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NEWS

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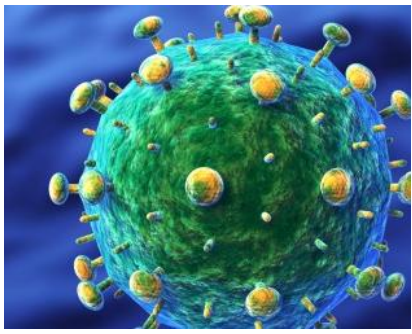
EDITOR'S CHOICE



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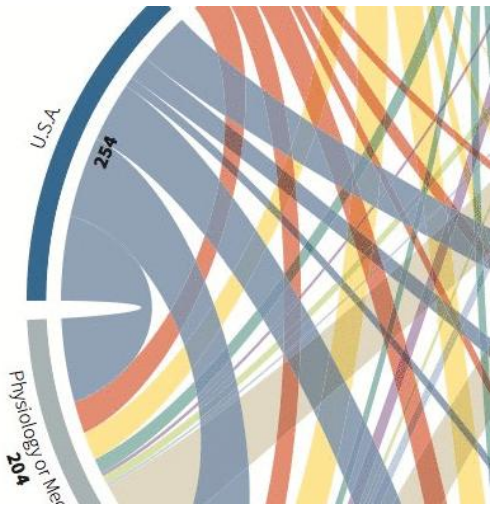
PICTURE STATION

ARTICLE

COMMON SCIENCE



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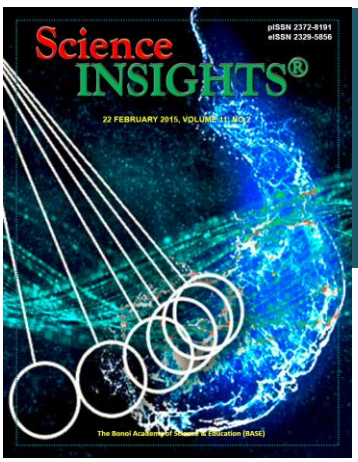

COVER
Flurbiprofen has superior analgesic effect over tramadol and butorphanol in locally-restricted injury like lumpectomy suggesting that conquering peripheral inflammatory responses evoked by surgical lesion is much more effective in controlling the pain than those drugs functioning through the CNS-associated mechanisms. See page 322.
Image: BASE illustrating group

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BASE

THE BONOI ACADEMY OF SCIENCE & EDUCATION

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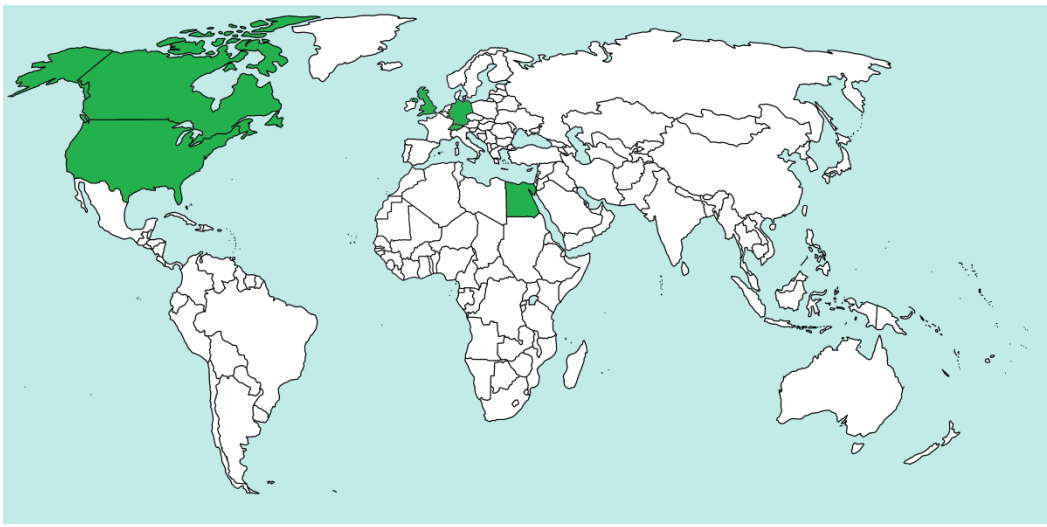
Love the Wave
Love the Earth

Seattle, USA

Andromeda Galaxy

The Hubble Space Telescope has captured a new photo of the Andromeda Galaxy showing striking details of the bright galaxy, which is located about 2.5 million light-years from Earth. While that may seem far away, Hubble usually trains its view on more distant targets. Because Andromeda fills up so much of Hubble's field of view, the telescope was able to capture incredible detail in its survey of the galaxy. The newly-released image stretches across about 48,000 light-years of the galaxy's disk, according to Hubble officials. In total, the image shows more than 100 million stars in the galaxy. Hubble officials revealed the new photo during a news conference here at the 225th meeting of the American Astronomical Society. "Hubble traces densely packed stars extending from the innermost hub of the galaxy, seen at left," Hubble representatives said in a statement. "Moving out from this central galactic bulge, the panorama sweeps from the galaxy's central bulge across lanes of stars and dust to the sparser outer disk." Scientists can use this image to help them interpret other spiral galaxies like the Andromeda galaxy that might have similar light signatures, but are farther from Earth. The panorama was created as part of the Panchromatic Hubble Andromeda Treasury program. This image was created as a mosaic of 7,398 exposures taken over the course of 411 pointings of the telescope, according to Hubble officials. "Large groups of young blue stars indicate the locations of star clusters and star-forming regions. The stars bunch up in the blue ring-like feature toward the right side of the image," Hubble representatives said in the same statement. "The dark silhouettes trace out complex



dust structures. Underlying the entire galaxy is a smooth distribution of cooler red stars that trace Andromeda's evolution over billions of years." Andromeda and the Milky Way are on the way toward a crash of cosmic proportions. The two galaxies will merge, forming one new galaxy billions of years from now. *By Miriam Kramer*. *Original article on Space.com.*■

London, UK

"God Particle" Higgs Boson Can Save the Universe?

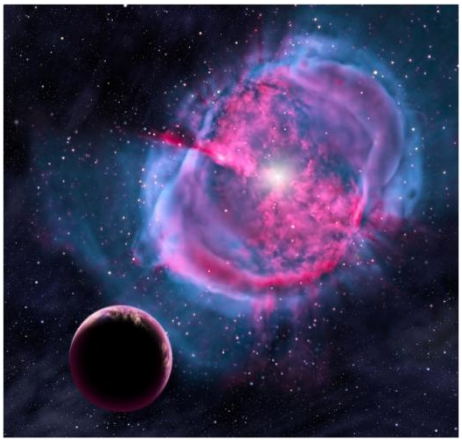
The recently discovered Higgs boson, which helps give particles their mass, could have destroyed the cosmos shortly after it was born, causing the universe to collapse just after the Big Bang. But gravity, the force that keeps planets and stars together, might have kept this from happening, scientists say. In 2012, scientists confirmed the detection of the long-sought Higgs boson, also known by its nickname the "God particle," at the Large Hadron Collider, the most powerful particle accelerator on the planet. This particle helps give mass to all elementary particles that have mass, such as electrons and protons. Elementary particles that do not have mass, such as the photons that make up light, do not get mass from the Higgs boson. The experiments that detected the Higgs boson revealed it had a mass of 125 billion electron-volts, or more than 130 times the mass of the proton. However, this discovery led to a mystery — at that mass, the Higgs boson should have destroyed the universe just after the Big Bang. This is because Higgs particles attract each other at high energies. For this to happen, the energies must be extraordinarily high, "at least a million times higher than the LHC can reach," study co-author Arttu Rajantie, a theoretical physicist at Imperial College London, told Space.com. Right after the Big Bang, however, there was easily enough energy to make Higgs bosons attract each other. This could have led the early universe to contract instead of expand, snuffing it out shortly after its birth. A number of scientists had suggested that new laws of physics or as-yet-undiscovered particles might have stabilized the universe from the peril posed by the Higgs boson. Now Rajantie and his colleagues have found that gravity

could solve this mystery instead. Gravity is a consequence of masses warping the fabric of space and time. To imagine this, think of how bowling balls would deform rubber mats they sit on. The early universe was very dense because it had not had a chance to expand much yet. This meant that space-time was greatly curved back then. The researchers' calculations revealed that when space-time is greatly curved, the Higgs boson increases in mass. This would have also raised the amount of energy needed to make Higgs bosons attract each other, preventing any instability that might have collapsed the early universe. By Charles Q. Choi. *Original article on* Space.com.■

Seattle, USA

Earth's Twin

Scientists found eight new planets in their stars' habitable zones, the region where liquid water can exist on a planetary surface. Three of these planets are similar in size to Earth, nearly doubling the number of possible Earth twins found so far. "We're now closer than we've ever been for finding a twin for Earth," said astronomer Fergal Mullally of the Kepler Science Office at a press conference here today at the meeting of the American Astronomical Society. The newly confirmed planets were discovered by the Kepler space telescope, bringing the mission's total to over 1,000. Previously, only five confirmed planets are similar to Earth in size and reside in the habitable zone. Of course, being in the habitable zone only means that it's possible for liquid water to exist, that it's not too hot or too cold. Just because these planets are in the zone doesn't mean they're covered with balmy seas. And even if a planet does have water, considered a prerequisite for life based on what we now about life in Earth, the planet still has to have the right chemical compositions, atmospheres, geology, and a host of other factors for life to exist. Two of the three new Earth-size planets, dubbed Kepler-438b and Kepler-442b, have a good chance of clearing one of those hurdles: having a solid surface. The third, Kepler 440b, is less likely to be a rocky planet. One of the new Earth-sized planets, Kepler-438b, is about 470 light-years away, has a diameter just 12 percent bigger than Earth's, gets 40 percent more light than our planet, and has a 70 percent chance of being in the habitable zone. Astronomers place the likelihood that this planet's surface is rocky at 70 percent. The second planet, Kepler-442b is 1,100 light-years away from Earth, is a third larger than our planet and receives a third less light. Its chance of being in the habitable zone is 97 percent, and the likelihood of being rocky is 60 percent. Both planets orbit M dwarfs, stars that are smaller and cooler than the sun. A year on those planets is quick: a year on Kepler-438b is only 35 days while a year on Kepler-442b is 112 days. Meanwhile, astronomers have sifted through more data from the planet-hunting Kepler space telescope and found 554 more objects that could be planets. Kepler has now found a total of more than 4,000 planet candidates, with more than 2,000 of them having radii less than twice that of Earth's. Among the new planet

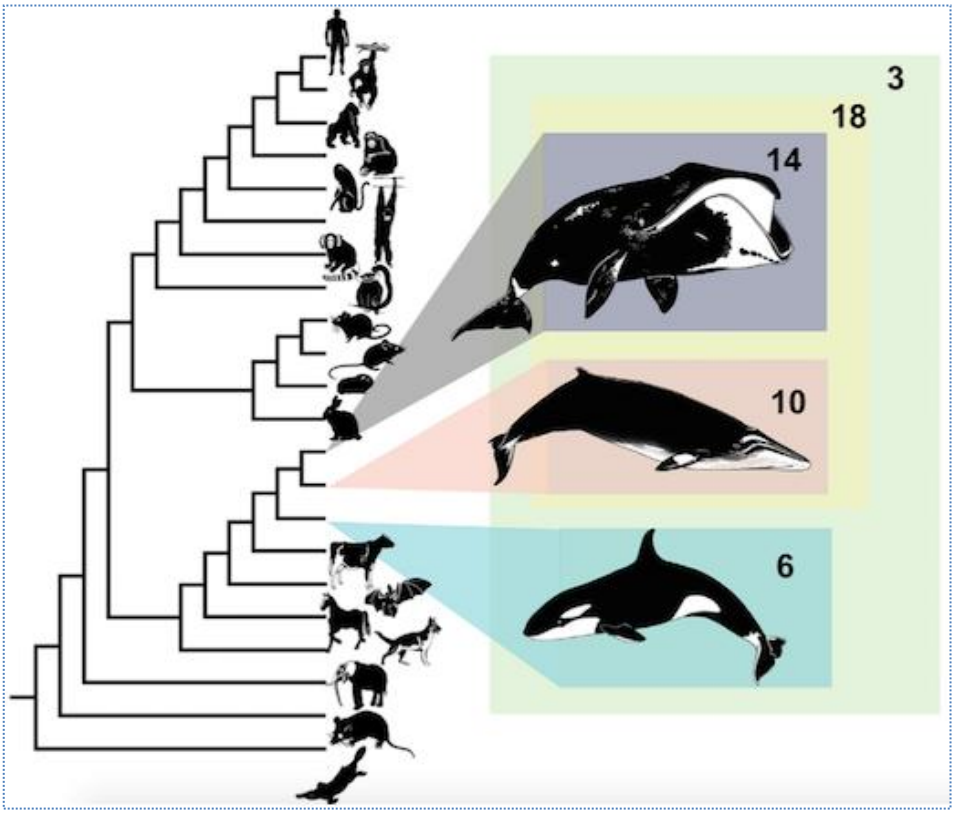


candidates are yet another eight that may be in their stars' habitable zones. And two of those may be even more similar to Earth than Kepler-438b and Kepler-442b, as they orbit stars more similar to our sun. One object (labeled 5737.01) circles its star every 376 days—not too different from a year on Earth—and has a radius of about 30 percent bigger than Earth's. The other (2194.03) is the third planet from its star, orbits every 445 days, and has a radius about 40 percent larger than Earth's. But these are only planet candidates. These objects have to go through a vigorous series of follow-up observations and analyses before they can be deemed confirmed planets. As astronomers learn more about these systems, the estimated radii and distance from their stars could change significantly, says astronomer Doug Caldwell of the SETI Institute. Or, they may turn out not to be planets at all. Still, the vast majority of the 554 new planet candidates are expected to be bona fide worlds, he says. BY Marcus Woo.■

Liverpool, UK

Why Bowhead Whale Lives So Long?

