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Lauding the 'perfect ten'

KOPPILLIL RADHAKRISHNAN, HEAD OF THE INDIAN SPACE RESEARCH ORGANISATION, IS IN NATURE'S LIST OF PEOPLE WHO MATTERED IN SCIENCE THIS YEAR, WRITES S ANANTHANARAYANAN

elected after much debate and consultation by its editors, Nature's 10 looks behind the major events and discoveries to show that, at its heart,

science is a human endeavour," says Helen Pearson, Nature's chief features editor. Here are the people who cut the mustard: Andrea Occomazo, a



former Italian military test pilot, joined the European Space Agency two decades ago and has spent the last 18 years researching the comet 67P/

Churyumov-Gerasimenko. Since 20-04, he has been guiding the robot spacecraft, Rosetta, and its landing craft, Philae, in their 6.4-billion km mission to the comet. In October 2014, Occomazo and his team brought Philae down to a landing within 120 metres of the spot selected.

Unfortunately, Philae did not anchor well and was blown into a shady place and its solar panel was rendered useless. But it sent back valuable data in the 64 hours that it worked and there is hope that the solar panels will work again at a later position of the comet in its orbit around the sun.



Suzanne Topalian is a US physician and researcher who has worked on a new approach to tackling the menace of cancer. Even as a medical student, she

says, she was fired with the idea of using the body's immune system to turn on cancer cells, in place of the convention therapy of attacking the tumour with drugs or radiation. The new drug she helped pioneer belongs to a class called PD-1 inhibitors (Programmed cell Death inhibitors), which block a defence of cancer cells to prevent the body's T-

cells from acting. The drug has been approved for use in Japan and the USA and analysts say it may become the cornerstone of cancer therapy in a few years.

India-born Radhika Nagpal leads a team of engineers at Harvard University in the field of biologyinspired robotics. Taking a cue from

a mentor when she was a student at the Massachusetts Institute of Technology, Nagpal built on the idea that the simple cell is the ultimate computer, with groups of cells taking cues from the environment and self-assembling to perform complex tasks. Her team has now got a swarm of 1,024 small, three-legged robots, called kilobits, just a few centimetres wide and tall, and communicate with neighbours through infra-red light to assemble themselves into different two-dimensional shapes. This level of cooperative behaviour in robots is seen as a remarkable achievement, which can be scaled up to create robotic teams that can rapidly move to deal with disasters or to aid environmental

clean-up operations. Sheik Hummar Khan was the heroic Sierra Leone doctor who succumbed to Ebola while treating patients during the outbreak in his country. He was part of

the team that carried out the first genetic sequencing studies of the virus in Sierra Leone. This research has shown how the virus is mutating and his team is installing sequencers all over West Africa to track its evolution. Khan had turned down attractive offers to work in Freetown or teach abroad.

He took the best precautions to protect himself but his empathy with patients, which extended to physical contact with survivors, may have been his undoing.

David Spergel, an astrophysicist at Pri-nceton, showed perseverance in pressing what he considered serious shortcomings in a discovery announced and

being hailed at high quarters. A team led by John Kovac of the Harvard-Smithsonian Centre for Astrophysics in Cambridge, Massachusetts, had called a press conference to announce a probable detection of gravitational waves from deep within space, which supports the position that the early universe had undergone a brief but enormous expansion. Spergel had a nagging feeling that there was something wrong with the evidence or the conclusion. He soon worked out where the error lay and expressed his reservation in a lecture and again in a publication where he and others analysed the signals that Kovac, et al, had relied on, to show that the features seen could be explained by reasons other than that ancient expansion.

Spergel's voice was soon heard by the astrophysics community and the euphoria was replaced by suspicion that there had been a cosmic error, and the announcement was prema-



mathematics. She had been exposed, while a graduate student, to a novel and complex work of abstract surfaces that could be folded into shapes that contained holes. With little appreciation of the complexity, she wondered why the result could not be extended to more general surfaces. She persisted, and 10 years later she coauthored a 172-page paper that

described a way, using wide ranging mathematical techniques, to do just this.

