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# Science INSIGHTS®

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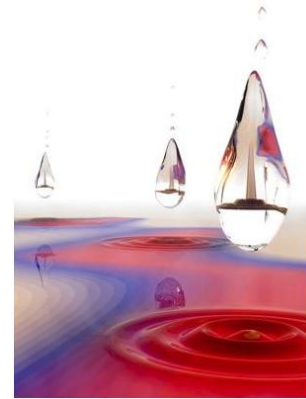
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### COVER

Regarding the cancer immune surveillance and cancer killing activity, the potential contribution of the innate immune system was largely unknown. The discovery of the SR/CR mice and the cancer killing mechanisms of which is mediated entirely by leukocytes from the innate immunity provides a powerful evidence for the significant role of the innate immune system in defending against cancer. See page 139.

*Image: BASE illustrating group*

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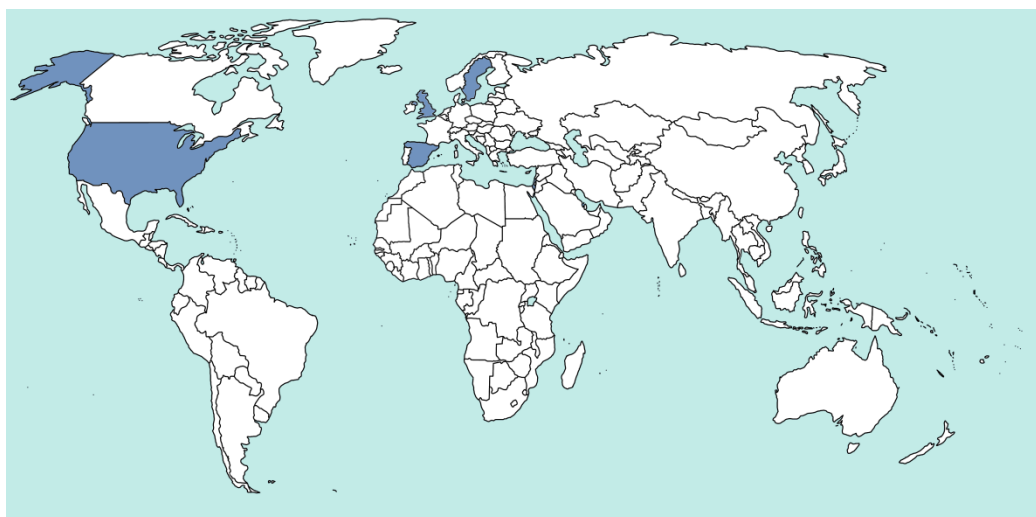
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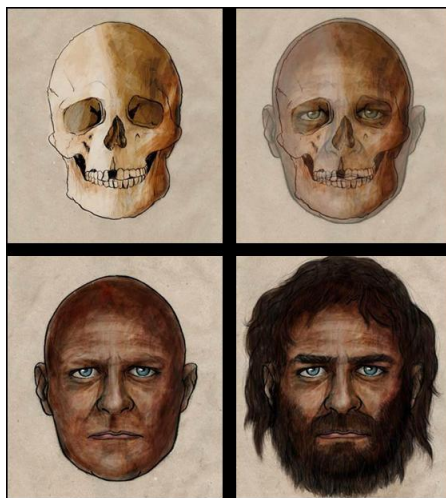
## Barcelona, SPAIN

### Image the 7,000-Year-Old Human

If you do not believe in the Creation of Man by God, please think about the human-oriented science from which we can figure out how old our forefathers were. A new study detailed in the journal *Nature* on January 26, 2014 that light skin evolved not to adjust to the lower-light conditions in Europe compared with Africa, but instead to the new diet that emerged after the agricultural revolution, said study co-author Carles Lalueza-Fox, a paleogenomics researcher at Pompeu Fabra University in Spain. The researchers gathered clue for this ancient European hunter-gatherer man who had dark skin and blue eyes, and lived in modern-day Spain only about 7,000 years ago. Many scientists have believed that lighter skin gradually arose in Europeans starting around 40,000 years ago, soon after people left tropical Africa for Europe's higher latitudes. The hunter-gatherer's dark skin pushes this date forward to only 7,000 years ago, suggesting that at least some humans lived considerably longer than thought in Europe before losing the dark pigmentation that evolved under Africa's sun. Scientists had assumed this was true because people need vitamin D for healthy bones, and can synthesize it in the skin with energy from the sun's UV rays, but darker skin, like that of the hunter-gatherer man, prevents UV-ray absorption. But the new discovery shows that latitude alone didn't drive the evolution of Europeans' light skin. If it had, light skin would have become widespread in Europeans millennia earlier, Lalueza-Fox said. The new analysis of that DNA now shows the man had the gene mutation for blue eyes, but not the European mutations for lighter skin. The DNA also shows that the man was more closely related to modern-day northern Europeans than to southern Europeans. The discovery may explain why baby



blues are more common in Scandinavia. It has been thought that poor conditions in northern Europe delayed the agricultural revolution there, so Scandinavians may have more genetic traces of their hunter-gatherer past – including a random blue-eye mutation that emerged in the small population of ancient hunter-gatherers. In the food-production theory, the cereal-rich diet of Neolithic farmers lacked vitamin D, so Europeans rapidly lost their dark-skin pigmentation only once they switched to agriculture, because it was only at that point that they had to synthesize vitamin D from the sun more readily. “The biggest surprise was to discover that this individual possessed African versions in the genes that determine the light pigmentation of the current Europeans,” Lalueza-Fox said. La Brana 1 was a hunter-gatherer subsisting on a low-starch diet and had trouble digesting milk. “The arrival



of the Neolithic, with a carbohydrate-based diet and new pathogens transmitted by domesticated animals, entailed metabolic and immunological challenges that were reflected in genetic adaptations of post-Mesolithic populations,” the study noted. “Among these is the ability to digest lactose, which La Brana individual could not do.” But the 7,000-year-old also had an advanced immune system normally associated with modern Europeans, the study found. ■

## Göteborg, SWEDEN

### First Womb Transplant Baby on Its Way

We are now facing the high-speeding development of medical science. After nine womb transplants in Sweden, the world's first baby from the procedure may be on its way: Doctors successfully placed an embryo into the transplanted womb of one of the patients last week. Now, “the best scenario is a baby in nine months,” says team leader Dr. Mats Brannstrom. “A success would be an important proof of principle that a procedure is now available to cure uterine infertility.” The embryo came from the patient's own egg; now the question is whether it will embed in the uterine wall, the *Daily Mail* notes. “Milestones through pregnancy how likely are success? Well, in the normal population,” Brannstrom says, “the chance for one embryo would be about 25%—so it may take some trials until we get



a pregnancy.” As for the other transplant recipients, “some of them say that it is fantastic just to have a period.” They say, “Now I feel like a real woman, a normal woman, for the first time.” Interesting note: The patient’s womb, the Telegraph notes, is from her mother – so a successful birth would mark the first time a woman has given birth using the womb from which she herself was born. ■

## New York, USA

### Pfizer Lung Cancer Drug Fails in Two Large Studies

New drug gives us hope to control over diseases, but the studying and testing processes are not that easy. Pfizer Inc. said recently that one of its experimental drugs had failed to meet its goals in two late-stage studies among patients who had received prior treatment for advanced non-small cell lung cancer, the most common form of the disease. Although Pfizer continues to test the drug, called dacomitinib, in another Phase III study, hopes for its success have now largely faded, according to ISI Group analyst Mark Schoenebaum. In one of the failed trials, called ARCHER 1009, patients given Pfizer’s once-daily pill did not show improved survival without the cancer worsening, compared with Roche Holding AG’s widely used Tarceva (erlotinib). Tarceva is the current standard of care in patients with mutated forms of a protein called Epidermal Growth Factor Receptor (EGFR). The protein plays a role in normal regulation of cell growth, but when mutated is believed to cause cells to proliferate and there-

by help spur various types of cancer. Dacomitinib is designed to block several types of Epidermal Growth Factor receptors, while Tarceva and similar treatments for lung cancer target only one type of receptor. Cowen and Co had forecast annual sales of \$500 million by 2020 for dacomitinib, if it were approved for lung cancer. That would make it a moderate-sized product for Pfizer, the largest U.S. drugmaker, which has annual revenue of \$50 billion. Schoenebaum said there has been little investor interest in the drug and that Wall Street had expected it to generate annual sales of only \$300 million by 2018. The second failed trial, named BR.26, involved patients that previously had failed to benefit from chemotherapy as well as from treatment with an EGFR inhibitor. Overall survival of patients taking the Pfizer drug was not prolonged in the study, compared with patients given a placebo. Pfizer said adverse events seen with dacomitinib were consistent with those seen in smaller earlier studies. In the meantime, Pfizer said dacomitinib is also being tested in a third late-stage trial, called ARCHER 1050, among patients with advanced non-small cell lung cancer who have not received prior treatment. The study will compare dacomitinib with Iressa (gefitinib), an EGFR inhibitor sold by AstraZeneca Plc. Results from that study are expected in 2015. ■