The bowhead whale can live well past the age of 200, yet we know very little about how it lives so long without experiencing many of the lethal diseases that humans often go through as they age. Now, re-

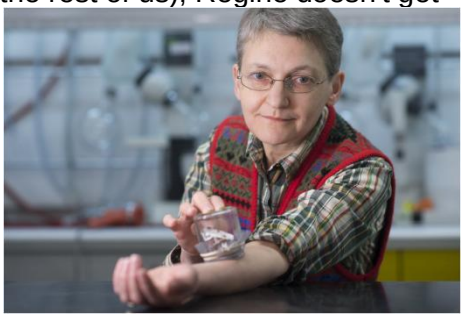


searchers have sequenced the entire genome of the 66-foot bowhead whale - a step that might finally yield some answers regarding its amazing longevity. In a study from the University of Liverpool, UK, the researchers chopped samples of bowhead whale DNA into 4 billion tiny pieces, called nucleotides. Then, they sequenced each of those DNA segments. Powerful computers then put the sequences together, "like a massive jigsaw puzzle," explains de Magalhaes. Finally, the researchers compared the resulting sequence to other whale genomes, like that of the smaller minke whale and the orca whale. Thanks to these comparisons, the scientists found alterations in key genes that might be biologically relevant to aging and cancer. "[The research] is sound," says Jong Bhak, a whale geneticist at Ulsan National Institute of Science and Technology in South Korea who didn't participate in the study. Soon, Bhak says, more scientists will do this kind of comparative genome analyses. "Whales are perhaps the most interesting genomes to study as they went through really severe environmental adaptations among mammals," because they went from from living a terrestrial life to an aquatic one, he says. And "genomics is perhaps the first such an automated way of pinpointing exact aging associated mutations in such a short time." The genome might help understand the population dynamics of this species, de Magalhaes says, and help estimate the effect of hunting on these animals. But the aging-related findings are what he finds more interesting. "By identifying novel maintenance and repair mechanisms we hope to learn what is the secret for living longer, healthier lives," he says. "[We] may be able apply this knowledge to improve human health and preserve human life." Now that the researchers have the sequence in hand, de Magalhaes and his team of researchers hope to use that information to create mice with bowhead whale genes. "Mouse studies, I think, would be ideal to determine if these genes emerging from the bowhead genome can protect against age-related diseases or even promote longevity," he says. The authors of the study aren't sure why it has taken so long to sequence the genome of a large whale, but de Magalhaes thinks that the availability of genetic material samples might have something to do with the delay. "Obtaining samples," he says, "was not easy and costs were also very high." But recent improvements in sequencing technology have made sequencing large genomes far cheaper. "I expect many more whale genomes — and of other species of course — to be sequenced in the next few years." By Arielle Duhaime-Ross.■

Vancouver, CANADA

A Bedbug Breakthrough After Subjecting Scientist Herself To 18,000 Bites

It was a sacrifice for science. After providing free meals to thousands of bedbugs, Simon Fraser University biologist Regine Gries has discovered the key to conquering the maddening pests. To study the insects, Gries partnered up with her husband Gerhard (who's also a biologist) and chemist Robert Britton, also of Simon Fraser. Regine served as the bedbug guinea pig, spending countless hours in a lab they had intentionally infested with bedbugs. After each of her stints, Regine would awaken to a mattress dotted with bedbug remains — delicate flakes of shredded skin and tiny sacs of blood-filled feces — the leftovers of the critters' feast. Unlike Gerhard (and the majority of the rest of us), Regine doesn't get



itchy when bit — she simply breaks out in a light rash. Gerhard and Regine swept up these remains to study the chemicals inside. He was looking for a key ingredient. Like humans and other animals, bedbugs produce and detect distinct smells. More importantly for Gerhard's purposes, they use these odors to communicate. Inside the bedbugs' shed skins and feces, the Gries team found the basic ingredients for a bug-alluring scent — a creepy-crawler J'adore Dior they could use to lure the bugs into a trap. Once they had recreated the smelly solution, they tried it out. To their dismay, it worked inside the lab — the bedbugs came running – but when they tried it out in dozens of bedbug-infested apartments in the metro area of Vancouver, it was useless. Something wasn't right. "We realized that a highly unusual component must be missing — one that we couldn't find using our regular ... tools," Gerhard said in a statement. That's when the couple teamed up with Britton, an expert at recreating nature's complex mixtures inside the lab. Using special technology that allowed him to take a closer look at the bedbug remains, magnifying them to the point where he could detect their individual atoms, Britton found the chemical clue the Gries team was looking for: histamine, which could freeze the bedbugs in their tracks. While five other scents the Gries team had identified before were able to successfully lure the nasty critters into their traps, only the histamine — the same chemical produced by our white blood cells as part of our immune response — stopped them from moving. The trifecta is still perfecting their solution, before they can start selling it commercially. Until then, we wait. In fear. By Erin Brodwin.■

Cairo, EGYPT

Passage to Egypt's Great Pyramid

An Egyptian citizen, identified as "Nagy" by Arabic news site, was illegally digging in his backyard when he found a tunnel leading to the Pyramid of Khufu. The pyramid, nicknamed the Great Pyramid, is the oldest and largest of the three Giza Pyramids. Nagy, a resident of the El Haraneya village, near the Giza Plateau, dug 33 feet beneath his house before he found the corridor, made from stone blocks. Egypt's Ministry of Antiquities sent

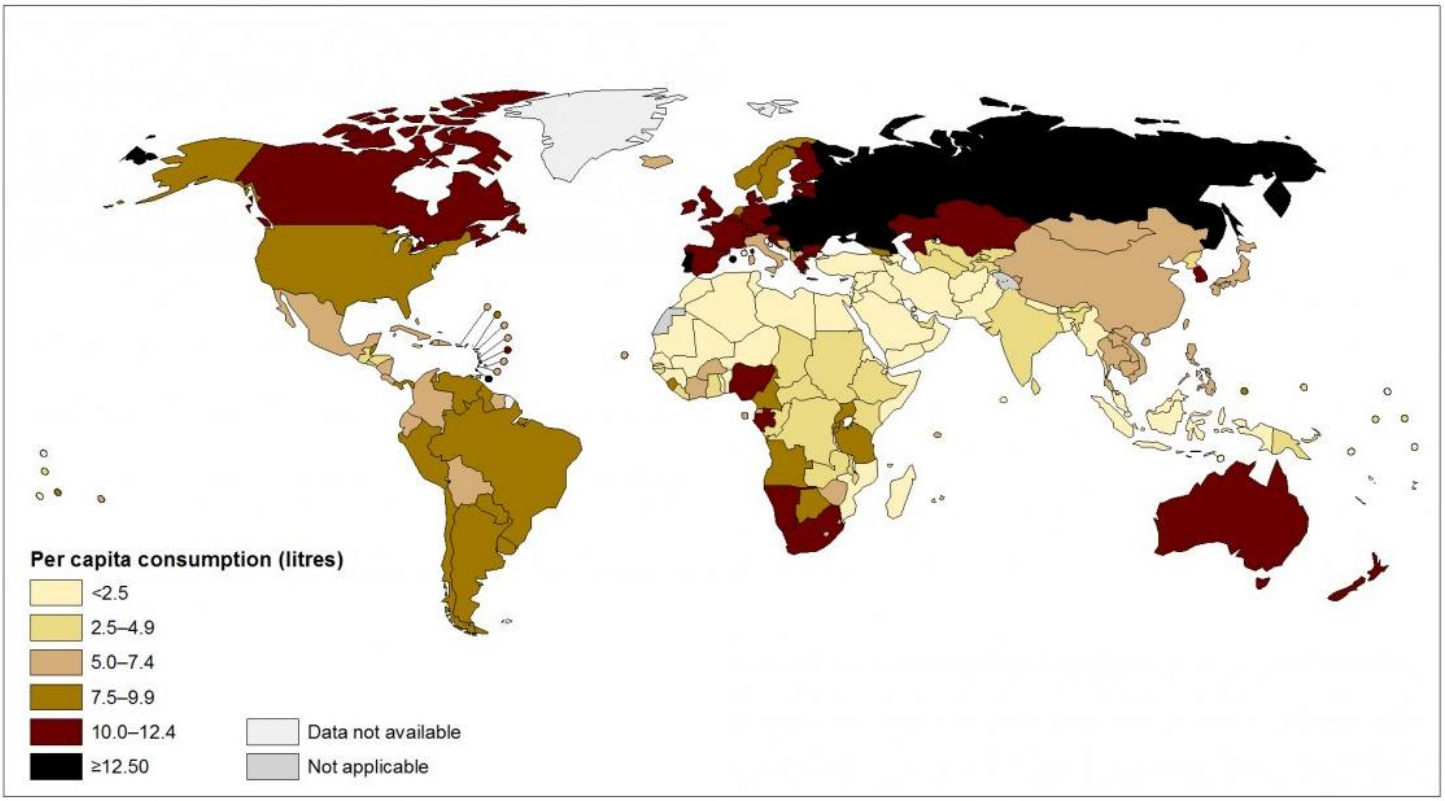
archaeologists to the scene, and a committee confirmed the passage to be the pyramid's legendary causeway. Archaeologists have searched for decades for the passage to the pyramid. The causeway is mentioned in the *Histories* by the Greek Herodotus, who claims to have visited it in the fifth century B.C.E. Herodotus wrote that the passage was enclosed and covered in reliefs, but before Nagy's excavation, only small remnants of the causeway had been found. The Khufu pyramid complex is known to have connected to an undiscovered temple near the Nile River. Thanks to the new discovery, archaeologists believe the temple may be buried beneath the village of Nazlet el-Samman. By Meghan DeMaria.■

Geneva, SWITZERLAND

The Drunkest Countries in the World

Alcohol consumption varies widely across the globe, and US drinkers can keep up with the residents of many other countries. As the map below from the World Health Organization shows, Russians and their neighbors drink more than almost everyone else in the world. Portugal, Grenada, and Andorra are also ranked in the highest category at more than 12.5 liters per person over the age of 15 in 2010. WHO notes in its 2014 report on alcohol and health that 48% of those included in this data abstain from drinking altogether. So if those people were excluded, per capita consumption among those who do drink would be even higher than what's shown on this map. Canadians drink more than Americans, keeping pace with most European countries. Alcohol consumption is low in northern Africa, but the southern half of the continent sees higher drinking rates, especially South Africa and Namibia. Alcohol consumption in Russia is a major concern. A study last year found that the high number of early deaths in Russia could be attributed to people drinking too much. Commons causes of early deaths include liver disease, alcohol poisoning, and getting into accidents or fights while drunk. Other countries near Russia, including Ukraine and Belarus, have similar levels of alcohol consumption. WHO's report notes that the European region contains just 14.7% of the world's population above the age of 15, but accounts for 25.7% of the total alcohol consumed worldwide. In addition to having some of the highest alcohol consumption rates in the world, Russia and Ukraine also have the most

Total alcohol per capita (15+ years) consumption, in litres of pure alcohol, 2010



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

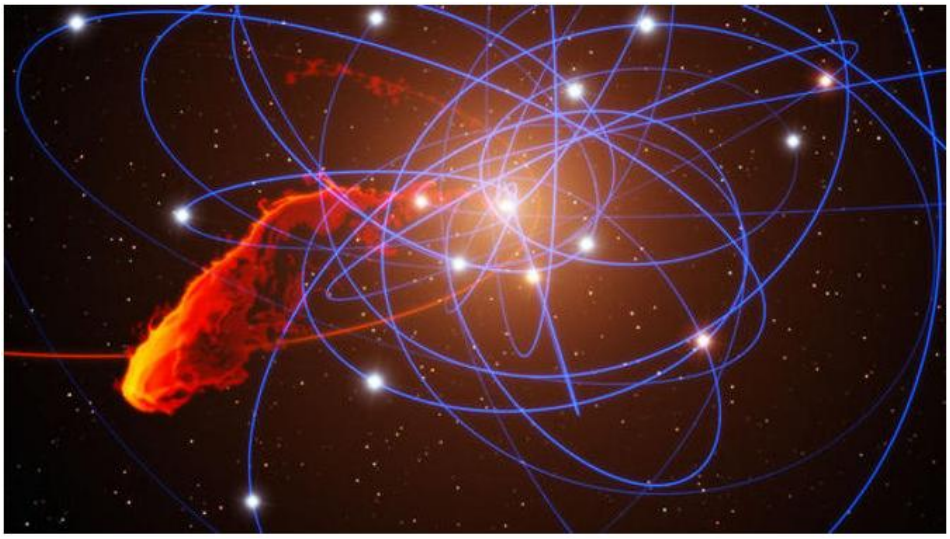
World Health Organization

risky patterns of drinking, according to WHO: To determine which countries have the riskiest drinking patterns, WHO considers the usual quantity of alcohol consumed per occasion, proportion of drinking events when drinkers get drunk, proportion of drinkers who drink daily or nearly daily, festive drinking, drinking with meals, and drinking in public places.■