The award of the Field's Medal to a woman is significant as there is a marked deficiency in the representation of women in the world of mathematics, apart from cultural bias.

The 30-year-old Pete Frates of Massachusetts, a graduate from Boston College and basketball player and coach, was

diagnosed with Amyotrophic Lateral Sclerosis in 2012. He lost the ability to speak or move, but he began campaigning to raise funds for awareness of the disease. With friend Pat Quinn of New York, they are now credited as the creators of the_Ice Bucket Challenge, an activity involving dumping a bucket of ice water on one's head to promote awareness of ALS, which went viral on social media during the summer of 2014. Over 17 million ice bucket videos have been posted and \$115 million has been collected. The drive has shown the need to

get people involved and has caught the attention of other advocacy groups. The National Organisation for Rare Disorders in Danbury, Connecticut, had held a seminar on viral fund-raising campaigns, and is planning a follow-up.



The award comes just before he retires, after 43 years of work on different Isro projects, from remote sensing satellites, Tsunami warning systems, the cryogenic engine. India's success in its very first attempt is creditable as over half the missions so far have failed. Radhakrishnan plays down his role.

"I was like the conductor of an orchestra," he says. But the achie-

vement has demonstrated India's ability to develop and implement high-technology enterprises.



pluripotent cells, that came from ordinary adult cells. to turn in sheets of retinal cells. Yamanaka had won the Nobel for the technique of reprogramming ordinary cells to become pluripotent, a method that makes it much easier to source than embryonic stem cells.

Takahashi has been working with getting stem cells to grow into retinal cells for more than 10 years. The work picked up speed with Yamanaka's technique of the induced pluripotent stem cell and after a series of trials with mice and monkeys and regulatory tests, Takahashi's lab-grown sheet of cells was transplanted in the retina of a human patient in September this year.



Sjors Scheres, at the Labaoratory for Molecular Biology, Cambridge, UK, brought mathematics and computers to help find the way through the interiors of cells and genetic material. The

method used in structural biology had been to first form crystals of gene regulating proteins and then to use X-ray scattering to probe the crystal structure. But cell material often defies crystalisation and a preferred technique is cryo-electron

microscopy, or cryo-EM, a low temperature method where the specimens are in a more native environment. But the images in cryo-EM are blurred and the computations called for to generate clear images are labo rious.

When methods were found to automate cryo-EM pictures, Scheres realised that normal computation of the data would not be feasible and he went to work on a computer programme. "We left him alone for a couple of years," says Nobel laureate and colleague Venki Ramakrishnan. And Sheres came up with Relion, a software package that Ramakrishnan describes as "a perfect saviour".

THE WRITER CAN BE CONTACTED AT

PLUS POINTS

Cloud cities

Despite the attention heaped on Mars, Venus might actually seem a better bet for space exploration and a new planet for us to eventually live on. It's nearer to us, a more similar size and has a density and chemical composition more like earth but it's also completely inhospitable.

Venus is far hotter than earth, at around 462° Celsius, and an atmospheric pressure over 92 times greater. It's also got huge volcanoes and an acidic cloud layer. Even probes that have been sent to the planet



have burnt up and died shortly after arriving. So instead, scientists at the national Aeronautics and Space Administration's Langley Researcher Center have proposed an alternative — a city in the clouds, built using huge balloons that look like passenger airships. They would carry two astronauts on a 30-day mission to explore the planet.

The project, named High Altitude Venus Operational Concept, or Havoc, is just a proposal at the moment, designed by the Systems Analysis and Concepts Directorate at the centre. But it hopes to keep working on it until it is ready to actually take astronauts to the planet, or just off it.

While the conditions on Venus keep humans from venturing down there, stay ing about 30 miles above the planet would keep astronauts in conditions mostly similar to earth. The atmospheric pressure is comparable, and gravity is just slightly lower. The temperature is warm but the ship would be able to keep the astronauts cool enough.