## Rehovot, ISRAEL

### The 300,000-Year-Old Caveman ‘Campfire’ in Israel

A newly discovered hearth full of ash and charred bone in a cave in modern-day Israel hints that early humans sat around fires as early as 300,000 years ago – before *Homo sapiens* arose in Africa. In and around the hearth, archaeologists say they also found bits of stone tools that were likely used for butchering and cutting animals. The finds could shed light on a turning point in the development

of culture “in which humans first began to regularly use fire both for cooking meat and as a focal point – a sort of campfire – for social gatherings,” said archaeologist Ruth Shahack-Gross of the Weizmann Institute of Science in Israel. The centrally located fire pit is about 6.5 feet in diameter at its widest point, and its ash layers suggest the hearth was used repeatedly over time, according to the study, which was detailed in the *Journal of Archaeological Science* on January 25, 2014. Shahack-Gross and colleagues think these features indicate the hearth may have been used by large groups of cave dwellers. Furthermore, its position implies some planning went into deciding where to put the fire pit, suggesting whoever built it must have had a certain level of intelligence. Qesem Cave was discovered more than a decade ago during the construction of a road some 7 miles east of Tel Aviv. At the site, excavators had previously uncovered other traces of fire (scattered deposits of ash and clumps of soil that had been heated to high temperatures) as well as the butchered bones of big game like deer, aurochs and horse left their by the prehistoric cave dwellers, possibly up to 400,000 years ago. Anthropologists have debated what constitutes the earliest evidence of controlled fire use – and which hominin species was responsible for it. Ash and burnt bone in Wonderwerk Cave in South Africa suggests human ancestors used fire at least 1 million years ago. Some researchers, meanwhile, have speculated that the teeth of *Homo erectus* suggest this early human was adapted to eat food cooked over a fire by 1.9 million years ago. A study out last year in the *Cambridge Archaeological Journal* argued that fire-builders would have needed some sophisticated abilities to keep their hearths burning, such as long-term planning (gathering firewood) and group cooperation. It is not entirely clear who was cooking at Qesem Cave. A study published about three years ago in the *American Journal of Physical An-*

thropology described teeth found in the cave dating to between 400,000 and 200,000 years ago. The authors speculated the teeth might have belonged to modern humans (*Homo sapiens*), Neanderthals or perhaps a different species, though they noted they couldn't draw a solid conclusion from their evidence. ■

## Oxford, UK

### New Stephen Hawking Theory on Black Holes

We are thinking about the universe, but we do not know the real things of it. Einstein's theory of general relativity predicts the existence of black holes – objects so incredibly massive and dense they pull everything nearby into themselves, and past a point known as the event horizon, not even light cannot escape them. But two years ago, theoretical physicist Joseph Polchinski of the Kavli Institute for Theoretical Physics at the University of California, Santa Barbara and colleagues discovered a wrinkle in the theory, dubbed the Firewall Paradox. The paradox relies on a thought experiment involving an astronaut drifting into a black hole. According to Einstein's theory of general relativity, the astronaut would approach the event horizon and then pass it, blissfully unaware of impending doom. That is because the astronaut would be in free fall, and should therefore feel the laws of physics the same as if he were anywhere else in the universe, Nature News reported. Once inside the hole, the astronaut would be sheared before being crushed at the black hole's infinitely dense core, known as the singularity. But quantum mechanics, the reigning physics theory that governs the behavior of very small particles, dictates that black holes are not perfect cosmic vacuum cleaners. Black holes may be even weirder than scientists had thought, according to a new paper by famed astrophysicist Stephen Hawking. The paper, which attempts to resolve a paradox between the theories of general relativity and quantum

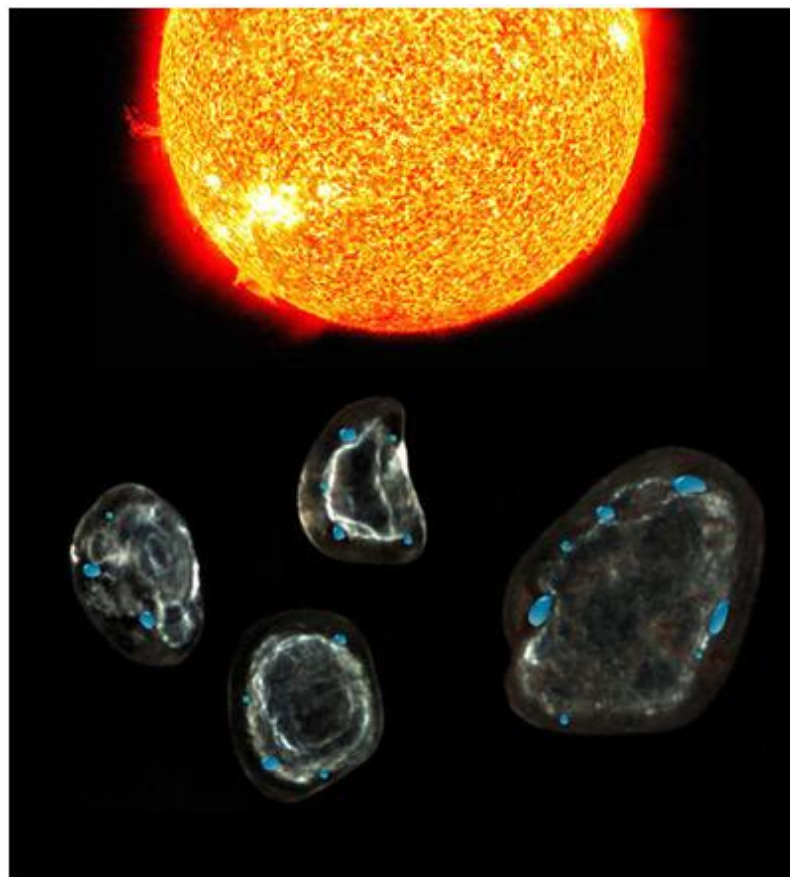
mechanics, was published January 22, 2014 in the preprint journal arXiv.org. In the article, Hawking contends that the notion that even light cannot escape a black hole's gravitational pull once it passes a certain point – known as the event horizon – may not be true. Still, not all physicists are convinced: Some say that doing away with the event-horizon concept doesn't resolve the black hole paradox at all. In 1974, Hawking theorized that black holes leak particles at their edges – a phenomenon known as Hawking Radiation. Given that these particles represent a type of “information” that can escape the event horizon, Polchinski and colleagues predicted that a fiery, energetic ring should exist just inside the event horizon – at least if quantum theory holds true. The firewall would incinerate the astronaut before the dense core compressed the astronaut to a tiny speck. The firewall messes up the notion of smooth, unwrinkled space-time at the event horizon. So, which is it: uneventful event horizon, or fiery ring of hell? To resolve the paradox, Hawking's new paper proposes that there is no fixed boundary of an event horizon. “The absence of event horizons means that there are no black holes – in the sense of regimes from which light cannot escape to infinity,” Hawking wrote in the paper. “There are, however, apparent horizons which persist for a period of time.” Rather than being fixed, these apparent horizons shift wildly with the behavior of quantum particles

inside the black hole. Energy and matter trying to escape the black hole's death grip would be stuck for a time, before eventually being released. So although information could escape a black hole's event horizon, the information would be so hopelessly scrambled that it would be very difficult to figure out what it originally came from, Hawking posits. But not everyone is convinced. For his part, Polchinski doesn't believe that black holes without event horizons are likely to exist in the universe, Nature News reported. Page also thinks Hawking's theory doesn't resolve the fundamental paradox, he told Nature News. ■