München, GERMANY

Mystery Object Appears Near Milky Way's Monster Black Hole

In yet another twist to a saga of astronomical proportions, astronomers have identified what they say is a gas cloud that made a tight orbit around the supermassive black hole at the center of the Milky Way galaxy 13 years ago. The object could be one in a series of gas clouds, the second of which may soon become a snack for the black hole. The newly discovered object has been dubbed G1. An object known as G2 has been in the news for more than a year, ever since astronomers at the Max Planck Institute for Extraterrestrial Physics in Germany hypothesized that it was a gas cloud. If that is true, it should lose some of its material to the supermassive black hole at the center of the Milky Way (known as Sagittarius A* or Sgr A*). This giant black hole — its name is pronounced Sagittarius A(star) — doesn't dine on material often, so the event would be a rare chance for astronomers to watch a black hole eat. While the scientists at Max Planck contend that G2 is a gas cloud, a group of researchers at the University of California, Los Angeles, led by astrophysicist Andrea Ghez, argue that G2 is more likely a star surrounded by a layer of dust and gas. Over the summer, G2 made its closest approach to the black hole and was not torn apart. Ghez and her group argued that this was a knockout punch for the gas cloud theory — clear evidence that G2 is a solid body. But the researchers at the Max Planck institute countered with an explanation for how G2 could have remained intact even if it is a gas cloud. Their theory incorporates the idea that G2 was once part of a larger gas cloud that subsequently broke up into smaller gas clouds that all follow the same path, like beads on a string. This "beading" of gas has been observed in the universe before. If additional clouds of gas could be identified following the same path as G2, that would strongly indicate that G2 is a gas cloud and not a star, the scientists say. In their newest paper, the Max Planck group provides a computer model that re-

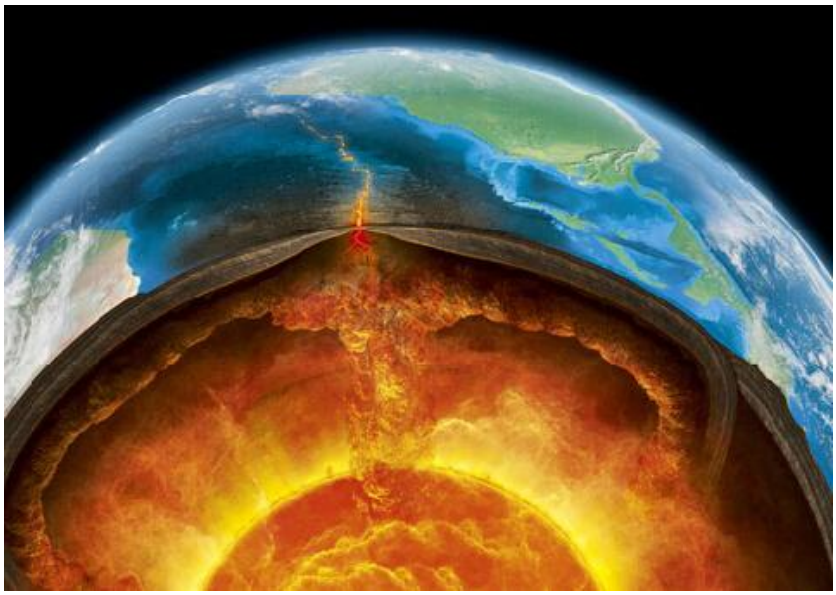


traces the path of G1. According to their research, G1 followed a path nearly identical to G2. The model does make certain assumptions about G1's motion — for example, that it decelerated near closest approach to the black hole. "The good agreement of the model with the data renders the idea that G1 and G2 are part of the same gas streamer highly plausible," Stefan Gillessen, a co-author on the new research, said a statement. By Calla Cofield. *Original article on Space.com.*■

Chicago, USA

"Oceans" Hiding Inside the Earth?

We know more about the surface of Mars than we do the mantle of the planet we live on. As little as 30kms (19 miles) below the surface – the distance between the centre of London and Heathrow Airport – the continental crust turns into the Earth's mantle, a layer some 2,900km (1,800 miles) thick that surrounds the Earth's molten outer core. Underneath the Earth's oceans, the crust can be as little as five kilometres (three miles) thick. And yet this trifling distance might as well be light years, for we know very little about this vital component of our planet. For example, is there more water down there than we thought? For decades, scientists have postulated that the Earth's oceans were created by comets striking the planet's surface. But now some, like Professor Steven Jacobsen of Northwestern University, think that the rocks in the Earth's mantle might have had a part to play as well; specifically a magnesium-rich silicate called ringwoodite. "I'm trying to ask big questions of where the Earth's water came from," he says. "One of the reasons I study rocks is they allow us to peer back in time." Jacobsen had tried to replicate in the lab the kind of ringwoodite formed hundreds of kilometres down, but was unable to – unless he added water. As Jacobsen explains, the chance discovery of a diamond containing a lump of ringwoodite that had been spewed out of a volcanic vent millions of years ago showed that the mineral held as much water as the examples he had reformed in the lab. Ringwoodite could hold 10 times as much water as previously thought – meaning there could be oceans of water still sitting in the mantle rocks beneath us.■



San Francisco, USA

Jupiter Moon Europa's Giant Geysers

Late last year, scientists announced that NASA's Hubble Space Telescope had detected plumes of water vapor spewing about 200 kilometers into space from Europa's south pole in December 2012. The news was met with a great deal of excitement, as it suggested that a robotic probe may be able to sample Europa's possibly life-supporting subsurface ocean without touching down. The researchers have trained Hubble on Europa repeatedly since then, trying to confirm and characterize the plumes during observations in January, February, November and December of this year. But they've come up empty. "We have not yet found any signals of waper vapor in the new images so far," team member Lorenz Roth, of the Southwest Research Institute in San Antonio, said Dec. 19 during a talk here at the annual fall meeting of the American Geophysical Union. Other research teams have also failed to confirm the

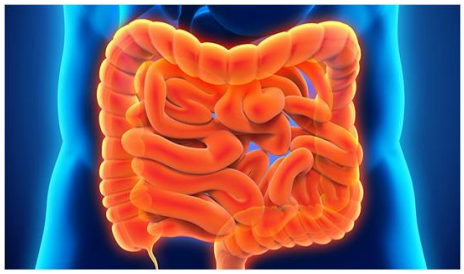
plumes. For example, a recent reanalysis of images gathered by NASA's Galileo probe, which studied the Jupiter system up close from 1995 through 2003, turned up no evidence of their existence, said Cynthia Phillips of the SETI Institute in Mountain View, California. Europa's plumes are thus unlikely to resemble the famous powerhouse geysers that erupt continuously from the south pole of Saturn's icy moon Enceladus, which also harbors an ocean of liquid water beneath its icy shell, she said. UVIS measurements also suggest that most of the hot gas surrounding the satellite originates from the neighboring volcanic moon Io, not Europa, and that Europa's wispy atmosphere is 100 times less dense than thought, the study found. However, none of this necessarily means that Europa's geysers don't exist. "It is certainly still possible that plume activity occurs, but that it is infrequent or the plumes are smaller than we see at Enceladus," Cassini UVIS team member and study co-author Amanda Hendrix, of the Planetary Science Institute in Tucson, Arizona, said in the NASA statement. "If eruptive activity was occurring at the time of Cassini's flyby, it was at a level too low to be detectable by UVIS." Indeed, the plume's discoverers had no expectation of constant and intense activity; Hubble observations in October 1999 and November 2012 did not detect any geysers, Roth said. By Mike Wall. Originally published on Space.com.■


Who feeds us?

BIOLOGY

How We Live in Harmony with Gut Bacteria

Stability in the composition of the hundred trillion bacterial cells in the human gastrointestinal tract is crucial to health, but scientists have been perplexed how our microbiota withstands an onslaught of toxins, dietary changes, and immune response to infections or antibiotics with little change. Research from Yale published in the January 9 issue of the journal Science identifies a strategy that commensal, or non-harmful, gut bacteria employ to preserve this stable relationship with their host during inflammation. "It has been a puzzle that many immune responses target all bacteria," said Andrew Goodman, assistant professor of microbial pathogenesis and a member of the Microbial Sciences Institute at Yale's West Campus. "Yet healthy individuals maintain the same beneficial microbes for decades even when exposed to a host of environmental disturbances." Research has shown that disruptions in the gut microbiome can lead to severe health consequences, including obesity, recurrent infections, and diseases such as irritable bowel syndrome. Instability in the microbiome has been linked to diseases as diverse as autism and cancer. Doctors may one day be able to manipulate the microbiome to treat patients, but scientists first need to understand the molecular machinery of the vast gut microbiome, which contains a hundred times more genes than the human genome. The new study represents a first step, Goodman said. The Yale team found that in mice and humans, microbiome stability is maintained by a single gene that allows bacteria to resist high levels of inflammation-associated antimicrobial



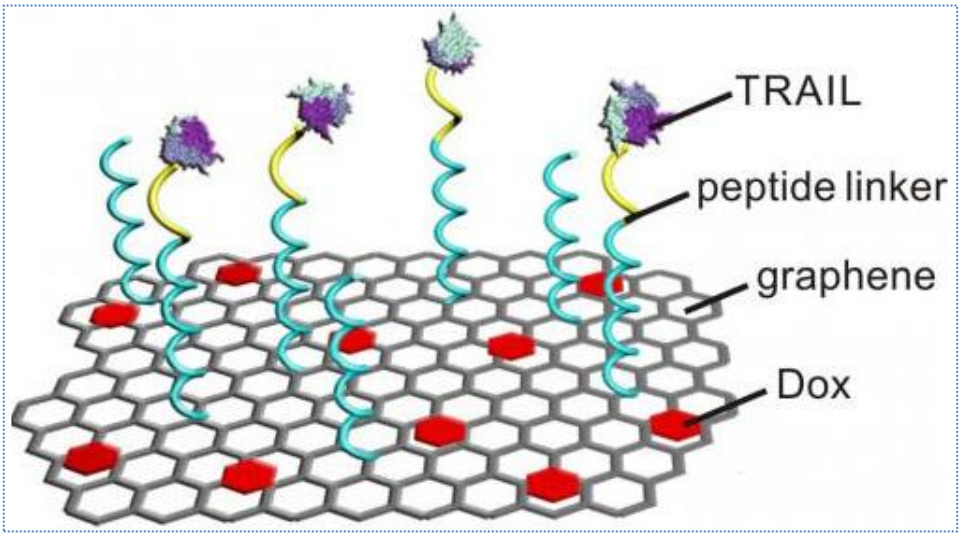
peptides. Commensal bacteria that lack this mechanism were promptly removed from the gut during inflammation in mice. "We were surprised that a single factor could have such a large effect," Goodman said. "This study opens the door for new approaches to understand how commensal bacteria interact with their hosts."

Science 2015; 347(6218):170

BIOMATERIAL

"Flying carpet" for delivering Anticancer Drugs

An international team of researchers has developed a drug delivery technique that utilizes graphene strips as "flying carpets" to deliver two anticancer drugs sequentially to cancer cells, with each drug targeting the distinct part of the cell where it will be most effective. The technique was found to perform better than either drug in isolation when tested in a mouse model targeting a human lung cancer tumor. The researchers also found that an anticancer protein, TRAIL, can serve as an active targeting molecule to bind directly to the surface of cancer cells, which had not been demonstrated previously. The work was done by researchers at North Carolina State University, the University of North Carolina at Chapel Hill, and China Pharmaceutical University (CPU). In this study, the researchers attached two drugs - TRAIL and doxorubicin (Dox) - onto graphene strips. Graphene is a two-dimensional sheet of carbon that is only one atom thick. Because TRAIL is most effective when delivered to the external membrane of a cancer cell, while Dox is most effective when delivered to the nucleus, the researchers wanted to deliver the drugs sequentially, with each drug hitting a cancer cell where it will do the most damage. The Dox is physically bound to the graphene due to similarities in the molecular structure of the drug and the graphene. The TRAIL is bound to the surface of the graphene by a chain of amino acids called peptides. "These drug-rich graphene strips are introduced into the bloodstream in solution, and then travel through the bloodstream like nanoscale flying carpets," explains Dr. Zhen Gu, senior author of a paper describing the work and an assistant professor in the joint biomedical engineering program at NC State and UNC-Chapel Hill. Once in the bloodstream, these flying carpets take advantage of the fact that cancer tumors cause nearby blood vessels to leak by using those leaks to penetrate into the tumor. When the flying carpet comes into contact with a cancer cell, receptors on the surface of the cell latch onto the TRAIL. Meanwhile, enzymes that are common on the surface of cancer cells sever the peptides linking the TRAIL and the graphene. This allows the cell to absorb the Dox-laden graphene and leaves the TRAIL on the surface, where it begins a process to trigger cell death. After the flying carpet is "swallowed" by the cell, the acidic environment inside the cell promotes the separation of the Dox from the graphene - freeing it to attack the nucleus. "We've demonstrated that TRAIL itself can be used to attach a drug delivery system to a cancer cell, without using intervening material - which is something we didn't know," Gu says. "And because graphene has a large surface area, this technique enhances our ability to apply TRAIL to its target on cancer cell membranes." The re-



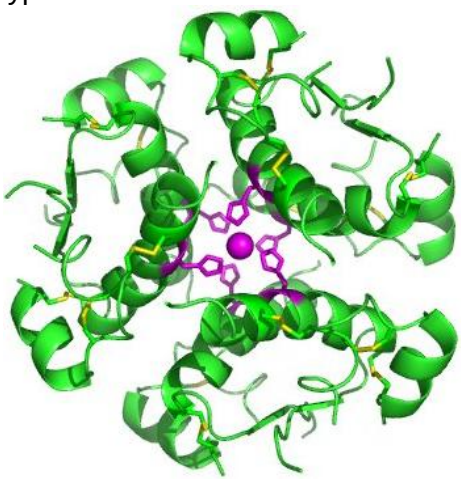
searchers tested the flying carpet drug delivery technique in preclinical trials against human lung cancer tumors (cell line A549) in laboratory mice. The technique was significantly more effective than Dox or TRAIL by themselves, or to a combination of Dox and TRAIL in which the peptide link between the graphene and the TRAIL couldn't be severed. "We're now trying to secure funding to support additional preclinical studies in order to determine how best to proceed with this new technique," Gu says.