The challenges for the mission would be getting the airship to Venus — and then, since it will be wrapped up, inflating it there. Before it is used scientists will also have to be confident that the ship and the solar panels that will power it can withstand the sulphuric acid in the atmosphere and the other strain it will be put under while it floats above the planet. But if they can work on the technology, "missions to the Venusian atmosphere can expand humanity's future in space". the SACD says.

Clues from a rock

A new analysis of a Martian rock that meteorite hunters plucked from an Antarctic ice field 30 years ago this month reveals a record of the planet's climate billions of years ago, back when water likely washed across its surface and any life that ever formed there might have emerged.

Scientists from the University of California, San Diego, the national Aeronautics and Space Administration and the Smithsonian Institution report



TOPIC OF CANCER Along came a spider RESEARCHERS ARE TURNING TO VENOM PEPTIDES TO PROTECT CROPS FROM THEIR MOST DEVASTATING PESTS.

TAPAN KUMAR MAITRA ELABORATES ON ONCOGENES AND MALIGNANCY

▲ alignancy or cancer is defined as an uncontrolled proliferation of cells that are capable of spreading b y in vasion and metastasis. In cancer cell popula tions, the balance between cell division and differentiation is disrupted, leading to a pr ogressive increase in the number of dividing cells. Cancer cells are anless susceptible than norchorage-independent.

plasma membrane GTP-binding pr oteins, nonreceptor pr otein kinases, transcription f actors and cell-cycle or cell-death regulators. Oncogenes code for abnormal forms or excessive quantities of such pr oteins, thereby leading to ex cessive stimulation of cell proliferation

ture, at any rate.



Iran-born mathematician Maryam Mirzakhani of Stanford University is the first woman recipient of the Fields Medal, regarded as

mal to density-dependent inhibition, and can replenish their telomeres.

Sustained tumor growth requires a blood supply w hose de velopment is trig gered b y an

increased pr oduction of angiogenesis activators and a decr eased production of angiogenesis inhibitors.

After triggering angiogenesis, cancer cells invade surrounding tissues, enter the cir culatory system and metastasise to distant sites. Invasion is f acili tated by decreased cell cell adhesion, increased motility and secr etion of proteases that degrade the extracellular ma trix and basal lamina

Only a tin y fraction of the cancer cells that enter the b loodstream survive the trip and establish successful me-

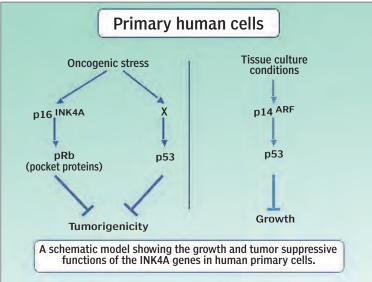
tastases. Sites of metastasis are deter mined by the location of the first capillary bed as well as organ-specific conditions tha t influence cancer cell growth.

A v ariety of different c hemicals, including those found in tobacco smok e, can cause cancer. Chemicals induce the de velopment of cancer through a multistep process involving initiation, promotion and tumor pr ogression. Initiation is based on DN A muta tion, whereas pr omotion involves proliferation of the initiated cells for a prolonged period of time, accompanied by a gradual selection of cells exhibiting enhanced growth pr operties. During tumor pr ogression, cells acquire additional muta tions and undergo changes in g ene expr ession that pr oduce cells with increasingly aberrant traits.

Cancers can also be caused by ionising radiation or sunlight, both of which cause DNA mutations, and by certain viruses, bacteria and parasites. Some cancer-causing viruses act by directly trig gering cell pr oliferation, either thr ough the action of viral genes or by altering the behaviour of cellular genes. Other infectious a gents create tissue destr uction that indirectly stimulates cell proliferation under conditions in which DNA damage is likely.