## Manoa, USA

### Solar Wind Creates Water in Star Dust

Could we really find new life outside the earth? We are trying every day, but we don't know because we just think about things using our human's manner. Solar wind can form water on interplanetary dust, potentially



adding to the primordial soup that gave rise to life on Earth, scientists say. On Earth, there is life virtually everywhere water is found. Past research suggests much of this water may have come to Earth from comets raining down on the planet. But scientists have suggested another source of water in the airless void of space – the continuous flow of charged particles from the sun, a stream known as the solar wind. This wind consists primarily of protons, the positively charged nuclei of hydrogen atoms. When these particles slam against oxygen-laden rocks – for instance, minerals known as silicates – they could in principle form water molecules. The creation of water via the solar wind could help explain the presence of water on the moon and on asteroids. The wind could also have formed water on interplanetary dust, which, in turn, could have rained water down on Earth and other rocky planets. Intriguingly, interplanetary dust is also known to possess more carbon-laden organic molecules than any other known class of meteoritic material. However, scientists have debated for decades whether or not the solar wind could generate water on the rims or surface layers of rocks in space. The scientists analyzed interplanetary dust collected in the dry stratosphere at an altitude of about 12 miles. Using flags coated in silicone oil mounted on the wing pylons of NASA aircraft, researchers gathered these particles as they rained down from the sky. The scientists detected water in the rims of interplanetary dust particles normally thought of as lacking water. These findings could have implications for distant planets and the prospect of alien life. The researchers noted that estimating how much water is or was deposited on Earth because of this effect remains difficult. This is because scientists do not know precisely how much of the surface area of in-

terplanetary dust particles is exposed to the solar wind or how long they are exposed to it. The brightness of the early sun also remains unknown, as does the amount of interplanetary dust that fell to Earth in the past. Both these factors would influence how much of this water Earth received. The scientists detailed their findings online Jan. 20 in the journal *Proceedings of the National Academy of Sciences*. ■

## Lubbock, USA

### New “Swamp Monster” Skull Found in Texas

A toothy, long-nosed skull found in Texas belonged to a “swamp monster” that lived more than 200 million years ago. The creature is a previously unknown type of phytosaur, an extinct creature that hunted fish and other prey along the shallow edges of rivers and lakes. Dubbed *Machaeroprotopus lottorum*, the phytosaur probably measured about 18 feet long. “They had basically the same lifestyle as the modern crocodile, by living in and around the water, eating fish, and whatever animals

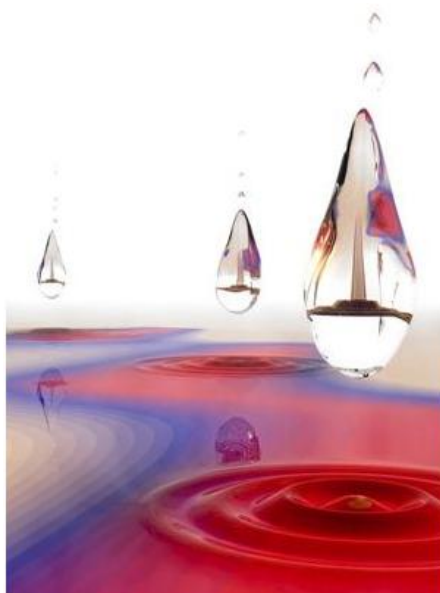
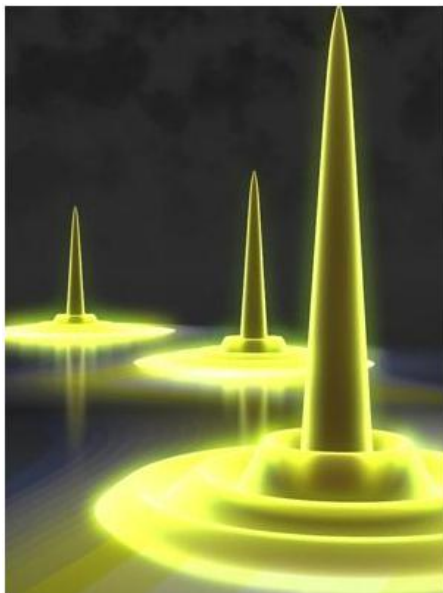


came to the margins of the rivers and lakes,” study researcher Bill Mueller, assistant curator of paleontology at the Museum of Texas Tech University, said in a statement. Phytosaurs are a common find in the Cooper Canyon formation in Garza County, Texas, where the new species was discovered. This area is now dry and scrubby, but in the late Triassic, it was a conifer forest with fern underbrush and an oxbow lake where phytosaurs

hunted. In 2001, Doug Cunningham, a research field assistant at the Texas Tech museum, unearthed the new skull during a dig. “When he found it, just the very back end of the skull was sticking out of the ground. The rest was buried,” Mueller said. “We excavated it and brought it into the museum to finish preparation.” That preparation took years. Once the skull was out of the rock surrounding it, Mueller and his colleagues compared the features of the skull with other phytosaur skulls (more than 200 have been found in North America). They also analyzed another phytosaur skull, found 120 feet (36 m) from the first. They discovered that their specimens represented a male and female from a new species, which they named *M. lottorum* in honor of the Lott family, the owners of the ranch where the fossil was found. Phytosaurs lived from about 230 million to 203 million years ago. They were one of the victims of the Triassic-Jurassic mass extinction, a huge die-off that wiped out many large land animals. The new female’s skull is about 3 feet (1 meter) long, and she would have grown to be about 17 feet (5.1 meters) total length, Mueller said. The male would have been about a foot longer. *M. lottorum*’s delicate snout suggests it ate mostly fish, and not more robust prey. It would have looked very much like an alligator or crocodile, but its nostrils were up near its eyes at the base of its snout, rather than at the end. The researchers reported their findings in the September 2013 issue of the journal *Earth and Environmental Science Transactions of the Royal Society of Edinburgh*. ■

## Washington DC, USA

### Science Academies Explain Global Warming Reality



We almost can hear about the global warming everywhere. Let's listen to the so-called scientific explanation that implies previous words on this topic were not science-based. The man-made global warming is worsening and will disrupt both the natural world and human society, warns a joint report of two of the world's leading scientific organizations. The U.S. National Academy of Sciences and the Royal Society, which is the national scientific academy of the United Kingdom, are releasing an unusual plain language report on climate change that addressed 20 issues in a question-and-answer format. The

**Marburg, GERMANY**  
**Boulder, USA**

### **Quantum Droplet: Weird New Particle Acts Like Liquid**

Physicists can spend years seeking new particles to illuminate aspects of nature's laws, but an international team decided instead to make their own particles. Called a dropletion or quantum droplet, the newly created "particle" is actually a short-lived cluster of electrons and positive charges called "holes". Like other so-called quasiparticles, dropletions act like single particles. An agglomeration of electrons and holes that was bigger than any created before – 200 nanometers, or billionths of a meter, across was made by scientists from the Philipps-University of Marburg, Germany, and Joint Institute for Lab Astrophysics at the University of Colorado, USA. That is almost big enough to see with a good microscope, about one-50th the thickness of a cotton fiber. Before now, physicists had created two-pair groups of electrons and holes, but never such an agglomeration that could form this liquid-like quantum droplet or dropletion. These dropletions behave according to the rules of quantum physics, and that means scientists can use the particles to investigate how light interacts with matter – a process also governed by quantum rules. Because the dropletions are so large, in particle terms, they might also help physicists locate the boundaries between the quantum world of the very small and the classical world of the human scale, the physicists report in the February 27, 2014 issue of the journal *Nature*. To make the dropletion, the researchers fired quick pulses of an extremely powerful laser at a block of gallium arsenide, the same material used in red light-emitting diodes (LEDs). Each pulse lasted less 100 femtoseconds, or billionths of a billionth of a second. When the light hit the gallium arsenide, the atoms released, or excited, electrons, which moved around in the gallium arsenide like a gas or plasma. When the negatively charged electrons exited their places around the atoms, they left behind regions of positive charge called holes. Since the dropletion is an artificial particle, containing a number of electrons, it acts something like a super-sized electron. That property means physicists could essentially modify the size of an electron for experiments. Of all the electron-hole particles that have been created, this is the first to ever hold enough pairs to form a liquid-like droplet. Electrons and holes, having opposite charges, tend to form pairs, called excitons. These pairs are familiar to anyone who has used some types of solar panels, which employ special materials to separate the electron-hole pairs, freeing up electrons and generating current. However, the excitons in this experiment were much more energetic. They had so much energy that they would clump together in groups as if they were water droplets clinging together. At that point, they were no longer excitons bound in pairs – they were dropletions. The electrons, unbound from single holes, formed a kind of standing wave pattern around them. It's similar to the patterns that ordinary molecules make in liquids. Dropletions don't last long, only 25 picoseconds, or trillionths of a second. But that's actually a relatively long time in terms of quantum-physical processes. In addition, because dropletions entangle with the photons used to make the quasiparticles, physicists can use them to study storage of quantum states – potentially useful in designing quantum-based communications devices in which such states serve as the bits of information. ■

report, released on Thursday, addresses new issues such as the recent slowing in the increase of world temperatures and how heat-trapping gases are connected to extreme weather. Increases in extreme weather, melting glaciers, rising seas and oceans getting more acidic are already happening, the 36-page report said. And those changes “are expected to increase greater warming and will threaten food production, freshwater supplies, coastal infrastructure and especially the welfare of the huge population currently living in low-lying areas,” the report said. The report said that while the rate of warming is slower in the 2000s than it was in the 1990s it does not negate the 150 years of observations that show the world is warming. The report also says that more the 90 percent of the heat trapped by greenhouse gases lately has been absorbed into the oceans’ deep water, which for a while slows surface warming but not the long-term trend. There is enough evidence on the science to warrant action, Sir Paul Nurse, president of the Royal Society, said in a news release. “We’ve changed the chemical composition of the atmosphere; that’s not a belief system. We know that beyond shadow of a doubt,” Santer said in an interview. “We ignore this at our peril.” ■