Adv Mater 2014; DOI: 10.1002/adma.201404498, In press

MEDICINE

Triglycerides Form in Liver despite Insulin Resistance

In type 2 diabetics, insulin fails to suppress blood sugar production by the liver while paradoxically allowing the production of hepatic triglycerides. This combination results in multiple health risks, including high blood sugar and fatty liver disease. For years, to gain insight into this phenomenon, researchers focused on the role of altered insulin action in the liver in the production of triglycerides. However, Yale researchers tested a theory that triglycerides formed in the liver were more dependent on the delivery of fatty acids to the liver than on insulin action. In their study, the Yale team—led by Gerald I. Shulman, the George R. Cowgill professor of medicine and cellular & molecular physiology—developed a novel method to measure the rate of triglyceride production from fatty acids in three types of animals: normal rats, insulin-resistant rats fed a high-fat diet, and rats with genetically modified insulin receptors. They found that in all of the animals tested increased triglyceride production was primarily dependent on fatty acid delivery and not on insulin action in the liver. The findings also explain the long-standing paradox of why insulin therapy does not exacerbate, but instead reduces, fatty liver disease in patients with type 2 diabetes. "These results



provide new insights into the pathogenesis of non-alcoholic liver disease and provides new approaches to treat fatty liver disease, which is now the most common liver disease in the world," said Shulman. Shulman and his team plan to apply similar methodology to translate their findings to insulin-resistant patients with type 2 diabetes, hyperlipidemia, and fatty liver disease.

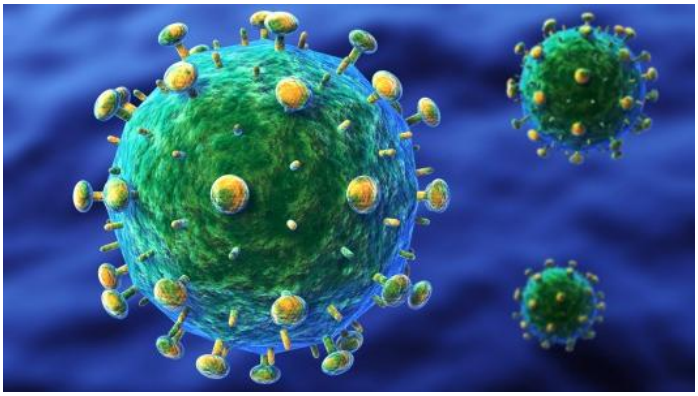
PNAS 2014; DOI: 10.1073/pnas.1423952112, In press

MEDICINE

The First and Only Person Cured of HIV

Timothy Ray Brown, long known only as the "Berlin Patient" had HIV for 12 years before he became the first person in the world to be cured of the infection following a stem cell transplant in 2007. He recalls his many years of illness, a series of difficult decisions, and his long road to recovery in the first-person account, Brown's Commentary describes the bold experiment of using a stem cell donor who was naturally resistant to HIV infection to treat the acute myeloid leukemia (AML) diagnosed 10 years after he became HIV-positive. The stem cell donor had a specific genetic mutation called CCR5 Delta 32 that can protect a person against HIV infection. The virus is not able to enter its target, the CD4 cells. After the stem cell transplant, Brown was able to stop all antiretroviral treatment and the HIV has not returned. "This is the first time that we get to read this important story written by the man who lived it," says Thomas Hope, PhD, Editor-in-Chief of *AIDS Research and Human Retroviruses* and Professor of Cell and Molecular Biology at Northwestern University, Feinberg School of Medicine, Chicago, IL. "It is a unique opportunity to share in the human side of this transformative experience."

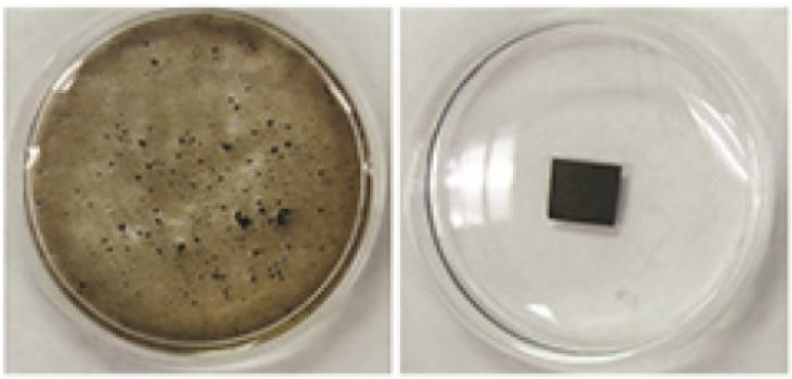
AIDS Res Human Retroviruses 2015; 31(1):2



CHEMISTRY

The Solubility Mystery of Graphene Oxide Films Solved

Like many scientists, Jiaxing Huang did not understand why graphene oxide (GO) films were highly stable in water. When submerged, the individual GO sheets become negatively charged and repel each other, which should cause membrane to disintegrate. But earlier papers noted that instead of disintegrating, the films stabilized. "It doesn't make any sense," said Huang, associate professor of materials science and engineering at the McCormick School of Engineering. "Many scientists have been very puzzled by this." Graphene oxide, a product of graphite oxidation, is often used to make graphene, a single-atom-layer thick sheet of carbon that is remarkably strong, lightweight, and has high potential in electronics and energy storage. Within the past three years, however, more scientists have become interested in GO itself, partially because of its potential for molecular separation applications. After studying the material for many years, Huang realized that the secret of GO's mysterious insolubility was the unintentional introduction of a common contaminant. To make a GO film, many scientists pass the acidic dispersion of individual sheets through porous anodized aluminum oxide filter discs, which are popularly used for preparing membranes of many nanomaterials. Huang's team found that during filtration, the aluminum filter discs corrode in acidic water to release a significant number of aluminum ions, Al^{3+}. The positively charged ion bonds with the negatively charged GO sheets to stabilize the resulting membranes. "We have solved the puzzle using essentially freshman-level inorganic chemistry," Huang said. "Now we know that graphene oxide films are indeed soluble in water. It's just a matter of sample purity." Other multivalent metal ions, such as manganese, which is a byproduct from the synthesis of GO, can also crosslink the sheets. Huang's research is described in "On the origin of stability of graphene-oxide membranes in water," published in *Nature Chemistry* on January 5. Other authors of the paper include graduate student Che-Ning Yeh, postdoc Kalyan Raidongia, former visiting graduate student Jiaojing Shao, and Shao's former adviser Quan-Hong Yang from Tianjin University in China. The National Science Foundation and Office of Naval Research funded different parts described in the paper. Huang's finding also indicated that GO films are not as strong as researchers once thought. The aluminum ions make the film much stiffer. Without the ions, GO is three to four times weaker.

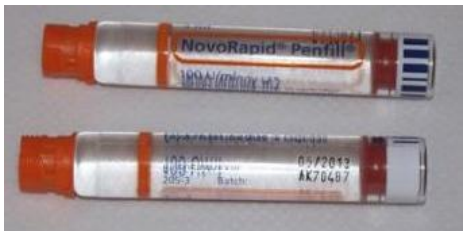


Nat Chem 2015; DOI: 10.1038/nchem.2145

BIOLOGY

Surprising New Clues to Insulin Resistance

In studying the cellular structure and function of insulin, a research team led by investigators at Beth Israel Deaconess Medical Center (BIDMC) has uncovered previously unknown steps in the development of insulin resistance, a hallmark of type 2 diabetes. Reported in the January 2015 issue of *Nature Cell Biology*, their surprising new findings identify two transcription factors—the glucocorticoid receptor (GR) and the vitamin D receptor (VDR) - that play a key role in insulin resistance, providing some of the first evidence that changes in the cellular nucleus underlie the condition and offering a promising new route for the development of drug therapies for type 2 diabetes. "We wanted to understand what was initially happening to cause the body to become unresponsive and stop 'listening' to insulin," explains senior author Evan Rosen of the Division of Endocrinology, Diabetes and Metabolism at BIDMC and Professor of Medicine at Harvard Medical School. "Insulin resistance has been intensively studied for decades, but most work has focused on rapid events that happen in cells immediately after the hormone is produced. Through epigenomic mapping, we have now identi-



fied events that take longer to develop and that involve previously unsuspected biological pathways. Perhaps most importantly, we found that these pathways work completely in the nucleus of the cell by regulating the expression of key target genes, a process that was felt by many to be irrelevant to the development of this widespread condition." Previous investigations of insulin resistance have focused almost exclusively on proteins and cellular functions at or near the surface of cells, where insulin binds. However, epidemiological and molecular data have suggested that events leading to insulin resistance might also take place in the nucleus, where the DNA blueprint is stored. One such piece of evidence comes from an observation surrounding fetal programming, says Rosen. "Fetal programming centers on a person's exposure in utero," he explains. "So, for example, whether a fetus has received too few or too many nutrients from the mother can lead to a person becoming obese or diabetic in adulthood, and this in turn can be passed along to the next generation. There is a lot of evidence that insulin resistance can be passed on this way and this type of intergenerational event almost certainly develops in the nucleus." Epigenomic modifications refer to changes in the structure of DNA that are distinct from mutations and can be passed from cell to cell as cells divide, and passed from one generation to the next. By mapping these modifications, scientists are able to gain important insights into the cell's nuclear function. To better understand how the epigenome is altered in states of insulin resistance, the research team treated fat cells with one of two chemicals, the steroid dexamethasone or the cytokine tumor necrosis factor-alpha (TNF). "By their nature, these agents would be predicted to cause almost opposite effects in cells, and yet we know that both cause insulin resistance," says Rosen. "This provided us with a unique opportunity to see how each agent was affecting the epigenome of cells. Then by focusing on changes that were shared by the two treatments, we could discern which epigenomic events might be at the core of insulin resistance." Because the types of epigenomic changes being analyzed occur at locations where transcription factors bind, the team was able use their data to infer which transcription factors might be involved in the development of insulin resistance. "The glucocorticoid receptor [GR] and the vitamin D [VDR] receptor fit the bill," says Rosen. A subsequent series of experiments confirmed that the GR and VDR receptors were indeed cooperating and working together to cause insulin resistance. "Our findings were unanticipated for several reasons," says Rosen. "First, TNF is a strong inducer of inflammation, while the GR protects against inflammation. Showing that TNF exerts at least some of its actions via the GR is somewhat heretical. Additionally, higher vitamin D levels have been correlated with better insulin sensitivity, so it was surprising to see the VDR associated with insulin resistance. These results call into question some of the basic assumptions surrounding the relationship between vitamin D and metabolic health. Most importantly, these data tell us that we have an awful lot still to learn about the basic mechanisms by which diabetes is triggered, and they reveal new ways in which we can approach drug therapy for this disorder."

Nat Cell Biol 2014; 17(1):44

INFECTION

Molecules That Can Block HIV Infection

This analogy illustrates the importance of the protective capsule, called the capsid, which surrounds the human immunodeficiency virus (HIV) genome. The capsid has to disassemble once the virus enters the cell, releasing its disease-causing cargo at precisely the right time and place. "It's still a matter of debate at what point the capsid falls apart in HIV-1 infection of cells," said Dmitri Ivanov, Ph.D., assistant professor of biochemistry in the School of Medicine at The University of Texas Health Science Center at San Antonio. Dr. Ivanov is a senior author on a study, published Dec. 15 in*Proceedings of the National Academy of Sciences,* that offers clues about HIV-1 capsid disassembly. The paper shows how an HIV-1 inhibitor called PF74 and a host protein called CPSF6 bind to a small pocket on the surface of the capsid and prevent it from disassembling. The suitcase, if you will, is locked. Viral information is kept inside. "We think that this process can be targeted for therapeutic purposes in HIV-1 infections," Dr. Ivanov said. In part of the study, researchers used X-ray crystallography at the UT Health Science Center to visualize the three-dimensional structure of the CPSF6 protein bound to the HIV-1 capsid. "Seeing molecules in 3-D is illuminating; it tells us something about their function," Dr. Ivanov said. "We now know how PF74 and CPSF6 interact with the adjacent building blocks of the HIV-1 capsid, thus stabilizing the entire capsid structure. It tells us that these molecules bind to the capsid before disassembly, blocking viral replication."