Oncogenes are those whose presence can cause cancer. While they ar e sometimes intr oduced into cells by viruses, more often they arise fr om normal cellular genes (proto-oncogenes) by point mutation, gene amplifica tion, chromosomal translocation, local DN A r earrangements or insertional muta genesis. Most pr oteins pr o-

Tumor suppressor genes are those whose loss or inactivation can lead to cancer. Susceptibility to developing cancer is incr eased in people w ho inherit defective tumor suppressor genes. Three



important tumor suppr essor genes are: the RB gene, which pr oduces a pr otein that r estrains passage from Gl into S phase; the p53 gene, which produces a protein that prevents cells with damaged DNA from proliferating; and the APC gene, which produces a protein that inhibits the Wnt pathway

Cancers arise through a stepwise accumulation of mutations in volving both onco genes and tumor suppressor genes. The genetic instability of cancer cells facilitates the acquisition of these multiple mutations. Some cancer cell properties that contrib ute to g enetic insta bility inc lude defects in DNA repair mechanisms, disruptions in pathways that trigger a poptosis and f ailures in the mec hanisms f or sor ting c hromosomes during mitosis.

Screening techniques, such as the P ap smear, can prevent cancer dea ths by detecting the disease bef ore it has spr ead. Treatment usuall v involves surgery to r emove the primary tumor followed, if necessary, by radia tion thera py and/or c hemotherapy to kill or inhibit the growth of any remaining cancer cells . Newer treatment approaches include immunotherapies that exploit the a bility of the immune system to attack cancer cells, molecular targ eting dr ugs aimed at proteins that are critical to the cancer cell and anti-angio genic a gents that a ttack a tumor's blood supply.

THE WRITER IS ASSOCIATE PROFESSOR, HEAD, DEPARTMENT OF BOTANY, ANANDA MOHAN COLLEGE, KOLKATA, AND ALSO FELLOW, BOTANICAL SOCIETY OF BENGAL, AND CAN BE CONTACTED AT tapanmaitra59

millions of acres of Bt corn cotton and potatoes every year, but the Bt pr oteins cannot pr otect against all pests, in particular species outside of Lepidoptera (moths and butterflies), and in recent years reports of Bt resistance in at least five major pest species ha ve scientists looking f or ways to enhance the crops' protection.

cific pests such as corn borers, cotton bollworms

and potato beetles. Farmers in the USA now grow

"You will have to produce new technologies to conquer the r esistance in insects ," says Inaam Ullah, a graduate student a t the Na tional Institute for Biotechnology and Genetic Engineering in Faisalabad, Pakistan. "It's a long ba ttle; (the introduced biopesticide) can 't be ne w forever.'

Some researchers have turned to spiders, the most speciose v enomous animal on the planet. for help. The Arachno Server, a database of sequence, structural and functional inf ormation for spider venom peptides and proteins, currently includes nearly 950 to xins from 86 species, and the insecticidal potential of a handful of these has been w ell documented, including that of hexatoxin-Hv1a (Hvt), a peptide in the venom of Australia's Blue Mountains funnel-w eb spider (Hadronyche versuta). As result, researchers at Nibge inser ted a synthetic v ersion of the Hvt gene into the g enomes of tobacco and cotton, yielding plants that produce the to xic peptide themselves

"It would be a f antastic adjunct to Bt plants because this to xin is effective a gainst a wide range of pests, including aphids, which Bt doesn't affect at all," says Glenn King, a biochemist at the University of Queensland in Australia, who studies spider to xin-armed Arabidopsis as a model system. It's particularly exciting, he adds, because Hvt, which blocks voltage-gated calcium channels in insects, works differently than pesticides already in use. "This is a completel y novel insecticide targ et... so ther e's no pr eexisting resistance.