## London, UK

### Chinese Jurassic Park Yields Incredible Feathered Dino

A fossil bed in China that contains some of the world’s most exquisitely



preserved feathered dinosaurs, early birds, reptiles and mammals may also be home to an equally rich set of older fossils from the Middle Jurassic, a new study finds. These older fossils, dating back about 160 million years, contain the earliest known gliding mammal, earliest swimming mammal, a flying reptile and the earliest feathered dinosaurs. Now, a new study classifies these fossils as belonging to a distinct ecological group, or biota. The new biota was found in layers of rock beneath the so-called Jehol Biota, a famous collection of 130-million-year-old fossils from China’s western Liaoning Province and nearby north-eastern China; the Jehol organisms are now thought to have been killed and preserved in a Pompeii-style eruption. In recent years, fossils that are 30 million years older have surfaced from beneath the Jehol Biota, but have not been definitively linked to

the same time period. The fossils from the Jehol Biota literally lie on top of the older specimens, said David Hone, a dinosaur biologist at Queen Mary University of London and leader of the study published on March 04, 2014 in the *Journal of Vertebrate Paleontology*. The researchers have catalogued and described the older fossils in unprecedented detail, naming them the Daohugou Biota after a village in Inner Mongolia near one of the six main fossil sites examined. Like the Jehol fossils, the Daohugou fossils have remarkably intact skeletons, often still containing soft tissues and even feathers. The fossil trove dates from the Middle-Upper Jurassic, a period when birds are thought to have evolved from feathered dinosaurs. The team found feathered dinosaurs that were extremely birdlike, though not any actual birds. ■

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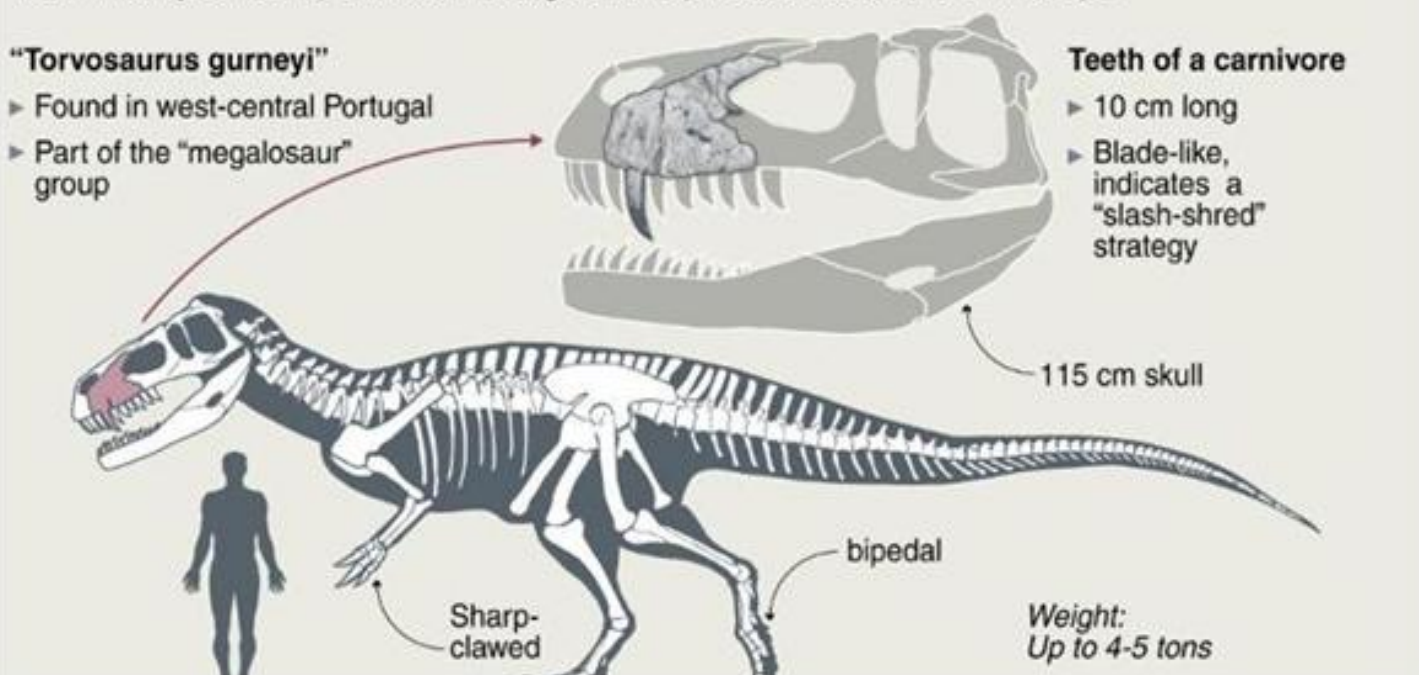
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## Predator king

150-million-year-old species is the largest land predator discovered in Europe

### "Torvosaurus gurneyi"

- ▶ Found in west-central Portugal
- ▶ Part of the "megalosaur" group



### Washington DC, USA

## Huge New Dinosaur in Portugal Was Predator King

A new dinosaur species discovered in Portugal dominated the food chain 150 million years ago – the Tyrannosaurus Rex of its time, researchers said Wednesday. The new species is the largest land predator discovered in Europe and one of the largest worldwide of the Jurassic era, said authors Christophe Hendrickx and Octavio Mateus of the Universidade Nova de Lisboa and Museu da Lourinha. The *Torvosaurus gurneyi*, like T. Rex, was a bipedal carnivore with blade-like teeth more than 4 inches (10 centimeters) in length, they said in a report published in the journal of PLOS ONE. The scientists estimate *Torvosaurus gurneyi* grew up to 33 feet (10 meters) long and weighed some 4 or 5 tons. Its skull measured nearly four-feet (115 centimeters) long, smaller than the T. Rex, but not by a huge margin. The fossils found in Portugal closely resemble those of a North American dinosaur – the *Torvosaurus tanneri* –

and indeed at first the scientists thought the two specimens must be from the same species. But upon closer analysis of the bones, the researchers determined the species must have evolved separately from the two sides of the proto-Atlantic Ocean over a few million years. Mateus said it is hard to know how different the two species would have looked when they were living – there may have been differences in coloring or behavior that would have easily distinguished them. The North American species has 11 or more teeth on its upper jaw, compared to fewer than 11 for the Portuguese dinosaur, the researchers explained. And the mouth bones are shaped and structured differently. Discovering such a large predator in this era could really be “a game changer” in terms of how scientists think of the Jurassic food chain, explained University of Kansas paleontologist David Burnham, who was not involved in the research. “These things were living with giant plant-eating dinosaurs,” or sauropods, Burnham explained, herbivores too big for other common Jurassic predators, like the *Allosaurus*, to attack. But if the estimates of the

new *Torvosaurus* are right, he said, the carnivore was certainly big and fast enough to catch a small sauropod. “The blade-like teeth of *Torvosaurus* are particularly nasty since they would seem to indicate a slash-shred strategy,” he added. The new species is also of interest to paleontologists, because it gives a more detailed picture of the interactions and connections between North America and Europe at the time. “Finding another (*Torvosaurus*) species in Portugal is pretty cool, because this is additional evidence that shows a similarity in Jurassic dinosaurs in Europe and in North America,” adding to finds of a *Stegosaurus* and an *Allosaurus* in both the US West and Portugal, said Ken Carpenter, paleontologist at Utah State University. ■





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## LIFE AND HEALTH

## Infant Mortality and Life Expectancy in China

With the rapid development of China economy, people's life is changing dramatically. For the most-populous country, people in the north and south regions have different life style and attitude toward living setting. Although the air pollution is a big problem for the China government to conquer it, the country's overall situation reached a new level. A study led by Dr. Zhengyan Zhao from Zhejiang University, China reported the infant mortality (IM) rate and the life expectancy (LE) of Chinese people. In this study, the authors reviewed the literatures on the history and current status of IM and LE in China and other major countries, the relationship between IM, LE, and per capita gross national income (GNI), and they found that the decline in IM from 30‰ to 15‰ took China only 7 years, which was faster than in developed countries. The leading causes of infant death in China were perinatal diseases, infectious and parasitic diseases, congenital anomalies, accidents, and signs, symptoms, and ill-defined conditions. Most under-5 mortality occurred during infancy (80%), particularly during the neonatal period (55%). LE was negatively correlated with IM and per capita GNI, while IM was negatively correlated with per capita GNI. However, healthcare capabilities and per capita GNI in China are still below the level of developing countries. Some countries have a comparable IM and healthcare capabilities, but they have a much higher per capita GNI than China. At last, the researchers concluded that in China, IM has decreased and LE increased rapidly. However, they were not in parallel with the current economic development. Deviation of these data might be attributed to many factors. In-house surveys and hospital-based follow-ups should be carried out to better understand infant death. ■