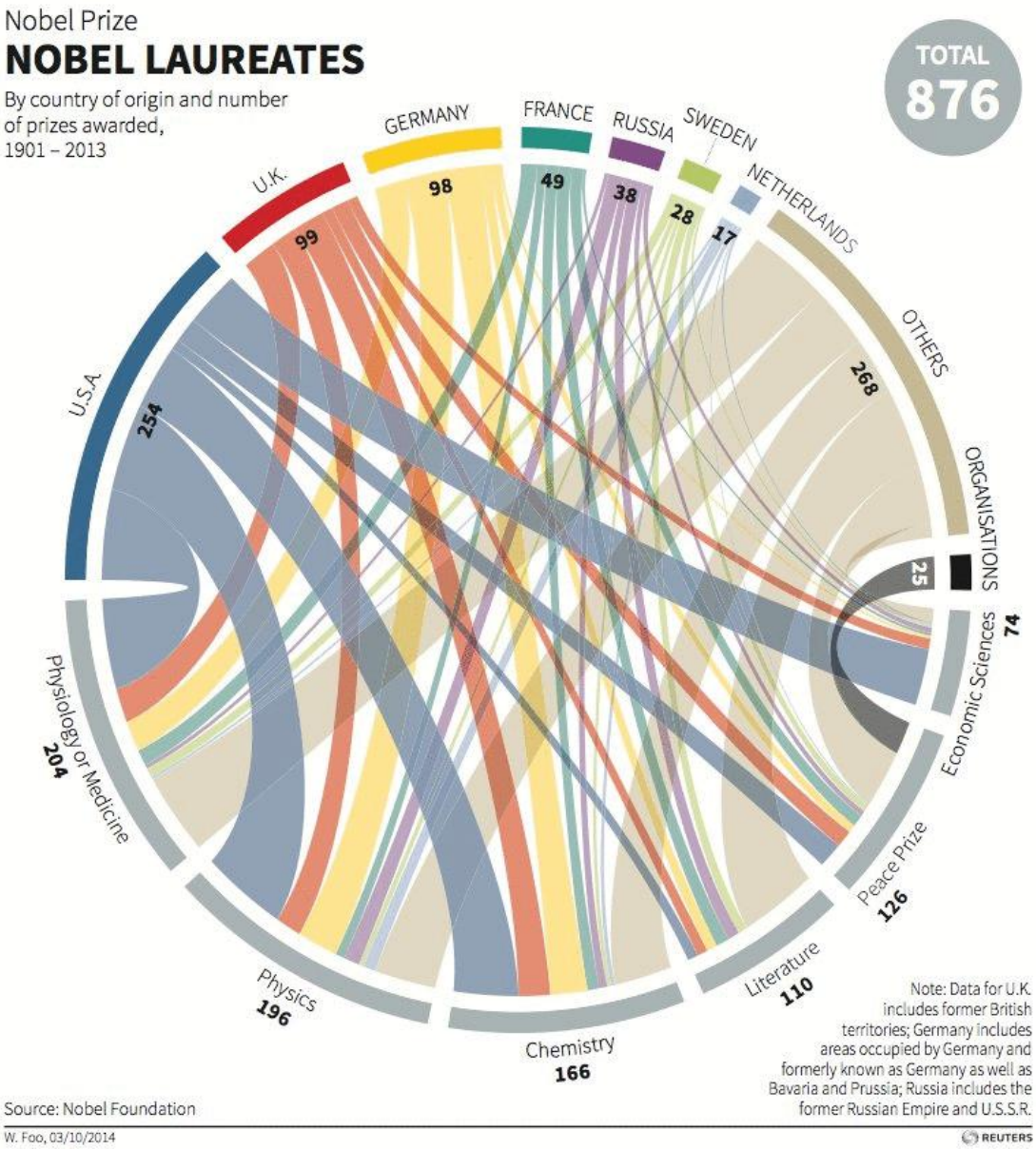
PNAS 2014; 111(52):1862


Working like a worker bee?
Relax yourself.....


When you face the eruption
Do you feel the ending of the world?

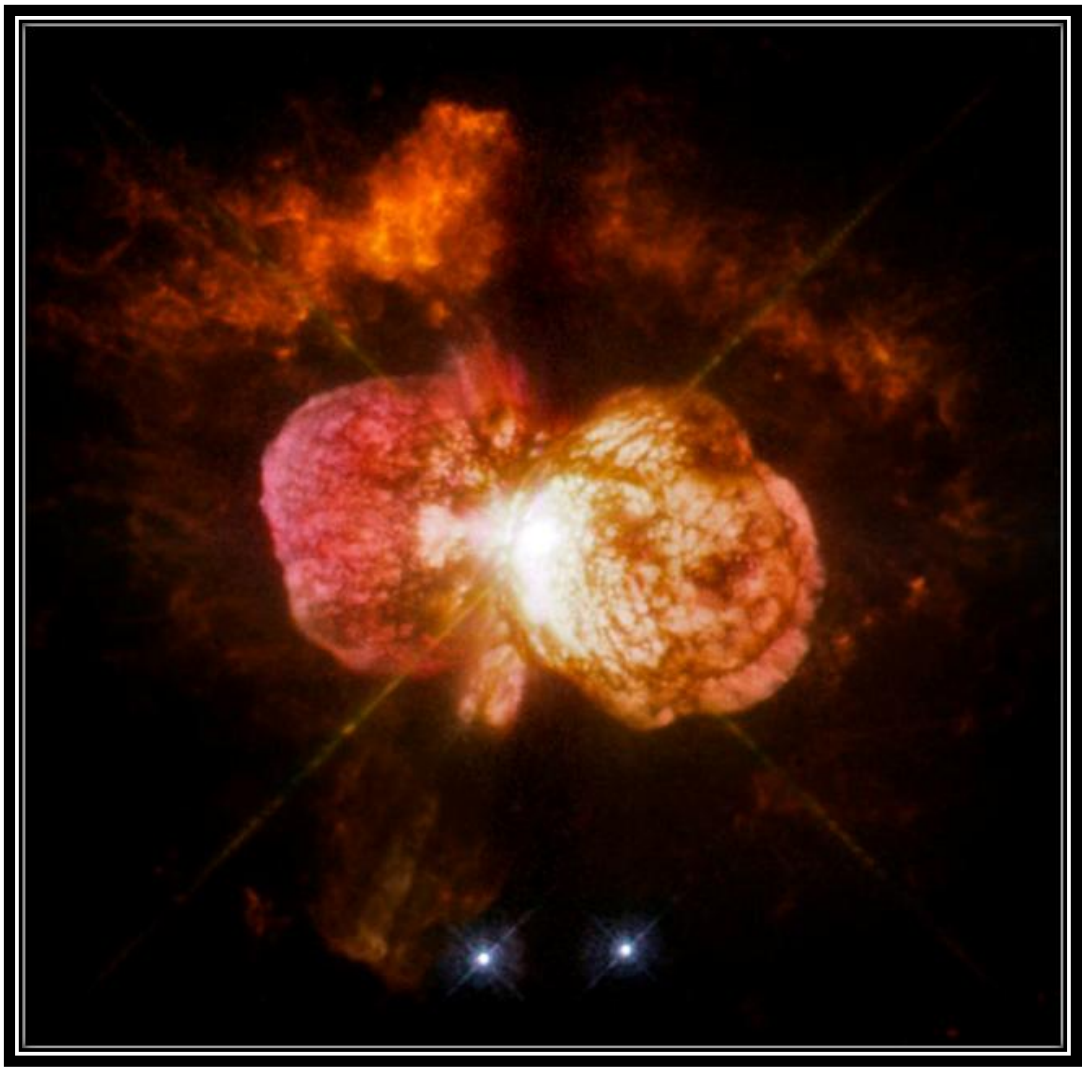
Nobel Prize Global

By Reuters (2014, USA)



Inside the Most Massive Star

By NASA (2015, USA)



A new long-term study of Eta Carinae—"the most luminous and massive star within 10,000 light-years"—has revealed amazing, never-before-seen features using data captured by multiple observatories during 11 years using multiple observatories, including the Swift and the Hubble. Located about 7,500 light-years away in the southern constellation of Carina, Eta Carinae comprises two massive stars whose eccentric orbits bring them unusually close every 5.5 years. [...] Astronomers have established that the brighter, cooler primary star has about 90 times the mass of the sun and outshines it by 5 million times. While the properties of its smaller, hotter companion are more contested, Goddard's Ted Gull and his colleagues think the star has about 30 solar masses and emits a million times the sun's light.■

“Pillars of Creation”

By NASA (2015, USA)

The Hubble Space Telescope's greatest-hits images would easily fill a coffee-table book with spiraling galaxies, ghostly nebulae and eye-catching stars. If you had to choose a cover image, then it most likely would be the famous "Pillars of Creation," an image captured in 1995 showing massive columns of cold gas reaching upward in the M16 nebula, popularly known as the Eagle Nebula. NASA notes how the original image captured the public's imagination, appearing on pillows, T-shirts and a postage stamp. It was the rock star of the Hubble image collection. Twenty years later, Hubble has revisited the stunning image and topped it with a fresh high-definition look at the columns in preparation for the space telescope's 25th anniversary in April. The new image is a combination of near-infrared and visible light, which enhances the otherworldly look of the pillars. Newborn stars are revealed to be lurking inside. The pillars are located about 6,500 light-years away, which is not terribly far in space terms.■

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Preemptive Analgesic Efficacy of Tramadol, Butorphanol, and Flurbiprofen in Lumpectomy: A Randomized, Controlled and Double-blind Trial

The BSAE Study Group

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Preemptive Analgesic Efficacy of Tramadol, Butorphanol, and Flurbiprofen in Lumpectomy: A Randomized, Controlled and Double-blind Trial

The BSAE Study Group *,†,Δ,1

BACKGROUND Preemptive medication prior surgical procedures has been proposed of the promising manner in controlling pain effectively, whereas different drugs given in this way produced varying effects in different contexts. We herein hypothesized that preoperative bolus injection of analgesics functioning through various mechanisms produced contrasting analgesic efficiency in patients undergoing lumpectomy.

METHODS After approval by the Institutional Ethical Committee, a total of 1,500 patients undergoing lumpectomy were screened and 1,336 were randomized into one of the four groups: saline, tramadol 100 mg, butorphanol 2 mg, and flurbiprofen 100 mg. All drugs were administered 15 min prior operation in 10 ml. Visual analog scale of pain at rest and during movement were rated, and analgesic indexes were calculated as the primary outcomes. Secondary outcomes include complementary morphine consumption, side effects, and overall satisfaction.

RESULTS Patients in the group of flurbiprofen experienced less intensity of pain at rest than the other three groups ($P < 0.01$), and also displayed a higher stationary analgesic index ($P < 0.05$). Besides, the pain scorings in both groups of tramadol and butorphanol showed effective analgesia began from the sixth hour after the surgery compared to the saline-delivered patients ($P < 0.05$). Correspondingly, patients treated with flurbiprofen reported less side effects than both tramadol and butorphanol, in which a lower satisfactory ratings were presented than the flurbiprofen-treated ones.

CONCLUSION Flurbiprofen has superior analgesic effect over tramadol and butorphanol in lumpectomy suggesting that conquering peripheral inflammatory responses evoked by surgical lesion is much more effective in controlling the pain than those drugs functioning through the CNS-associated mechanisms.■

*: The members of the BSAE Study Group are disclosed at the end of the paper.

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1: These authors contributed equally to this work (see Appendix 1).

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Keywords: Lumpectomy – Analgesic – Opioids – NSAIDs – Preemptive

WITH THE area of the lumpectomy "wakes up" after the anesthesia, it can recover some of its senses, which can cause mild discomfort in the breast, and the pain improves slowly and can linger for a long time (1). In general, benign breast masses were excised under local anesthesia at the day-surgical department with less treatment of the pain from breast incision. While several reports concerned the postoperative pain management after breast surgeries, their major focuses were on the nerve blocking manners (2, 3). In contrast, little information is available regarding the preemptive injection of analgesics intravenously referring to post-surgical analgesia in breast masses excision. We herein purposed that a bolus injection of the analgesics, opioids or non-opioids, would produce effective analgesia after lumpectomy.

Tramadol is a synthetic, centrally acting opioid analgesic with a potent active opioid metabolite (4). It produces less respiratory depression than other opioids and has no significant cardiac effects. Parenteral and oral tramadol has been proven effective and well tolerated in the management of moderate to severe acute postoperative pain in adults (5). Preemptive administration of tramadol with a single dose in postoperative pain management was evaluated that it was effective in the earlier period of time after surgeries (6, 7). Butorphanol, a totally synthetic morphinan, is considered to be a mixed agonist-antagonist opioid analgesic (8). WHO suggests that therapeutic categories for butorphanol in humans are as an anesthesia or preanesthesia adjunct, narcotic analgesic for postoperative pain (9). It has been shown to be several advantages of few side effects, including vomiting and respiratory depression, of minimal potential for abuse and low toxicity (10, 11). Flurbiprofen axetil is a member of the phenylalkanoic acid derivative family of nonsteroidal anti-inflammatory drugs (NSAIDs), and functions by suppressing the local production of prostaglandin (12). It produced superior analgesic effect when used preemptively than postoperative administration (13, 14). As thus, the preemptive bolus injection of tramadol, butorphanol and flurbiprofen may produce effective analgesia after surgical procedures. The aim of this study was to objectively compare the analgesic efficacy of these three drugs with the 100-mm chiroscience gauge of visual analog scale (VAS) in the context of lumpectomy.

MATERIALS AND METHODS

Participants and Ethics

With the approval of the Institutional Ethics Examining Committee of Human Research, a total of 1,500 American Society of Anesthesiologists physical status I-II patients who underwent elective lumpectomy were screened, and 1,336 of them were randomized, followed-up in this double-blind and controlled study. All participants signed an approved consent and a full explanation was given about tramadol, butorphanol, flurbiprofen axetil, general anesthesia and the linear VAS scoring of pain, sedation, and satisfaction.

Exclusion Criteria

Patients were excluded from the study if one or more following criteria were met: (i) Allergy to opioids, a history of the use of centrally-acting drugs of any sort, chronic pain and psychiatric diseases records. (ii) Participants younger than 18yr，older than 65yr or pregnancy. (iii) Those who were not willing to or could not finish the whole study at any time. (iv) The post-anesthetic care unit (PACU) assessing score was under 6 on a scale of 10 (measuring somnolence, respiration, movement, color, and blood pressure on 0-2 scales), and arterial oxygen saturation measured by pulse oximetry (SaO_2) was 92% or lower (supplemental oxygen was permitted). (v) Using or used in the past 14 days of the monoamine oxidase inhibitors (MAOIs). (vi) Alcohol addictive or narcotinum dependent patients were excluded for its influence on the analgesic efficacy of the study substances. (vii) Subjects with gastrointestinal ulcers and asthma, or receiving therapy with quinolone antibiotics.

