time in my retirement and I am happily busy. I keep fit by dancing four times a week and walking. I keep my mind active by involvement in the University of the Third Age, teaching computer skills and dancing to the oldies, most of them are younger than me.

"My answering machine message is 'I am out enjoying my retirement'," he said.

Dr Ding hopes the research will encourage people to think positively about retirement.

"We hope this information could translate to better health in older Australians, preventing cardiovascular disease and diabetes," she said.

"Retirement is a good time for doctors to talk their patients about making positive lifestyle changes that could add years to their life.

"The findings suggest that both health professionals and policy makers should consider developing special programs for retirees to capitalise on the health transitions through retirement," Dr Ding said.

http://www.eurekalert.org/pub_releases/2016-03/ip-dko030916.php

Different kinds of physical activity shown to improve brain volume & cut Alzheimer's risk in half

Combined UCLA and University of Pittsburgh study links increased brain volumes with improved memory health

LOS ANGELES, CA/PITTSBURGH, PA - A new study shows that a variety of physical activities from walking to gardening and dancing can improve brain volume and cut the risk of Alzheimer's disease by 50%.

This research, conducted by investigators at UCLA Medical Center and the University of Pittsburgh, is the first to show that virtually any type of aerobic physical activity can improve brain structure and reduce Alzheimer's risk. The study, funded by the National Institute of Aging, was published on March 11 in the Journal of Alzheimer's Disease.

The researchers studied a long-term cohort of patients in the 30-year Cardiovascular Health Study, 876 in all, across four research sites in the United States. These participants had longitudinal memory follow up, which also included standard questionnaires about their physical activity habits. The research participants, age 78 on average, also had MRI scans of the brain analyzed by advanced computer algorithms to measure the volumes of brain structures including those implicated in memory and Alzheimer's such as the hippocampus. The physical activities performed by the participants were correlated to the brain volumes and spanned a wide variety of interests from gardening and dancing to

riding an exercise cycle at the gym. Weekly caloric output from these activities was summarized.

The results of the analysis showed that increasing physical activity was correlated with larger brain volumes in the frontal, temporal, and parietal lobes including the hippocampus. Individuals experiencing this brain benefit from increasing their physical activity experienced a 50% reduction in their risk of Alzheimer's dementia. Of the roughly 25% in the sample who had mild cognitive impairment associated with Alzheimer's, increasing physical activity also benefitted their brain volumes.

Said lead author Cyrus A. Raji, MD, PhD, of UCLA, "This is the first study in which we have been able to correlate the predictive benefit of different kinds of physical activity with the reduction of Alzheimer's risk through specific relationships with better brain volume in such a large sample."

George Perry, PhD, Editor in Chief of Journal of Alzheimer's Disease, added, "Currently the greatest promise in Alzheimer's disease research is lifestyle intervention including increased exercise. Raji et al present a landmark study that links exercise to increases in grey mater and opens the field of lifestyle intervention to objective biological measurement."

According to the Alzheimer's Association, Alzheimer's disease currently affects 5.1 million Americans and is projected to increase to13.8 million over the next 30 years. Dr. Raji commented, "We have no magic bullet cure for Alzheimer's disease. Our focus needs to be on prevention."

http://www.bbc.com/news/science-environment-35783598

Fossil reptile discovery 'something extraordinary'

A newly discovered 250-million-year-old fossil reptile from Brazil gives an "extraordinary" insight into life just before the dinosaurs appeared.

By Helen Briggs BBC News

The reptile lived near lakes and rivers, feeding on smaller reptiles **Voltaire Neto**

At the time, the world was recovering from a massive extinction that wiped out most living species.

The reptile, named Teyujagua or "fierce lizard", is the close relative of a group that gave rise to dinosaurs, crocodiles and birds.

The fossil is "beautiful" and fills an evolutionary gap, say scientists.

Dr Richard Butler from the University of Birmingham said the animal is a new species that has not been previously known. "It's very close to the ancestry of a very important group of reptiles called archosauriforms," the co-researcher on the study, published in the journal Scientific Reports, told BBC News. "It helps us understand how that group evolved."

The skull of the reptile is exceptionally well preserved **Scientific Reports**

'Beautiful skull'

Teyujagua paradoxa was a small crocodile-like animal that probably lived at the side of lakes, feeding on fish.

The ancient reptile lived just after a mass extinction event 252 million years ago that was thought to have been triggered by a string of volcanic eruptions.

About 90% of living species were lost, creating a niche for other animals, such as Teyujagua, to flourish. The reptile - and its close relatives the archosauriforms - became the dominant animals on land and eventually gave rise to the dinosaurs.

Dr Felipe Pinheiro, from Universidade Federal do Pampa, São Gabriel, Rio Grande do Sul, is among the scientists from three Brazilian universities who discovered the well-preserved fossil skull near the southern city of São Francisco de Assis. "The discovery of Teyujagua was really exciting," he said.

"Ever since we saw that beautiful skull for the first time in the field, still mostly covered by rock, we knew we had something extraordinary in our hands. "Back in the lab, after slowly exposing the bones, the fossil exceeded our expectations.

"It had a combination of features never seen before, indicating the unique position of Teyujagua in the evolutionary tree of an important group of vertebrates."

Teyujagua is different from other fossils from the same era.

Its anatomy is somewhere between that of more primitive reptiles and the archosauriforms, which include all dinosaurs and pterosaurs (flying reptiles), along with modern day birds and crocodiles.