**Med Sci Monit 2014;20:379.**



## NEUROSCIENCE

## Noise and Errors in Working Memory

Are there special maneuvers that can help us enhance our memory? Short-term recall of basic visual features declines steadily in precision as the number of features held in memory increases. In visual memory, attempts to account for errors in terms of allocation of a limited pool of working memory resources have met with some success, whereas the biological basis for this cognitive architecture is yet to be known. A new study conducted by Dr. Paul M. Bays of the University College London, UK and University of California at Berkeley, USA examined the errors produced by an ideal observer decoding stimulus parameters from the activity of probabilistically spiking neurons. As the gain of the neural population decreases, error distributions deviate from normality in the manner characteristic of human working memory. The author tested the ability of a population coding model to describe errors in short-term memory for displays consisting of multiple orientation stimuli. Memorization of the display was

modeled as encoding of the stimulus orientations in the activity of a population of idealized memory neurons, with spatial selectivity and orientation tuning. Each orientation stimulus provided a feedforward input to a discrete subpopulation of neurons selective to its location. Within that subpopulation, the driving input to each neuron was determined by the deviation between the stimulus orientation and the preferred orientation of the cell, following a bell-shaped tuning function. To compare the predictions of the population coding model to human memory performance, observers in Experiment 1 were presented with displays consisting of between one and eight oriented bars. After a brief blank display, one location was probed, and subjects reported the remembered orientation of the item at that location using a response dial. Recall error was quantified as the angular deviation between the reported orientation and its true value in the memory array. To test the effect of both increasing recall fidelity for the preferred stimulus and reducing precision for other items in memory compared with the situation with equal inputs, the author performed a second experiment. The task



was identical to Experiment 1, except that one item on each trial was highlighted by a visual cue appearing before the array, and this cued item was more likely to be probed on the subsequent test than other items in the array. Based on previous results, I expected that observers would prioritize accurate storage of the cued item to maximize their overall response precision. In the study, the population coding model allowed the research to make quantitative predictions regarding the optimal weighting of stimuli in memory that would minimize errors on the task. For a fixed ratio of cued/uncued test probability, the author found that observers should increasingly weight memory representation in favor of the cued stimulus as load increased. This prediction was borne out in the distributions of observers' errors, demonstrating that human observers can fine-tune the contents of working memory to attain behavioral goals. For this model, the author finally concluded that one testable prediction of this account is that rate of decay should increase with memory load. A corollary is that boosting the gain of neurons encoding one particular stimulus during maintenance would protect that stimulus from decay, at the cost of more rapid decay for other stimuli – this might provide an explanation for the “retro-cue effect,” i.e., the recall advantage seen for an item cued long after its presentation. ■

**J Neurosci 2014;34(10):3632.**

## ADOLESCENCE HEALTH

### Children in High-Poverty with Subsequent Mental

## Disorders during Adolescence

Poverty is spreading over the world even in the developed countries. The youth from poverty environment shows high rates of emotional problems. However, how to intervene this and improve their mental health is a thorny problem. A new study led by Dr. Ronald C. Kessler from Harvard Medical School, USA performed an exploratory analysis of associations between housing mobility interventions for children in high-poverty neighborhoods and subsequent mental disorders during adolescence, and found that interventions to encourage moving out of high-poverty neighborhoods were associated with increased rates of depression, posttraumatic stress disorder (PTSD), and conduct disorder among boys and reduced rates of depression and conduct disorder among girls. Better understanding of interactions among individual, family, and neighborhood risk factors is needed to guide future public housing policy changes. In this study, the researchers randomized 4,604 volunteer public housing families with 3,689 children in high-poverty neighborhoods into 1 of 2 housing mobility intervention groups (a low-poverty voucher group versus a traditional voucher group) or a control group from 1994 to 1998. The low-poverty voucher group (n=1,430) received

vouchers to move to low-poverty neighborhoods with enhanced mobility counseling. The traditional voucher group (n=1,081) received geographically unrestricted vouchers. Controls (n=1,178) received no intervention. Follow-up evaluation was performed 10 to 15 years later (June 2008-April 2010) with participants aged 13 to 19 years (0-8 years at randomization). After follow-up, the researchers evaluated the presence of mental disorders from the Diagnostic and Statistical Manual of Mental Disorders (4th Edition) within the past 12 months, including major depressive disorder, panic disorder, PTSD, oppositional-defiant disorder, intermittent explosive disorder, and conduct disorder, as assessed post hoc with a validated diagnostic interview. Of the results, the authors presented that of the 3,689 adolescents randomized, 2,872 were interviewed (1,407 boys and 1,465 girls). Compared with the control group, boys in the low-poverty voucher group had significantly increased rates of major depression (7.1% vs 3.5%; odds ratio (OR), 2.2 [95% CI, 1.2-3.9]), PTSD (6.2% vs 1.9%; OR, 3.4 [95% CI, 1.6-7.4]), and conduct disorder (6.4% vs 2.1%; OR, 3.1 [95% CI, 1.7-5.8]). Boys in the traditional voucher group had increased rates of PTSD compared with the control group (4.9% vs 1.9%, OR, 2.7 [95% CI, 1.2-5.8]). However, compared



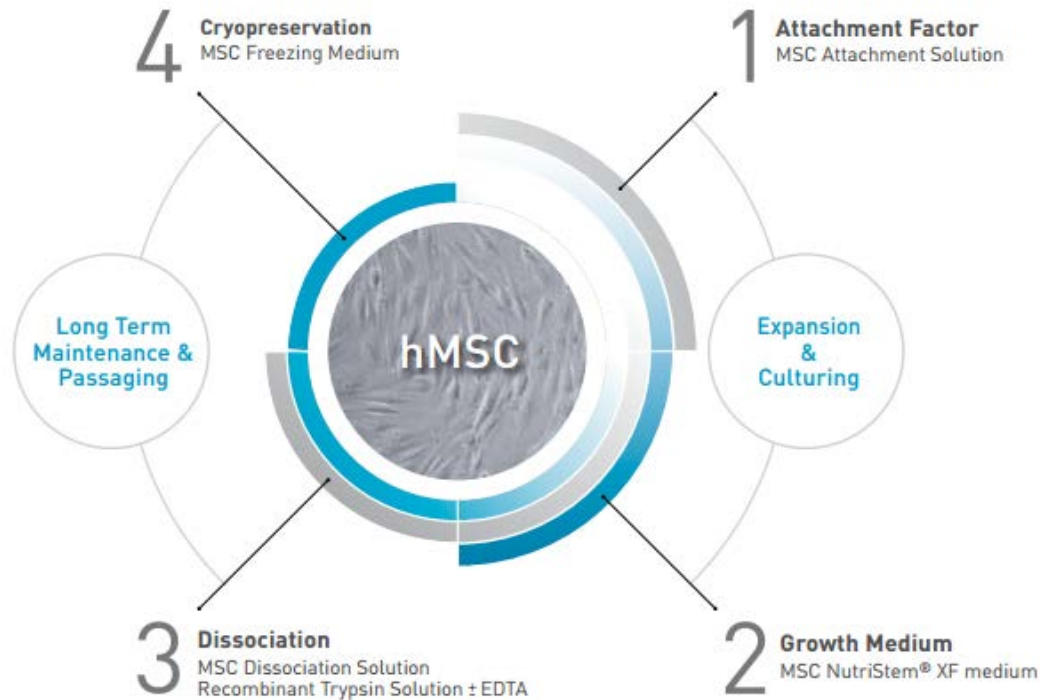
with the control group, girls in the traditional voucher group had decreased rates of major depression (6.5% vs 10.9%; OR, 0.6 [95% CI, 0.3-0.9]) and conduct disorder (0.3% vs 2.9%; OR, 0.1 [95% CI, 0.0-0.4]). From these results, the researchers concluded that interventions to encourage moving out of high-poverty neighborhoods were associated with increased rates of major depression, PTSD, and conduct disorder among boys and reduced rates of major depression and conduct disorder among girls. Better understanding of interactions among individual, family, and neighborhood risk factors is needed to guide future public housing policy changes in light of these sex differences. ■