Study Design

All enrolled patients were randomly divided into one of four groups according to SNOSE way (15) for preemptive injection of the drugs, one of control group (Saline), one of tramadol group (tramadol hydrochloride 100 mg), one of butorphanol group (butorphanol tartrate 2 mg) and one of flurbiprofen group (flurbiprofen axetil 100 mg). Each drug was injected in a volume of 10 ml 15 min prior to the operation. The randomized envelopes were maintained in opaque until 15 min before the operation started. All research staff, data collectors and nurses, and drug delivery populations were kept from the contents of the brown syringe except for the drug numbers, No. 1, No.2, No.3 or No.4 for each time (different in drug allocation each time), until the end of the study. The corresponding drug name and number were sealed in an envelope and administrated by the institutional ethical department. Each syringe received saline, tramadol, butorphanol or flurbiprofen contained into similar brown ampoule with same volume. We adopted brown syringe and ampoule for keeping the contents from being recognized by the research staff due to the white emulsion of flurbiprofen axetil.

Baseline measurements of pain were recorded immediately prior to return to surgical wards. The study drugs were administered as a 10ml

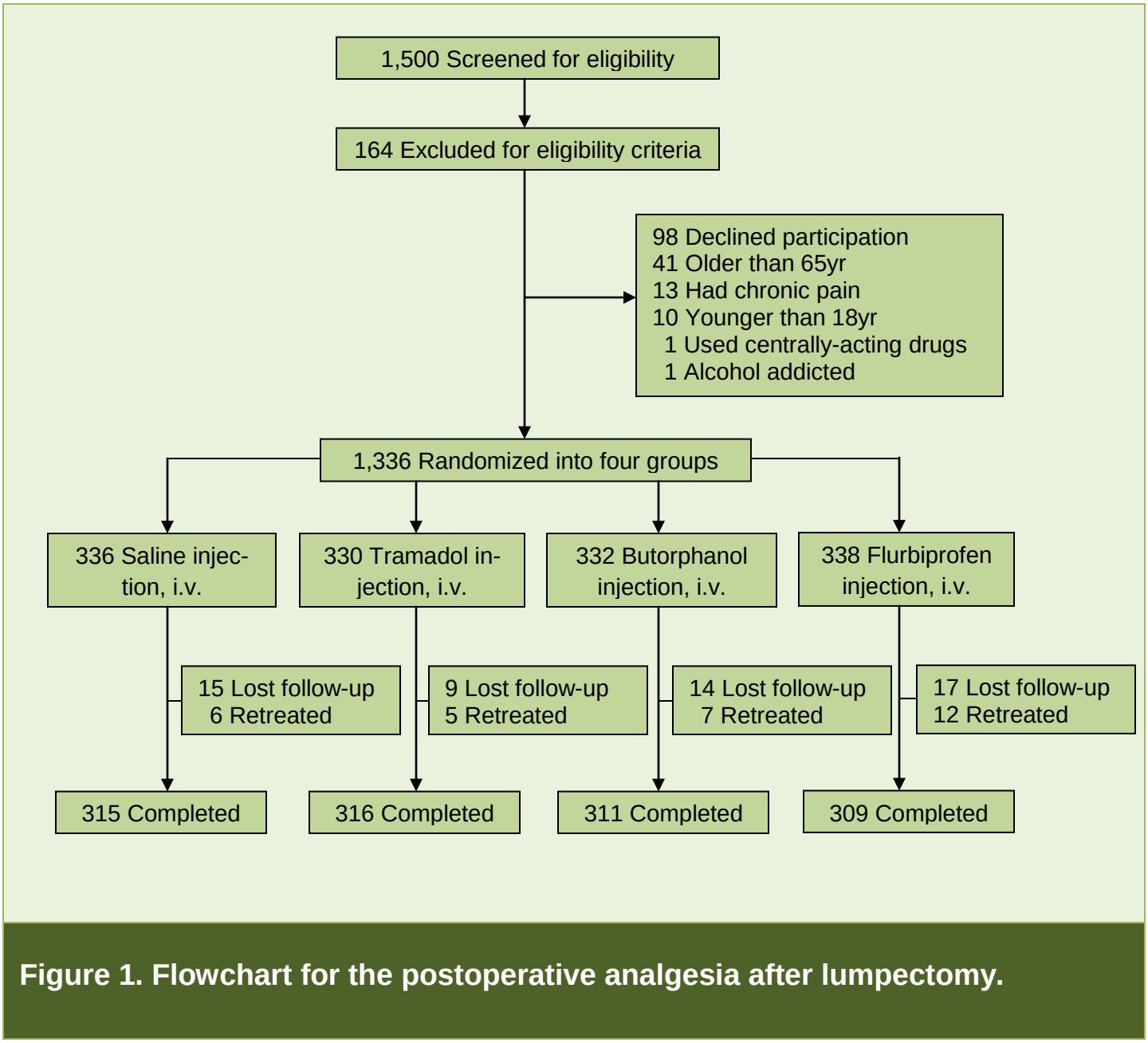

Figure 1. Flowchart for the postoperative analgesia after lumpectomy.

bolus over 20-30 sec, followed by a continuous follow-up up to 24 h. Additional drugs were not allowed except for 0.04 mg/kg morphine as rescue drug of uncontrolled pain. Ondansetron 0.15 mg/kg was administered prophylactically, but patients still could receive metoclopramide 10 mg i.v. every 6 h administered at the discretion of the nursing staff. Diphenhydramine 25 mg was delivered intravenously (i.v.) for conquering pruritus. Patients received supplemental oxygen therapy via nasal tube (40% O_2 2-4 l/min) after returning to the surgical wards to maintain SaO_2 above 92%.

The monitoring parameters during the whole study included the measurement of heart rate by 3-lead electrocardiograph, respiratory rate, noninvasive systolic and diastolic blood pressure, mean arterial pressure and fingertip pulse oximetry (Nihon Kohden, TL-201T, Tokyo, Japan).

Anesthesia and Perioperative Management

Total intravenous anesthesia (TIVA) was performed to each patient. Sufentanil 0.20 μg/kg, midazolam 0.05 mg/kg, and propofol 1.5-2.0 mg/kg slowly injected i.v. for induction. The maintenance of anesthetics was consisted of propofol was infused intraoperatively at a rate of 30-50 μg/kg/min, and remifentanil at a rate of 0.15 μg/kg/min. During the process of anesthesia, spontaneous respiration was maintained, and artificial support was given timely if only the respiratory rate was lower than 8 breaths per minute which was defined as the respiration depression. The pump of propofol was stopped at ~10 min before the end of the operation, and remifentanil was stopped at approximately 5 min before the end of the surgery. No neuromuscular relaxants were used.

All the participants underwent mono-lateral single incision. A catheter was inserted in a right or left antecubital vein for fluid and drug administration. Intra- and post-

Table 1. Base-line characteristics of the patients.

	Saline (n=336)	Tramadol (n=330)	Buborphanol (n=332)	Flurbiprofen (n=338)
Age – yr	32 ± 11	34 ± 13	32 ± 9	35 ± 15
Weight – kg	58 ± 9	61 ± 13	59 ± 9	60 ± 11
Height – cm	158 ± 8	157 ± 5	161 ± 9	158 ± 9
Education – yr	7 ± 5	7 ± 4	8 ± 5	6 ± 5
ASA physical status I/II	328/8	324/6	320/12	331/7
Intraoperative propofol – mg	155 ± 45	147 ± 58	152 ± 52	161 ± 63
Intraoperative sufentanil – μg	16 ± 5	16 ± 6	15 ± 4	16 ± 5
Intraoperative remifentanil – μg	46 ± 9	51 ± 11	48 ± 10	48 ± 9
Intraoperative midazolam – mg	3 ± 1	3 ± 1	3 ± 1	3 ± 1
Intraoperative fluid therapy				
Crystalloids – ml	419 ± 114	421 ± 105	408 ± 121	417 ± 112
Colloids – ml	229 ± 101	211 ± 95	230 ± 114	222 ± 118
Surgical duration – min	58 ± 15	57 ± 21	61 ± 16	55 ± 18
Estimated blood loss – ml	62 ± 27	57 ± 15	66 ± 18	64 ± 21
Volumes of urine – ml	115 ± 39	127 ± 44	109 ± 48	118 ± 47
Preoperative blood pressure				
Systolic pressure – mmHg	125 ± 8	113 ± 9	118 ± 11	124 ± 13
Diastolic pressure – mmHg	73 ± 12	71 ± 14	69 ± 11	71 ± 10
Preoperative heart rate – bpm	75 ± 14	67 ± 9	78 ± 16	74 ± 11
Preoperative respiratory rate – bpm	19 ± 4	20 ± 3	18 ± 2	20 ± 4

Data are mean ± SD or numbers. No significant differences among the four groups.

operative fluid management included replacement of preexisting fluid deficits, of normal losses (maintenance requirements), and of surgical wound losses including blood loss and the amount of urine collected via an indwelling urinary catheter, of hemodynamic variables and hemoglobin concentration. No additional drugs were administrated perioperatively except for the routine administration of atropine sulfate 8.0 μg/kg and phenobarbital sodium 1.5 mg/kg used intramuscularly prior to surgery 30 min.

Postoperative Measurements

During the study, the patient-derived VAS scorings of pain at rest and during movement, and VAS ratings of satisfaction, and vital signs were recorded hourly from 1 h until 12 h after the surgical procedures and six-hourly up to the 24th h. Additional morphine consumption was calculated every 4 h after the operation, and the total morphine usage was recorded eventually. At the end of the study, an overall maximal pain intensity score and the occurrence of the side effects throughout the study were evaluated by the follow-up physicians.

Primary Outcome

The VAS of pain at rest and during movement with the 100-mm chiroscience gauge as reported previously (16) was measured as the primary outcome, i.e. subjective pain intensity ratings, based on a 0-100mm linear VAS (0 = no pain; 100 = worst pain imaginable). A VAS pain score of less than or equal to 3 was considered to represent effective analgesia. Patients were explained to understand that one end of the scale represented no impact of pain at all and the other end was representative of extreme or severe impact of it.

Secondary Outcomes

The following measures were selected as the secondary outcomes: (i) Overall subjective satisfaction, a 1-100mm linear VAS used (1 = sad; 100 = happy). (ii) Morphine consumption in four groups were calculated and expressed with median and corresponding 95% confidence interval (95% CI). (iii) Incidence of side effects.

Statistical Analysis

Analyses were performed using GraphPad Prism version 5.0 (GraphPad Software Inc., San Diego, CA, USA). Values are expressed as mean, median, standard deviation (SD), 95% CI or numbers. The demographic data and background characteristics (age, weight, baseline heart and respiratory rates, SpO_2, blood pressure and education status), the ASA physical status, the duration of surgery, the amounts of perioperative drugs administration and morphine consumption, fluids therapy and blood transfusion were compared with two-way analysis of variance (ANOVA). The effects of the study drugs on patient's self-rated VAS pain and satisfaction were analyzed using two-way

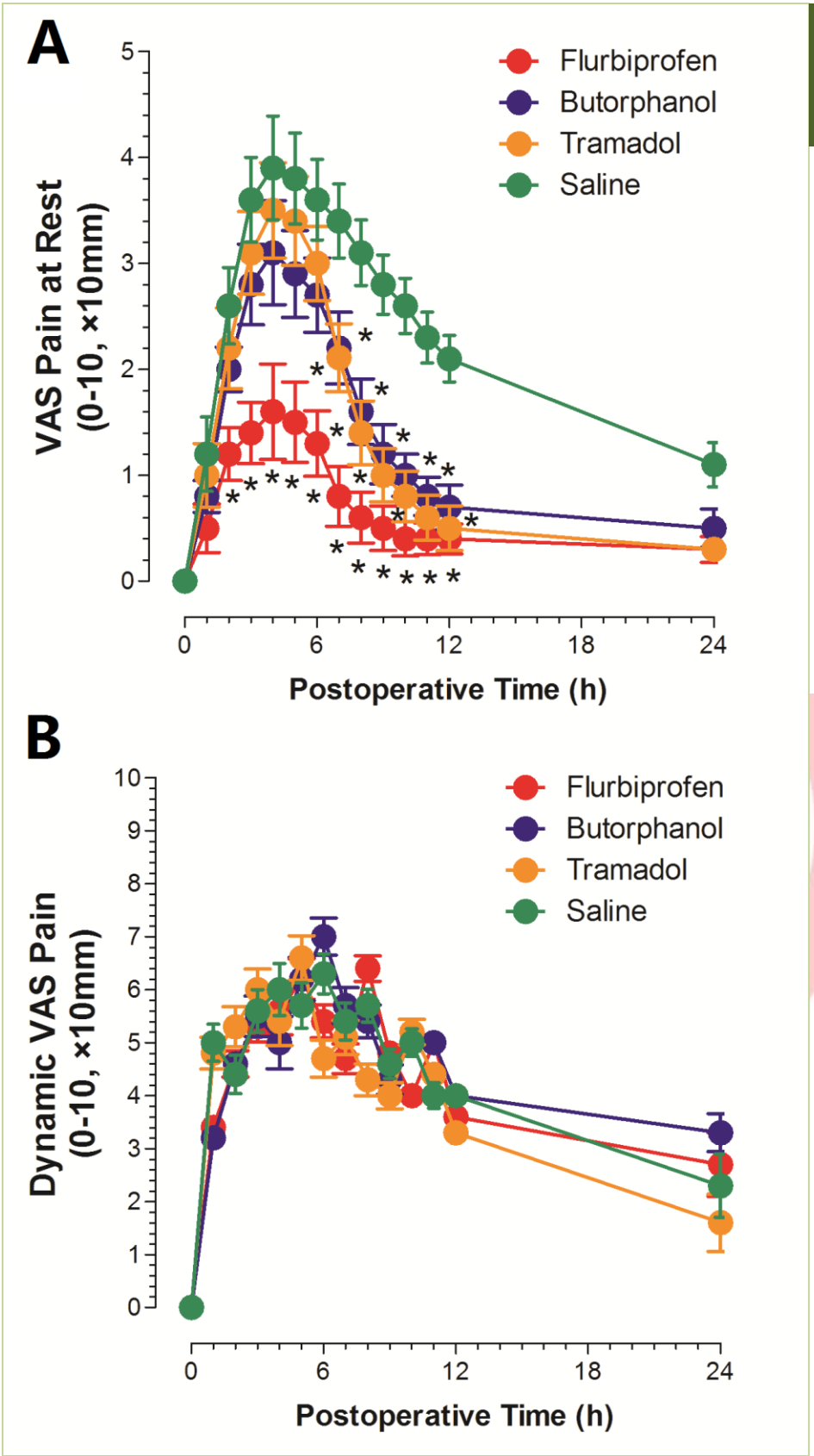

Figure 2. Analgesic scorings in patients at rest and during movement.

