

Technology Scan

Focus: Biotechnology

ASIA-PACIFIC

INDIA

Neem to cure oral cancer

India's traditional toothbrush, the neem, has properties that can prevent oral cancer, scientists from the biochemistry and biotechnology department at Annamalai University in Chidambaram have found. While neem's anti-cancer properties have been demonstrated several times by a number of researchers, scientists in Annamalai University demonstrated that a bio-active ingredient, nimbolide, activates a tumour suppressor protein called RECK (Reversion-inducing Cysteine-rich Protein with Kazal Motifs), which is found in all normal tissues but is low or absent in malignant tumours. The research, they hope, will help them find drugs that improve survival rates and treatment outcomes in patients with oral cancer.

The research study, published in a peer-reviewed journal, *Scientific Reports*, Nature Publication Group in May, said nimbolide, derived from the leaves and flowers of the neem tree, could be used effectively to treat oral cancer, said biochemistry and biotechnology professor Siddavaram Nagini. In the laboratory, a team of researchers showed that nimbolide prevents cancer progression by preventing growth of uncontrolled malignant cells. It also spreads to other tissues through new blood vessels and kills cancer cells.

"RECK has tumour suppressing properties. In normal cells, it maintains tissue architecture and prevents infiltration and spread of tumour cells to other organs. In cancer, an array of molecules inhibits the function of Reck. Nimbolide suppresses the functions of the molecules that inhibit the function of RECK," Nagini said.

<http://timesofindia.indiatimes.com>

Edible dal from wild legume

Scientists in the National Botanical Research Institute (NBRI), a constituent laboratory of the Council of Scientific and Industrial Research (CSIR), have managed to knock off certain undesirable genetic material from a wild variety of legume

crop making its grains edible and nutritious. Winged beans (*P. tetragonolobus*), also called Goa beans, is a highly nutritious legume crop that normally grows wild. It is also cultivated in a small way in western and northeastern parts of the country. Almost all parts of this plant – leaves, pods, seeds and tubers – are edible. As the nutrients in this legume offers are very similar to those present in soybean, it is also billed as soybean of tropics.

Despite its high nutritional value, the legume is inedible beyond a limit. This is because a certain class of anti-nutrients called condensed tannins present in the plant can induce flatulence and stomach disorder, says Dr Chandra Sekhar Mohanty of NBRI, who led the study.

Now, NBRI researchers led by Dr Mohanty and their counterparts of the biotechnology department of the Kumaun University in Nainital, may have found a way to reduce, if not completely rid of, condensed tannins – whose primary jobs is to confer protection against predation and pathogen attacks – in winged beans. Their research work, which appeared recently in the journal *Scientific Reports*, has shown that it is possible to knock off genes that are responsible for the production of condensed tannins. "It would be ideal to produce a variety of winged bean that is high in protein content but less in condensed tannin," says Dr Mohanty. To do this, the scientists are planning to use a sophisticated technique called gene silencing.

Over the years, least attention being paid for improvement of legume crops in general orphan legumes in particular when compared with cereal crops of commercial importance, he observes. "Even though there are some 20,000 species of legumes, only 20 different types of legumes come to our daily diet for consumption," says Dr Mohanty.

<http://www.downtoearth.org.in>

JAPAN

Drought resistant, higher yielding GM rice

Scientists at the RIKEN Center for Sustainable Resource Science have developed strains of

rice that are resistant to drought in real-world situations. Published in *Plant Biotechnology Journal*, the study reports that transgenic rice modified with a gene from the *Arabidopsis* plant yield more rice than unmodified rice when subjected to stress brought by natural drought.

In previous work, RIKEN scientists showed that *Arabidopsis* plants express the *AtGols2* gene in response to drought and salinity stress. For this study, they created several lines of transgenic Brazilian and African rice that over-express this gene, and with their collaborators, tested how well the rice grew in different conditions in different years.

When might we see this useful rice on the market? According to [RIKEN scientist Fuminori] Takahashi, the greatest barrier to commercial availability is that they used genetically modified (GM) technology to generate the *Gols2* transgenic rice. "Now, we have begun our next collaborative project, in which we will generate useful rice without GM technology. It might take 5–10 years to reach our goal, but we must keep pressing forward because droughts and climate change might get worse in the future."

<https://geneticliteracyproject.org>

REPUBLIC OF KOREA

Technology to control protein therapeutics

Republic of Korean researchers have developed a technology, which leads protein therapeutics to tumor cells safely and accurately by using lights, to treat cancer. The Korea Advanced Institute of Science and Technology (KAIST) announced on August 9 that its research team led by Choi Chul-hee and Jeong Kyung-sun, professors of the Department of Bio and Brain Engineering, developed such a new technology and released it in the online version of *Nature Communications*, a renowned international scientific journal, on July 22.

The research team used proteins CRY2 and CIBN that stick to each other when blue lights with a wavelength of 450 to 490 nanometers were illuminated on them. It combined protein therapeutics with CRY2

and exosome, a nanoparticle which is used to deliver protein between cells, with CIBN, and then shoot the blue lights with the wavelength of 450 to 490 nm. In this case, protein therapeutics and exosome mingle together as CRY2 and CIBM combine together. In short, it is like guiding customers, or protein therapeutics, who head to the destination of tumor cells with lights, and helping them to get on the bus, or exosome, to the destination.

The traditional way is to inject protein, which is refined the outside of cells, into exosome. However, the new technology can reduce costs and time as it doesn't require a refining process. Moreover, it can increase the loading rate of protein therapeutics by more than 1,000 times, according to the KAIST. Unlike the traditional method, the new technology doesn't have to control the immune reaction to protein therapeutics and leads protein therapeutics to target cells.