**JAMA 2014;311(9):937.**

**BIOENGINEERING**

**Method for Harvesting hMSCs from Microcarriers**

Biotechnology poises the development of biology and medical science. Stem cell engineering is a promising means in treating diseases. However, how to get adequate dynamic cells using different techniques is a biological and engineering problem. Cumulating emphases were focused on improving human mesenchymal stem cell (hMSC) expansion techniques. A group headed by Dr. Christopher J. Hewitt from Loughborough University, UK studied and found a potentially scalable method based on agitation theory for harvesting hMSCs from microcarriers. The use of hMSCs for allogeneic ther-



apies requiring lot sizes of billions of cells will necessitate large-scale culture techniques such as the expansion of cells on microcarriers in bioreactors. Whilst much research investigating hMSC culture on microcarriers has focused on growth, much less involves their harvesting for passaging or as a step towards cryopreservation and storage. A successful new harvesting method has recently been outlined for cells grown on SoloHill microcarriers in a 5 l bioreactor. Here, this new method is set out in detail, harvesting being defined as a two-step process involving cell “detachment” from the microcarriers’ surface followed by the “separation” of the two entities. The new detachment method is based on theoretical concepts originally developed for secondary nucleation due to

agitation. Based on this theory, it is suggested that a short period (here 7 min) of intense agitation in the presence of a suitable enzyme should detach the cells from the relatively large microcarriers. In addition, once detached, the cells should not be damaged because they are smaller than the Kolmogorov microscale. Detachment was then successfully achieved for hMSCs from two different donors using microcarrier/cell suspensions up to 100 ml in a spinner flask. In both cases, harvesting was completed by separating cells from microcarriers using a Steriflip® vacuum filter. The overall harvesting efficiency was >95% and after harvesting, the cells maintained all the attributes expected of hMSC cells. ■

**Biochem Eng J 2014;85:79.**



Love the Wave  
Love the Earth



# Saturn's "Yin and Yang" Moon

By NASA



**Saturn's "Yin and Yang" Moon.** Call it cosmic zen. Yin and yang appear to meet on one of Saturn's moons in a photo taken by a spacecraft exploring the ringed planet and its many moons. The new Cassini photo of Saturn's moon Iapetus shows the satellite's dark and light sides as comma-shaped features that bear a striking resemblance to the yin and yang symbol in Chinese philosophy. The image was released in December 2013, but actually taken by the Cassini spacecraft in August 2013. "This view looks toward the Saturn-facing hemisphere of Iapetus," NASA officials wrote in an image description. "North on Iapetus is up and rotated 30 degrees to the right. The image was taken in visible light with the Cassini spacecraft narrow-angle camera on Aug. 30, 2013." Some scientists think that the two faces of Iapetus probably get their distinct appearances from the moon's slow rotation, meaning that the dark surfaces of the moon absorb more heat and have time to warm. Any icy materials that mix with the hotter surfaces turn gaseous and then fall back into the cooler regions, meaning that the dark side gets darker while the bright side becomes brighter. Giovanni Cassini first spotted Iapetus in 1672. The odd moon is shaped somewhat like a walnut, with a huge ridge running along its equator. It is likely that the ridge was created when a giant impact flung chunks of Iapetus out into space at the end of its planetary growth more than 4.5 billion years ago. The debris may have re-formed around the moon, creating a new moon orbiting Iapetus. Eventually, Iapetus' gravity tore its moon apart and the rubble rained down, creating the moon's distinctive ridge. It's also possible that the ridge formed early in the moon's history when it was spinning more quickly than it does now. The Cassini spacecraft launched in 1997 and made it into orbit around Saturn in 2004. The spacecraft is expected to continue studying Saturn and its moons until 2017, after which it will burn up in Saturn's atmosphere.



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## **Granulocyte Therapy for Cancer: A Prospective Review** Dong Wang, Wen-ying Wang, Lei Ren

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# Granulocyte Therapy for Cancer: A Prospective Review

Dong Wang,<sup>\*A</sup> Wen-ying Wang,<sup>†</sup> Lei Ren<sup>\*</sup>

A powerful and complicated defense system exists within the cell and the whole body to protect against “irresponsible” cell growth and to deal harshly with most wannabe cancerous cells. However, occasionally the malfunction of one of these systems may result in an uncontrolled cell growth, which has been found taking the first step toward becoming carcinogenesis. Immune system is the most important defense system to protect the host from diseases. There is strong evidence showing that immune system also plays an essential role in providing significant protection against cancer. However, how the immune system works in defending and fighting against cancer and what is the exact molecular mechanisms of this process are still unknown. We herein review the historical change of the immune-associated cancer therapy and then provide evidence on the exploration of the relationship between the immune system and cancer disease. Moreover, an outline about the serendipity discovery of the Spontaneous Regression/Complete Resistant mice and the corresponding selective cancer killing mechanism of which is mediated entirely by leukocytes from the innate immunity is discussed. In addition, based on the outstanding curative effect on the animal model, a promising anti-tumor therapy method, Leukocyte Infusion Therapy, has been approved by FDA and is being preceded in conducting clinical trials. ■

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**Keywords:** Cancer immunotherapy – Immune surveillance – Spontaneous regression – Granulocyte – Cancer Killing Activity

IT is well known that cancer is predominately a disease of elder individuals, the human above their 50 years of age have a higher risk for cancer (1). It is also not uncommon that some people remain cancer-free into their 80s and 90s, even if they are regularly exposed to environmental carcinogens such as

air pollutants and heavy cigarette smoking etc. Like most of the epidemic diseases, they spread in a large area or among a large population especially in the winter. As reported that human mortality is much higher in winter than in summer (2), this phenomenon seems never changing since data have been recorded (3).

Immune system, an essential evolutionary protective composition of our surveillance mechanism, plays the foremost important role in protecting the host from attacking by different types of diseases, especially the infectious diseases. The immunity seems vary with the seasons, which means people needs limited activity and more sleep to compensate the weaker immunity in the winter. In addition, there is strong evidence showing that a weakened immune

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system will increase one's chances of getting blood-cell and virus-associated cancer (4).

### From spontaneous regression of cancer to cancer immune surveillance

What is the exact relationship between immune system and cancerous diseases? This is a frequently asked question but without a clear answer. We herein briefly review the development of its history and give some typical events about the question.

From the historical records, the spontaneous regression of cancer is a well-documented, even are rare, event for many types of cancer (5, 6). While great efforts have been taken over the past decades, the mechanisms of spontaneous regression have remained elusive. However, one interesting thing is that many reported cases of spontaneous regression of malignancy occurred along with infection (7, 8).

In the 1890s, William Coley, a New York pioneer surgeon, began exploring the immunotherapeutic approach to cancer. Coley developed a vaccine, now referred to as "Coley's toxins", consisting of extracts of killed gram-positive streptococcus pyogenes and gram-negative serratia marcescens, can evoke many symptoms of bacterial infection such as fever and chills without the actual infectious problems. Tumors, especially the soft-tissue sarcomas and lymphosarcomas or lymphomas, were observed to partially or completely be regressed following treatment with Coley's toxins (9).

Although the reasons why sarcomas responded preferentially to the treatment of Coley's toxins are unanswered, it has been suggested that sarcomas have a higher probability of being immunogenic (10). The application of Coley's toxins in clinical practice eventually stopped due to his death and some inconsistent results, whereas Coley's efforts to stimulate the immune system to combat cancer

credited him being as the father of today's cancer immunotherapy.

In 1909, Paul Ehrlich, the 1908 Nobel Prize laureate in Physiology and Medicine, suggested that cancer and the functional capacity of an individual's immune system are interdependent. He proposed that in a normal human body there existed cancer cells, but an inherent system also existed that could identify and remove cancer cells before they accumulate into detectable cancer lesion in the absence of external therapeutic intervention. After then, Ehrlich named his hypothesis as "cancer surveillance" (11), which means the existence of few cancer cells in normal human body may not threaten daily health only if the growth of cancer cell and the cancer surveillance are in the dynamic balance of supersession and remodeling.

The hypothesis of tumor immune surveillance was then formalized in the 1950s by Sir MacFarlane Burnet, the 1960 Nobel Prize laureate in Physiology and Medicine, and Lewis Thomas on the basis of the advanced mechanisms of the role of cellular immunity in eliminating allergenic or altered cells including cancerous cells. They then hypothesized that lymphocytes were the critical component for recognizing and eliminating the continuously arising and newly transformed cancerous cell. (12). However, the theory of tumor immune surveillance subsequently remained controversial and found difficult to be demonstrated experimentally. The newly developed basic and clinical evidence supported the significant effect of immune system, mainly the lymphocytes, on the cancer immune surveillance, but the potential contribution of other leukocyte populations was largely unknown.