Preemptive administration of tramadol, butorphanol, and flurbiprofen in patients undergoing lumpectomy produced different effects on conquering postoperative pain. Flurbiprofen displayed significant lower VAS scorings of pain at rest than the other three groups (*P < 0.05 versus Saline; Panel A). Of interest, tramadol and butorphanol expressed significant analgesia since the 6th h after the surgical procedures, and during the first six hours, both of them had little effects on the pain relief after lumpectomy (*P < 0.05 versus Saline; Panel A). However, all three drug-treated groups displayed almost same pain scorings during movement (Panel B). Data were presented with mean ± SD.

ANOVA with repeated measures. Finally, a Chi-square t-test was performed to compare side effects among groups. Statistical significance was accepted at the level of $P < 0.05$.

RESULTS

Participants

The flowchart in Figure 1 shows the most common reasons for exclusion for the 1,500 patients who were screened but not randomized and the follow-up for the 1,336 patients who were randomly assigned to the four groups. Finally, 315 patients in saline, 316 patients in the group of tramadol, 311 subjects in the group of butorphanol, and 309 subjects in the group of flurbiprofen axetil completed the study.

Baseline Characteristics

The demographic, background, surgical, anesthesia and intraoperative management data, baseline vital signs all were within the physiological ranges throughout the anesthesia and surgical process and were no significant difference amongst the four groups (Table 1).

Flurbiprofen Axetil Expressed the Most Significant Analgesic Effect at Rest

Preemptive flurbiprofen axetil evidenced significant lower VAS scorings of pain at rest during the whole follow-up period than the other three groups ($P < 0.05$, Figure 2A). The average scoring was 1.1 ± 0.5 in the group of flurbiprofen versus 4.2 ± 1.3 in the Saline patients, and versus 2.3 ± 0.8 and 2.1 ± 0.9 in the groups of tramadol and butorphanol, respectively (Figure 2A). Of interest, tramadol and

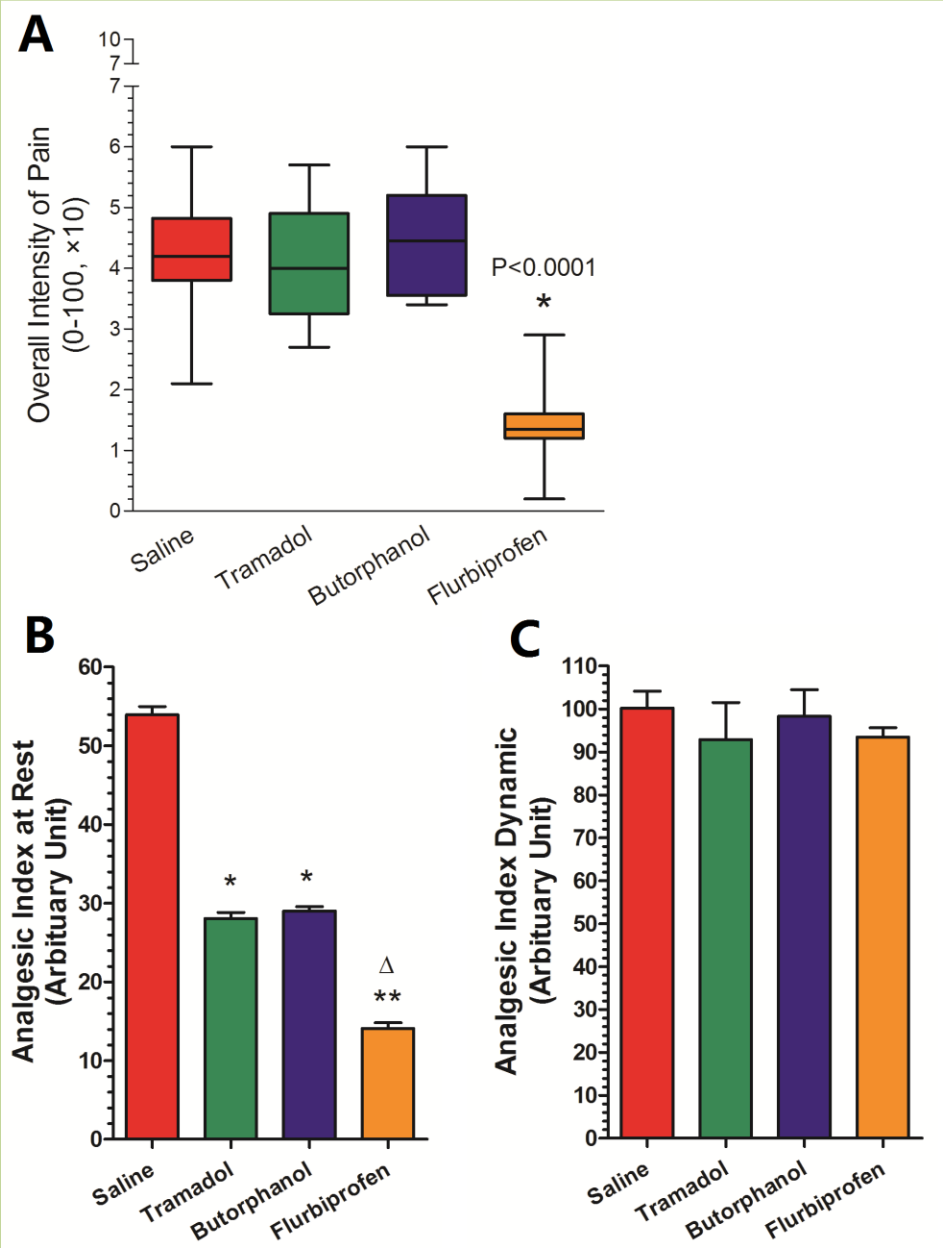

Figure 3. Overall analgesic ratings and analgesic indexes.

At the end of the study, the overall intensity of pain was evaluated, and flurbiprofen expressed the lowest scoring (*P < 0.0001), which was followed by the tramadol and butorphanol groups evidenced relative lower scorings compared with the saline group (Panel A). Although the three study drugs produced different analgesic effects after lumpectomy individually at different time points, the overall intensity of pain also showed big difference (Panel A). In addition, the area under the curve (AUC) of the analgesic scorings as the index of pain control was calculated, and the results showed that all three interventions had lower analgesic indexes at rest, and flurbiprofen showed the most significant analgesia (**P < 0.01 versus Saline, $^{\Delta}$P < 0.05 versus both Tramadol and Butorphanol, *P < 0.05 versus Saline; Panel B), but the dynamic analgesic indexes showed no significant difference among the four groups (Panel C). Data were presented with mean ± SD.

butorphanol expressed significant analgesia since the 6th h after the surgical procedures, and during the first six hours, both of them had little effects on the pain relief after lumpectomy (Figure 2A). However, all three drug-treated groups displayed almost same analgesic effects during movement (Figure 2B).

In addition, the overall intensity of pain was evaluated at the end of the study, and flurbiprofen axetil expressed the lowest scoring ($P < 0.0001$), which was followed by the tramadol and butorphanol groups evidenced relative lower scorings compared with the saline group ($P < 0.05$, Figure 3A). Although the three study drugs produced different analgesic effects after lumpectomy individually at different time points, the overall intensity of pain also showed big difference (Figure 3A). Besides, we calculated the area under the curve (AUC) of the analgesic scorings as the index of pain control, and the results showed that all three interventions had lower analgesic indexes at rest, and flurbiprofen showed the most significant analgesia depicted as the analgesic index ($P < 0.01$, Figure 3B), but the dynamic analgesic indexes showed no significant difference among the four groups (Figure 3C).

Additional Morphine Requirement and Overall Satisfaction

Additional morphine was delivered timely if the patients were under insufficient analgesia and the total morphine consumption was calculated. flurbiprofen axetil-treated subjects consumed the least morphine than saline ones ($P < 0.01$, Table 2), and the tramadol and butorphanol patients required relatively more morphine than flurbiprofen ones ($P < 0.05$, Table 2).

Patients' overall feeling of satisfaction was best in the group of flurbiprofen than the other three groups ($P < 0.01$, Table 2), and tramadol and butor-phanol groups showed relative higher scorings than the saline group ($P < 0.05$, Table 2).

Table 2. Total morphine consumption and overall satisfaction.

	Saline (n=315)	Tramadol (n=316)	Buborphanol (n=311)	Flurbiprofen (n=309)
Additional total morphine consumption – mg*	8.5 (4.2-12.4)	4.6 (1.5-7.2) †‡	4.1 (1.2-6.3) †‡	1.1 (0.7-2.5) †
Overall VAS satisfaction scorings (1-100mm)**	24.1 ± 9	54.6 ± 15 †‡	56.8 ± 12 †‡	70.7 ±11.5 †

* Denotes the median and 95% confidence interval (95% CI) of morphine consumption.
** Denotes data are mean ± SD.
† Denotes compared with the group of Saline (P<0.01).
‡ Denotes compared with the group of Flurbiprofen (P<0.01).

Table 3. Incidence of side effects.

Side effect	Saline (n=315)	Tramadol (n=316)	Bbutorphanol (n=311)	Flurbiprofen (n=309)
Nausea	36 (11)	32 (10)	27 (9)	11 (4)
Vomiting	11 (3)	9 (3)	12 (4)	4 (1)
Dry mouth	44 (14)	26 (8)	31 (10)	14 (5)
Dizziness	27 (9)	21 (7)	17 (5)	7 (2)
Drowsiness	24 (8)	30 (9)	25 (8)	6 (2)
Pruritus (Itching)	9 (3)	12 (4)	18 (6)	3 (1)
Sweating	8 (2)	6 (2)	14 (5)	2 (0.6)
Constipation	4 (1)	1 (0.3)	1 (0.3)	2 (0.6)
Urinary retention	1 (0.3)	1 (0.3)	2 (0.6)	0
Respiratory depression	1 (0.3)	1 (0.3)	0	0
Miosis	0	0	0	0
Memory and cognitive impairment	0	0	0	0

Data are number of patients and %.

Side Effects

The incidence of different side effects was expressed in table 3. The total incidence of side effects in the group of flurbiprofen was the lowest (P < 0.01, Table 3), and no significant difference was observed among the other three groups.

DISCUSSION

The results of this study demonstrate that tramadol and butorphanol expressed similar analgesic manner with bolus injection preemptively after breast masses excision, i.e. the effective analgesia started from the 6th h and almost no pain relief role in the early 6 hours after the surgical procedures. In contrast, flurbiprofen axetil produced more effective analgesia since from the end of the operation to up to 24 h post surgical procedures. Although so, the overall pain intensity in the three study drug groups evidenced significant alleviation. Consistent with the analgesic data, the additional morphine requirement was saline > tramadol > butorphanol > flurbiprofen, on the contrary, the overall scoring of satisfaction was flurbiprofen > butorphanol > tramadol > saline. Finally, the incidence of side effects in flurbiprofen was the lowest than the other three groups.

To our knowledge, this is the first time to find that the analgesic effect of tramadol and butorphanol expressed nearly parallel manner after surgeries, and even more interesting thing is the later-occurring analgesia at least 6 hours after operation. While previous studies displayed effective analgesia of the premedication of tramadol and butorphanol, in general, such therapies mainly based on the conditions as that the preemptive delivery of the drugs followed by continuous infusion or patient-controlled analgesia (PCA) (17). In our study, the single bolus injection prior operation demonstrated an easy-to-conduct analgesic regimen

with emphasis on the short-durational surgeries.

Our data depicted a functional situation in which flurbiprofen, a nonsteroidal anti-inflammatory drug (NSAID) taking function through inhibiting cyclooxygenase (COX), mainly plays the role peripherally especially at the injury-induced inflammatory sites as in this study context – lumpectomy. Contrarily, both centrally-functioning drugs, tramadol and butorphanol, did not show high analgesic indexes. All these tell us a fact that peripheral inflammatory responses resulted from regional lesion is superior to the central sensitization suggesting the local inflammatory "soup" at the peripheral injured sites was the major contributor to such kind of pain condition rather than the central involvement which generally is the key composition of the large surgical wound-associated pain.

In addition, centrally-functioning medications showed more incidences of central nervous system (CNS)-related side effects such as sedation and drowsing make these drugs unwanted by patients than the peripherally-functioning ones, of which showed much less undesirable side effects. In some patients, they even preferred to have pain than experience the sufferings of side effects.