But any toxin peptide that is to be truly useful in an a gricultural setting must be mor e than a good pesticide. It's also impor tant that the spi-



Australia's Blue Mountains Funnel-web spider, which can grow up to four centimetres long, lies in wait for prey

der-venom peptides do not harm non-target spe-

cies, especially those tha t pr ovide ecosystem

services such as pollination. Hvt is known to be

highly arthropod-specific — "there are very low

chances, if any, that they can af fect any higher

organisms," says Ullah - b ut what about non-

target insects

Interested in these biosafety issues, Ullah emailed the biosafety g roup at Agroscope, a Swiss federal a gricultural research centre in Zürich. In 2011, he secur ed funding from the Higher Education Commission of Pakistan and hopped on a plane to Switzerland to work with Jörg Romeis and others a tAg roscope's Institute f or Sustainability Sciences. He shipped himself seeds of Hvt-carrying cotton and tobacco plants de veloped by his colleagues at Nibge, then grew the plants in g reenhouses, measured the Hvt pr oduced by each species and tested the ef fects of ingesting the toxin peptide or plants expressing it on both target and non-target insects.

As expected, the toxin effectively killed pests: ingestion of either the purified pe ptide or the leaves of the Hvt-transgenic plants had fatal effects on the African cotton leafw orm (Spodo*ptera littor alis*) and the tobacco b udworm (Heliothis virescens). More importantly, the purified toxin peptide did not harm any of four beneficial non-targ et species: the common g reen lacewing (Chrysoperla car nea), the a phid parasitoid (Aphidius colemani), the seven-spot ladybird (*Coccinella septempunctata*) — three aphid predators used f or biological control - or the Western honey bee (Apis mellifera). "We tested the non-target (insects) with the same concentration (of toxin peptide that killed the pests), and it did not af fect them in an y way," says Ullah.

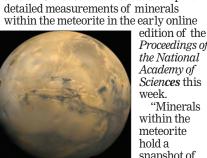
The results confirm research published this June in *Proceedings of the Royal Society B* in which a group of UK researchers demonstrated that Hvt, linked to a car rier molecule called GNA from the common sno wdrop plant (Galanthus ni valis), did not r educe honey bee survival or ra tes of learning and memory. "They did a whole range of studies that show that it has absolutely no effect at all," says King. "All of the data is looking very, very strong.

But w hile the science is pr omising, public acceptance of crops carrying spider to xin genes

is another issue entir ely. "The big question of course is regulation and public concer n a bout transgenic plants in general," says King.

Transgenic cr ops carrying pe ptides from spider v enom ma y not hit the market for several years yet, but the use of spider-venom pe ptides to protect crops "is not a theoretical thing", says King. "This is r eally happening.'

THE SCIENTIST



The surface of Mars was once wet, but no water flows there now. UC San Diego chemists and others took a close look at meteorite that may have been blasted from this huge rift across the planet's surface. The image is a composite of hundreds of photos taken by Nasa's Viking missions in the 1970s.

"Minerals within the meteorite hold a snapshot of the planet's ancient chemistry of interactions between water and atmosphere,"

said Robina

Shaheen, a

project scientist at UC, San Diego, and lead author of the report.

The unlovely stone, which fell to earth 13,000 years ago, looks a lot like a potato and has quite a history. Designated ALH84001, it is the oldest meteorite we have from Mars, a chunk of solidified magma from a volcano that erupted four billion years ago. Since then something liquid, probably water, seeped through pores in the rock and deposited globules of carbonates and other minerals.

The carbonates vary subtly depending on the sources of their carbon and oxygen atoms. Both carbon and oxygen occur in heavier and lighter versions, or isotopes. The relative abundances of isotopes forms a chemical signature that careful analysis and sensitive measurements can uncover.

Mars's atmosphere is mostly carbon dioxide but contains some ozone. The balance of oxygen isotopes within ozone are strikingly weird with enrichment of heavy isotopes through a physical chemical phenomenon first described by co-author Mark Thiemens, a professor of chemistry at UC, San Diego, and colleagues 25 years ago.

"When ozone reacts with carbon dioxide in the atmosphere, it transfers its isotopic weirdness to the new molecule,' said Shaheen, who investigated this process of oxygen isotope exchange as a graduate student at the University of Heidelberg in Germany. When carbon dioxide reacts with water to make carbonates, the isotopic signature continues to be preserved.