For the existence of cancer immune surveillance, Chester Southam provided another piece of evidence (13). Southam injected a tumor cell line (Hela cells) into humans who were divided into two groups. The study showed that non-cancerous patients rejected the tumor cells; in con-

trast, subjects with advanced cancer were able to sustain tumor growth for a considerably longer period of time from the cancerous transplants, which suggested that the later had impaired immune function against cancer. Moreover, the impaired immune function was not resulted from the immunosuppression, as the production of antibodies against viral infection was found to be the same in non-cancer patients as those with cancer. The study discussed and argued that the decline in immune function was cancer specific. Otherwise, there naturally exists an immune surveillance system in some people's body, and this surveillance is cancer specific. However, it does not exist in all people's body.

### A serendipity discovery of the Spontaneous Regression/Complete Resistant (SR/CR) super mice

The exploration of the relation between the immune system and cancerous diseases continued, and 50 years later, a serendipity discovery and a series of research work put this hypothesis on spot again. (14)

In 1999, Dr. Cui and colleagues injected mice with an ultra-virulent ascites carcinoma cells, Sarcoma 180 (S180), during a routine experiment designed to generate ascites for enhancing antibody production. Unexpectedly, one male mouse survived with S180 and remained ascites free after repeated injection. S180 is a historically wide-used mouse cancerous cell line that was originally derived from the connective tissue of Swiss mice and is reported to express negligible levels of Major Histocompatibility Complex (MHC) surface proteins, thus enabling it to demonstrate unrestricted growth within several different genetic strains of mice. Due to its aggressive nature, no reports there regarding the resistance to S180 induced ascites. After then, confirmation studies were carried out and found the original mouse survived after increasing the does up to

$2 \times 10^9$  S180 and remained ascites free.

Since then thousands of mice in about 50 generations have been bred from the original cancer-free super mouse and approximately 30 percent of the offsprings have inherited the cancer resistant trait in an autosomal manner.

These mice strain were named later by Dr. Cui as Spontaneous Regression/Complete Resistant (SR/CR) mice. The purpose in naming the mice SR/CR was due to the age-dependent responses witnessed at the time of cancer screening. Among offsprings that eventually showed to be SR/CR, those that are screened at 6 weeks of age quickly demonstrate complete resistance (CR), whereas approximately half that go on to be initially screened at 12 weeks of age would develop S180-induced ascites before demonstrating spontaneous regression (SR).

Further studies in Dr. Cui's lab have shown that the cancer resistance in SR/CR mice is mediated by the special immune system, exactly as the innate immune system with neutrophils, macrophages, and natural killer cell among the most abundant responding cell types (15).

What is the evidence about the innate immune system, rather than adaptive immune system or others, in response to the action unit? Before discussing the novel discovery and the scientific explanation, we will first present some basic concepts of the immune system.

The innate immune system, also known as non-specific immune system, is capable of providing an immediate first line defense over the host from infection by external organisms through recognizing common features of pathogens in a non-specific manner. In contrast, the adaptive immune system permits the recognition of novel pathogens through the clonal selection of antigen-specific receptors. The adaptive response is retained after elimination

of the pathogen in the form of immunological memory, which provides enhanced levels of protection from subsequent re-infection from the same pathogen. The innate immune system plays an important role in both the activation of the adaptive immune system and the control of infections before the initial adaptive immune response taking effect (16).

The resistance against cancer mediated by innate immunity is supported by a lot of evidenced facts as fol-

...What an amazing unbelievable scene that the elder cancer resistant mouse developed ascites like the other commons and then the ascites disappeared suddenly overnight at about 15th day after the cancer cell challenged...

lows (15, 16): (i) The SR/CR mice survived the initial challenge with cancer cells without any prior exposure suggests that the anticancer response is innate immunity, and the innate immune cells remain as the major responding effector cells during repeated cancer cell challenges. (ii) The rupture of cancer cells by leukocyte subsets was clearly, visually characterized by transmission electron microscopy and immunofluorescence microscopy (17). On this video, the yellow arrow pointed out that granulocyte is killing cervical cancer cells. For this process, it was shown that some rosettes was formed between leukocyte subsets and cancer cells, and the composition in the rosettes was identified by using flow cytometry and surface marker labeled to indentify polymorpho-nuclear leukocytes (PMN, 38%), natural killer cells (NK, 35%), and macrophages (26%). Formation of rosettes between leukocytes and cancer cells is a specific property of the anticancer response in SR/CR mice and has not been observed in wild type (WT) mice challenged with cancer cells. (iii) The independent depletion of any of

these sub-types cannot abolish cancer resistance, while the total immune depletion resulted in tumor formation which could be reversed when the immune system was allowed to recover. (iv) Half of the offspring crossed from SR/CR mice and the nude mice in which the maturation of T lymphocyte is blocked by the absence of a thymus show the similar ascites resistance phenotype to the SR/CR mice. (v) Highly purified NK cells, macrophages, and neutrophils from the SR/CR mice independently kill cancerous cells in vitro. Besides, the purified populations of SR/CR macrophages have been shown can be transferred to WT mice to offer protection from S180 tumor formation. Thus it is clear that in the SR/CR mouse model, the innate immune cells, especially the neutrophils, are capable of mediating cancer immune surveillance.

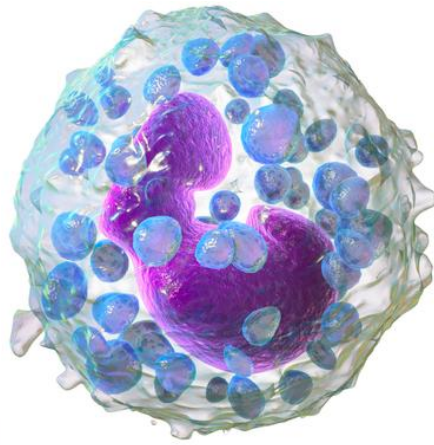
The innate immune response of SR/CR mice to S180 occurs in three distinct phases: infiltration, tight contact and tumor destruction (15, 16). First, upon challenges with cancerous cells, predominant innate host leukocytes can detect the unique signals of cancerous cells and migrate directly to the cancer site in response to the reversed chemical concentration gradient. The varieties of protein pieces specifically produced by cancerous cell may mainly be the chemo-attractants play a role in this process. In addition to S180, SR/CR mice were found to be resistant to EL-4 lymphoma, MethA sarcoma, P851 mastocytoma, and LL2 lung carcinoma etc, although there was a large difference in the maximum tolerated dose (MTD) to different types of tumor cells. The tumor cells with intense chemotaxis to attract leukocytes have a higher MTD, which leads to an escape from resistance. These results indicated that the chemo-attractants of tumorous cells and the chemotaxis function of leukocytes together play a pivotal role in the process of cancer killing (18). Second,

once they arrive at the sites of cancer, the host leukocytes tightly contact with the cancerous cells via surface recognition, of which is mediated by the cellular membrane charge difference between them. The surface recognition by leukocytes results in a suspended cellular aggregate and then formed the rosettes. The presence of the rosette provides a crucial experimental means showing that direct cell contact is essential for leukocyte-mediated cancer killing in SR/CR mice (18). Third, once they are engaged with cancerous cells, leukocytes undergo rapid transformation into effector cells, in which the effector molecules such as cytotoxic granules and perforin, and other cytolytic effectors like superoxides, and nitric oxides are generated. Such effector molecules cause damage to the plasma membranes swelling and eventual rupture of cancerous cells through both cytolysis and apoptosis pathways (18). The third process may not unique to SR/CR mice since these effector mechanisms have been reported previously in WT mice in killing the cancerous cells (18). However, the first two processes were unique to SR/CR mice since WT leukocytes are unable to respond to the same cancerous cells with either infiltration or rosette formation. Research on elucidating the exact mechanism of SR/CR resistance is still ongoing.

Another intriguing property of the resistance of SR/CR mice is that they are healthy even in an extended lifespan suggesting that normal cells in these mice are not harmed by the anticancer response that only targets on cancerous cells with exceptional high specificity. The cancer resistant phenotype can be retained for life if the mice are frequently challenged with cancerous cells (16).

### Leukocyte infusion therapy for cancer

The exact mechanism and the roles of innate and adaptive immune system in SR/CR resistance are not so clear. However, the therapeutic potential



for cancer is apparent and absolutely exciting.

Granulocytes are the most abundant type of white blood cells that account for as much as 60% of total circulating white blood cells in healthy people, and up to 95% of granulocytes are neutrophils. Donors can give granulocytes specifically without losing other components of blood through a process called leukapheresis that separates granulocytes and returns other blood components back to donors. This is an established procedure that has been in use for more than 40 years with very good safety records. According to the FDA regulation, a healthy donor can give granulocytes by apheresis blood donation 24 times a year.