In sum, flurbiprofen has superior analgesic effect over tramadol and butorphanol in locally-restricted injury like lumpectomy suggesting that conquering peripheral inflammatory responses evoked by surgical lesion is much more effective in controlling the pain than those drugs functioning through the CNS-associated mechanisms. Our findings and conclusions only derived from lumpectomy-related analgesic context. Whether such analgesic regimen also plays an effective role or not in other types of surgeries needs further investigation.■

Acknowledgement

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Conflict of Interests

None

APPENDIX 1

Members of the Breast Surgery Analgesia Evaluation (BSAE) group:

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References

1. Surgery and Radiation Pain. http://www.breastcancer.org/tips/pain/.
2. Dabbagh A, Elyasi H. The role of paravertebral block in decreasing postoperative pain in elective breast surgeries. Med Sci Monit 2007; 13: CR464-CR467.
3. Visser WA, Fanyar Z, Luiten EJ. Thoracic paravertebral block for awake breast surgery in a patient with congenital central hypoventilation syndrome (Ondine's Curse). J Clin Anesth 2013; 25: 604-605.
4. Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL. Trends in Opioid Analgesic Abuse and Mortality in the United States. N Engl J Med 2015; 372: 241-248.
5. Gibbison B, Bailey CR, Klein AA. Tramadol - the Marmite(™) drug. Anaesthesia 2015; 70: 125-130.
6. Ong KS, Tan JM. Preoperative intravenous tramadol versus ketorolac for preventing postoperative pain after third molar surgery. Int J Oral Maxillofac Surg 2004; 33: 274-278.
7. Mastrocinque S, Fantoni DT. A comparison of preoperative tramadol and morphine for the control of early postoperative pain in canine ovariohysterectomy. Vet Anaesth Analg 2003; 30: 220-228.
8. Smith MA, Pennock MM, Pitts EG, Walker KL, Lang KC. The effects of amphetamine, butorphanol, and their combination on cocaine self-administration. Behav Brain Res 2014; 274: 158-163.
9. WHO Expert Committee on Drug Dependence. WHO Expert Committee on Drug Dependence. World Health Organ Tech Rep Se 2006; 942: i, 1-21, 23-24 passim.
10. Rosow CE. Butorphanol in perspective. Acute Care 1986; 12: S2-S7.
11. Nelson KE, Eisenach JC. Intravenous butorphanol, meperidine, and their combination relieve pain and distress in women in labor. Anesthesiology 2005; 102: 1008-1013.
12. Idrees A, Rahman NU, Javaid Z, Kashif M, Aslam I, Abbas K, Hussain T. In vitro evaluation of transdermal patches of flurbiprofen with ethyl cellulose. Acta Pol Pharm 2014; 71: 287-295.
13. Yamashita K, Fukusaki M, Ando Y, Fujinaga A, Tanabe T, Terao Y, Sumikawa K. Preoperative administration of intravenous flurbiprofen axetil reduces postoperative pain for spinal fusion surgery. J Anesth 2006; 20: 92-95.
14. Yilmaz B, Sahin H, Akba V, Erdem AF. Determination of flurbiprofen in human plasma by gas chromatography with mass spectrometry and its pharmacokinetics. J AOAC Int 2014; 97: 1061-1066.
15. Doig GS, Simpson F. Randomization and allocation concealment: A practical guide for researchers. J Crit Care 2005; 20: 191-193.
16. Weinbroum AA, Bender B, Nirkin A, Chazan S, Meller I, Kollender Y. Dextromethorphan- associated epidural patient-controlled analgesia provides better pain- and analgesics-sparing effects than dextromethorphan-associated intravenous patient-controlled analgesia after bone-malignancy resection: a randomized, placebo-controlled, double-blinded study. Anesth Analg 2004; 98: 714-722.
17. Wordliczek J, Banach M, Garlicki J, Jakowicka-Wordliczek J, Dobrogowski J. Influence of pre- or intraoperational use of tramadol (preemptive or preventive analgesia) on tramadol requirement in the early postoperative period. Pol J Pharmacol 2002; 54: 693-697.■

Doi: 10.15354/si.15.ar006


help those in need...

Stop wasting foods

The Three Worst Things Must Avoid Slowing the Aging Process

THERE ARE countless men and women who have cracked the code on aging and have literally slowed down their biological clock to a crawl. And I'll show you all the effective anti-aging tips and tricks in just a minute, but first let's look at what happens as you age…

Your metabolism slows down to a snail's pace as you age. This makes burning fat and losing weight next to impossible.

The hormones responsible for all of your youth-like qualities such as healthy skin tone, strong lean muscle, robust energy and insatiable sex drive, start declining more and more each year that goes by. And if you're not proactive, your youth enhancing hormone levels may drop so low that there is no turning back.

Aging makes your bones weaker and more brittle by robbing your body of vital minerals that are essential for strong bones. This is why so many elderly people suffer from hip fractures that can lead to even more serious medical complications.

It's not just your physical qualities that get negatively affected by aging…your brain suffers as well. Your memory, your ability to solve problems, and your decision making skills all start to decline and worsen each year. And here's the real kicker: After 40, your biological age starts to speed up and age faster than your chronological age! In fact, for every year that passes you can age up to 6 months extra. That means when you turn 42, your body is essentially turning 43…if you keep this up, at 48 your body could be as old as 52.

These are the harsh facts, but it's the truth. However, it doesn't need to be this way. YOU have the power to slow aging and prolong your youth. When you apply my anti-aging strategies, you'll be able to REVERSE the aging process by greatly slowing down yourbiological aging well below your chronological aging.

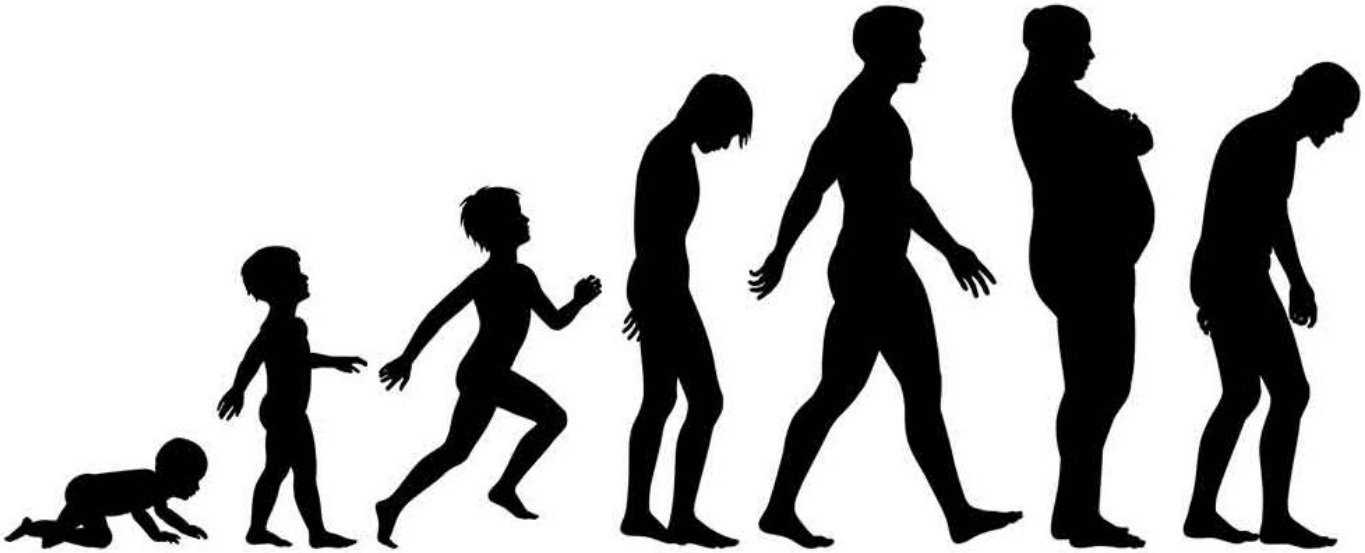
Here's what you can expect when you use some of my anti-aging strategies:

You'll re-ignite your metabolism, reprogramming your body so you can readily start burning fat right away.

You'll reboot your endocrine system, creating a resurgence of youth enhancing hormones so can get infinitely more energy—and replace flab with lean, strong muscle while boosting your sex drive

You'll fortify your body by regaining bone density and building a solid foundation.

Boost your brain power, enhancing memory and improving your cognitive function making



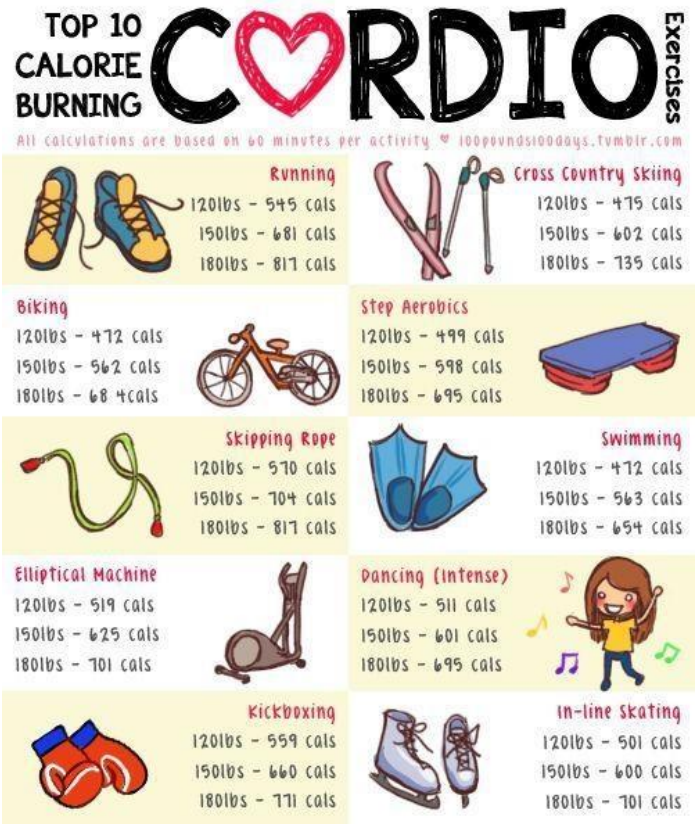
you as sharp as a tack

You'll dramatically decelerate your body's aging process. So, your biological age will age slower than your chronological age—making you look and feel younger each year that passes.

Now I need to warn you… what you're going to read next is probably going to go against everything you've ever heard before. But that's because very few people actually know how to slow their aging process. Think about the so-called "experts" giving you anti-aging tips… what do they look like? If they don't look 10 - 15 years younger than their actual age, do you really think they have the right knowledge? Look, I'm not one to judge by looks alone, but as far as anti-aging is concerned I'm taking advice from people that look the part and live the part…

Now, here are the three worst mistakes you must avoid if you want to slow the aging process and increase your metabolism to burn fat, boost your youth enhancing hormones to get more energy & stamina, and build a lean, strong, healthy body:

CARDIO



Too many people think that cardio is the answer to everything related to weight-loss and fat-loss. And although cardio can be helpful (if done properly), it does nothing to slow the aging process. In fact, it does the exact opposite. Doing long frequent cardio sessions will break down your muscles and increase the production of free radicals. These free radicals are nasty little things that damage the cells in your body and accelerate aging. Don't worry if you're concerned about your heart health. There is a much more effective way to improve your cardiovascular health, which I'll cover in just a minute. And here's the best part: it takes only 1/3 the time of a conventional cardio workout AND it also triggers your youth enhancing hormones instead of those nasty free radicals that age you faster.

LOW-FAT DIET

It's hard to believe that "low-fat" is still a dietary recommendation because science has proven that fat is not the cause of weight gain or heart disease. In fact, since the introduction of the fat-free diet, the world has gotten more fat and sick than it has ever been before. Fat is not the enemy. Fat does NOT make you fat. In fact, fat is an *absolute must* if you want your body to look and feel younger! Why? Because healthy fats are an essential source of *good* cholesterol, which is KEY to producing the hormones that enhance your youthful qualities. (Not all cholesterol is bad, by the way — *good* cholesterol is a crucial component of healthy skin tissue, making your skin more supple, glowing, and youthful). If you're following a low-fat diet, you're depriving your body of the nutrients it needs to slow aging and keep your youth.

YOGA

Yoga has been around for thousands of years and it's still around after all this time because it's very effective for things like improving your inner consciousness, mind-body connection and spiritual health. However, it should NOT be considered an effective form of exercise. Sure, some movements are difficult and physically challenging. BUT strictly physiologically speaking, yoga lacks the necessary components to stimulate your body to build lean muscle, burn fat and most importantly… trigger your youth-enhancing hormones to help slow aging. Yoga can improve your flexibility and calm your mind, but it will NOT stimulate your "youth" hormones.

WHAT TO DO NEXT

If you want to reverse the aging process, you need to know HOW to trigger your youth-enhancing hormones to slough away old, dead cells while elevating your metabolic process so you can burn away stubborn, flabby fat and replace it with lean, toned muscle.

The answer is *metabolic training*. Don't worry, it's not as technical as it sounds. Let me explain…

Metabolic training involves doing certain types of exercises that involve your entire body, so you can activate as many muscles as you can in a short amount of time. It's completely different from doing traditional isolated body building exercises (like biceps curls or leg curls) where you're only using one muscle at a time. This form of exercise takes way too long and doesn't stimulate enough muscle fibers to increase your fat-burning and youth-enhancing hormones.

Here's the key: *the more muscles you're able to activate at the same time, the more you'll be able to trigger your youth-enhancing hormones*. This is why using exercises that involve your entire body (upper body and lower body) at the same time is crucial.

That's not all…there's a particular way you want perform these exercises, because doing so will trigger your most effective fat burning hormones, so you can burn off your old excess fat that's been hanging around way too long.
And here's the best part… you can replace your flabby body parts with lean, toned muscle by simply following these exercise protocols, because not only do they trigger your youth-enhancing hormones and fat-burning hormones—they also boosts your testosterone. Testosterone is your ultimate lean-muscle building—hormone for BOTH men and women. And much like other hormones, your testosterone levels naturally start to decline after the age of 40, which is why it's so difficult to gain lean muscle and maintain that youthful body tone as you get older.

Turning back the clock is easy when you know HOW to trigger the right hormones in your body. And I'll show you the specifics behind this easy, *insanely effective* method on the next page. Soon you'll be able to trigger your youth enhancing hormones, along with your fat-burning and lean-muscle building hormones so you can defy the aging process and look and feel 10 years younger! By Shin Ohtake, Fitness & Fat Loss Expert, Author of *MAX Workouts*■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who should pay for this…

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