To normalize the cancer resistance ability, an *in vitro* assay of Cancer Killing Activity (CKA) has been developed by Dr. Cui's research team (19). The CKA was normalized as percentages of total target cells during selected periods of incubation time and at selected effector/target cell ratios in comparison to non-effector cell controls. The CKA assay was initially used in SR/CR mouse phenotype test, and then investigated successfully in human leukocytes. The existence of CKA in humans is an initial step to the goal that can translate the anti-cancer therapeutic effect into human being.

In a human study with small sample volunteers, Dr. Cui and colleagues found that the cancer-killing activity of the granulocytes was in the highest level in people under the age 50. One of the unexpected dis-

coveries is that the CKA in some volunteers is higher than that in the SR/CR mice, although it is in the same low level in some people as in the WT mice. They also found that this activity can be decreased by factors like winter weather or emotional stress (19). The research raised a prospect that cancer-killing immune cells from donors can be used to significantly boost the cancer-killing ability of cancer patients to fight their diseases until cure them.

In the study, volunteers who are selected as donors, based on the observed potential CKA of their white blood cells, will complete the leukapheresis blood donation to collect their "super strength" granulocytes. The cancer patients will then receive the granulocytes through a transfusion, a safe process that is often used for patients who have antibiotic-resistant infectious diseases for many years. Dr. Cui named the therapy Leukocyte Infusion Therapy (LIFT). The concept makes us think again about our preconceived notions that how the immune system works against cancer. The clinical trial of Leukocyte Infusion Therapy has been approved by FDA with a ClinicalTrials.gov Identifier of NCT00003243 and is preceded in South Florida Bone Marrow/Stem Cell Transplant Institute (20). The study was to see if simple blood transfusions can transfer cancer immunity from people with strong cancer immunity to those without such strong immunity.

The key to the success for such a new therapy is to transfuse sufficient granulocytes from healthy donors while their cancer-killing activities are at the peak level. It is important that the donors and recipients are unrelated and the human leukocyte antigen (HLA) mismatched to avoid the possibility of transfusion-associated graft versus host diseases.

How can we collect sufficient "super strength" cancer resistance granulocytes? Whether patients can tolerate the sufficient amount of transfused granulocytes for the treat-

ment? Whether the treatment can result in significant clinical benefits for the patients? Which types of cancer are suitable for such treatment? All these questions are needed to be investigated by future studies.

In summary, cancer immune surveillance is a long historical but controversial topic in the progress of anti-cancer area. The fast-developing basic and clinical researches have been being focused on the effect of immune system, particularly the adaptive immune system. Regarding the cancer immune surveillance and cancer killing activity, the potential contribution of the innate immune system was largely unknown. The discovery of the SR/CR mice and the cancer killing mechanisms of which is mediated entirely by leukocytes from the innate immunity provides a powerful evidence for the significant role of the innate immune system in defending against cancer. Although the exact genetic and molecular mechanisms of the SR/CR “super mouse” family are still unclear, the therapeutic potential of LIFT for cancer are absolutely promising, not only for the clinical, but also for the fundamental knowledge about the relationship between the immune system and cancerous diseases. ■

### Conflict of Interests

None

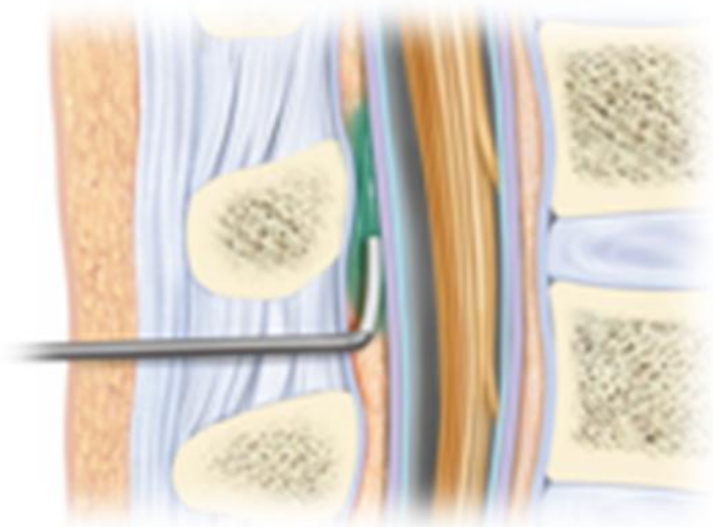
### Abbreviations

SR: Spontaneous Regression; CR: Complete Resistant; WT: wild type; S180: Sarcoma 180; MHC: Major Histocompatibility Complex; PMN: polymorphonuclear leukocytes; NK: natural killer cells; MTD: maximum

tolerated dose; CKA: Cancer Killing Activity; LITF: Leukocyte Infusion Therapy; HLA: human leukocyte antigen

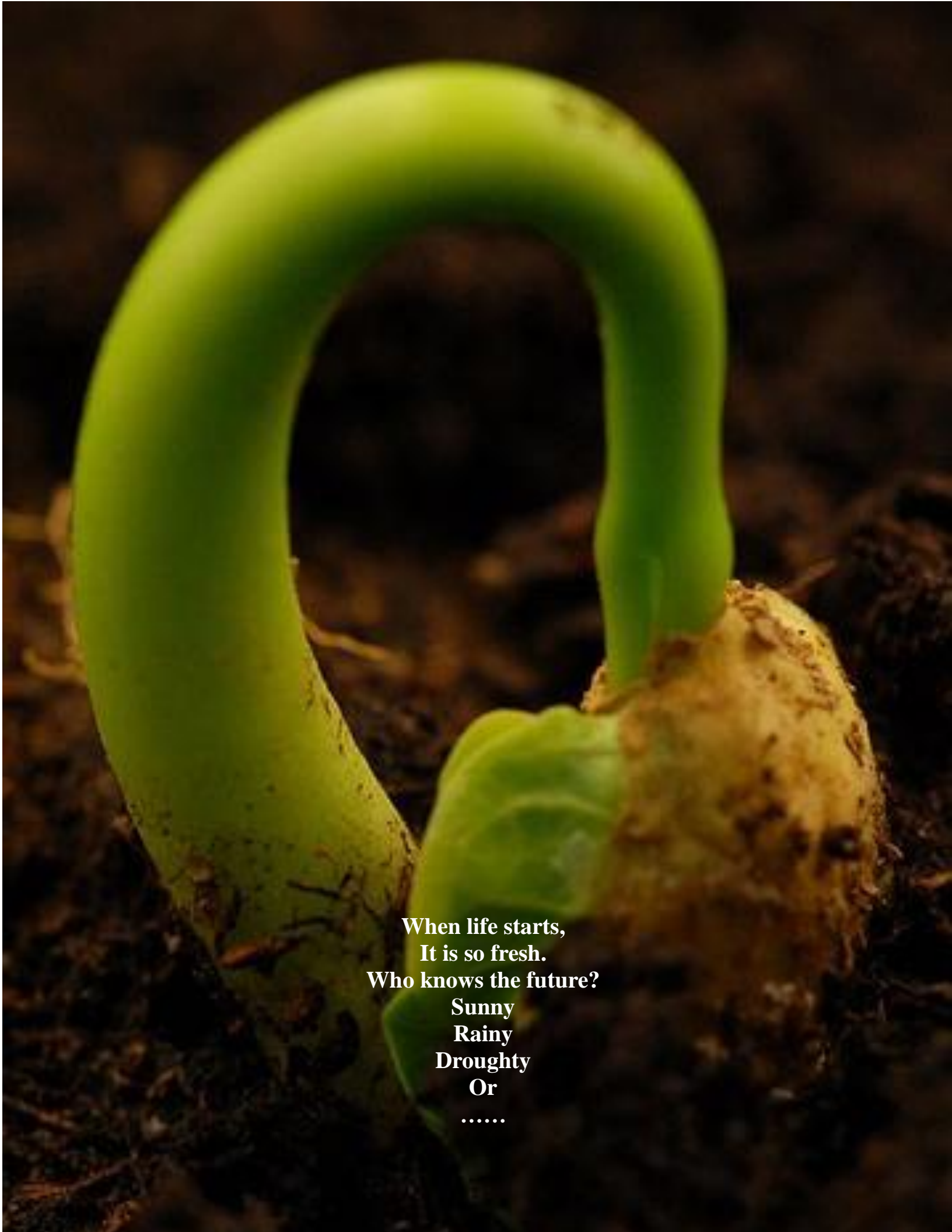
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**FORTHCOMING ISSUE**  
**12 APRIL 2014**



A young green plant with a curved stem and a root ball, growing in dark soil. The stem is bright green and arches over, forming a loop. The root ball is light brown and textured. The background is dark and out of focus.

**When life starts,  
It is so fresh.  
Who knows the future?  
Sunny  
Rainy  
Droughty  
Or  
.....**

**RIOT**

TODAY'S WORLD

*who should pay for this...*



*FREEDOM*



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