In regard to the new technology, Professor Jeong said, "This is an innovative source technology which can mass produce safe and superior protein therapeutics." The technology has been transferred to Celex Life Science, a company founded by the KAIST, and the company is currently using it to optimize the manufacturing technology of exosome drugs.

<http://www.businesskorea.co.kr>

Stem cells to treat spinal cord injuries

A team of Republic of Korean researchers developed a new technology to produce customized stem cells that can be used in the treatment of severe diseases, such as a spinal cord injuries. A team led by professor Kim Jeong-beom of the Bio Science Division at the Ulsan Institute of Science and Technology (UNIST) announced on October 27 that his team successfully developed oligodendrocyte precursor cells (OPCs) by utilizing one particular gene.

An OPC is a spinal cord cell that is composed of myelin, a protective layer that surrounds spinal nerves. The use of this cell can regenerate myelin destroyed due to spinal cord

injuries and finally lead to the treatment of damaged spinal cords. The research team attempted direct reprogramming with OPCs by injecting the gene Oct4 to skin cells, a core gene of a stem cell. Direct reprogramming differentiates a desired stem cell from skin cells. An OPC differentiated through this technology cannot turn into a cancer cell or a teratoma, since the OPC does not go through a pluripotent state where it can differentiate into all kinds of cells.

The research team directly proved its genetic stability and treatment effects by way of ten months of animal tests. "It took four years for us to publish our thesis after proving the characteristics of the cell and its treatment effects," Professor Kim said. "This means we developed a new cell production technology that overcomes the limitations of current OPC production methods," Professor Kim continued. "The go-ahead was given to the treatment of refractory diseases." These research results will lead to methods to treat patients with spinal cord injuries with the addition of bio 3D printing technology that produces biological tissues with a 3D printer.

"We will produce spinal cord tissues with a bio 3D printer and the produced OPC. The direct transplantation of the spinal tissues in damaged parts of patients will maximize the efficiency of spinal cord injuries," Kim added. "When the Ulsan Hospital for Industrial Disaster Victims opens, its technological commercialization will be possible. So this technology will contribute to treating and rehabilitating patients with injured spinal cords." The research results appeared in the online edition of the journal of the European Molecular Biology Organization (EMBO).

<http://www.businesskorea.co.kr>

SINGAPORE

DNA technology for infectious diseases, cancer

A more efficient DNA technology to detect and treat infectious diseases and cancer has been developed by Singapore researchers at the Institute of Bioengineering and Nanotechnology (IBN) of A*STAR, the agency said in a press release. The researchers

improved on existing technologies to create a modified single-stranded DNA molecule called aptamer. DNA aptamers are ideal for pharmaceutical applications because they can specifically bind to any molecular target in the body such as proteins, viruses, bacteria and cells.

Once DNA aptamers are artificially generated for each target, they will bind to it and inhibit its activity. This makes DNA aptamers a promising technology for disease detection and drug delivery. But no DNA aptamers have been approved for clinical use yet because current aptamers do not bind well to molecular targets and are easily digested by enzymes. "To overcome these challenges, we have created a DNA aptamer with strong binding ability and stability with superior efficacy. We hope to use our DNA aptamers as the platform technology for diagnostics and new drug development," said IBN Executive Director Professor Jackie Y. Ying.

This study, led by IBN principal research scientist and team leader Dr Ichiro Hirao, was recently published in the journal *Scientific Reports*. To tackle the weak binding problem, the research team added a new artificial component called unnatural base to a standard DNA aptamer, which typically has four components. The addition of the fifth component greatly enhanced the binding ability to the molecular target by 100 times as compared to conventional DNA aptamers.

Furthermore, to prevent the aptamer from being digested easily by enzymes, a unique and small DNA called "mini-hairpin DNA" was added to the DNA aptamer. "The mini-hairpin DNAs have an unusually stable and compact stem-loop structure, like a hairpin, of small DNA fragments. Their structure strongly resists the digestive enzymes, so I added them to specific positions on the DNA aptamer to act as a protective shield," Dr Hirao explained. "Usually DNAs are digested within one hour in blood at body temperature. With the mini-hairpin DNA, our DNA aptamers can survive for days instead of hours. This is important for pharmaceutical applications, which require the therapeutic to remain in

the body for a longer period." If successfully commercialized, DNA aptamers could replace or complement the existing use of antibodies in drugs for targeted disease treatment.

<http://news.xinhuanet.com>

EUROPE DENMARK

New robust oilseed crop

Researchers have successfully developed a new oilseed crop that is much more resistant to heat, drought and diseases than oilseed rape. University of Copenhagen and the global player Bayer CropScience have successfully developed a new oilseed crop that is much more resistant to heat, drought and diseases than oilseed rape. The breakthrough is so big that it will feature as cover story of the April issue of *Nature Biotechnology*, a journal about biotechnology research.

Should the global warming continue, a golden rape field under the summer sun may soon become but a distant memory. Researchers have now developed a mustard crop with all the good properties of rape, but which, in addition, also is resistant to drought and heat.

Professor Barbara Ann Halkier, Head of DynaMo Center of Excellence, University of Copenhagen, is one of the scientists who has worked on developing a new oilseed crop with better properties. She explains: "Oilseed rape does not grow very well in warm and dry areas. We are very happy that we have succeeded in using a groundbreaking technology on a mustard plant, which is a close relative to rape. The result is an oilseed crop with improved agronomic traits that is tolerant to global warming. The new crop will enable cultivation in areas that today is not suitable for oilseed crops, such as the Western part of Canada, parts of Eastern Europe, Australia and India."

In close collaboration with Bayer CropScience – one of the major global players within plant biotechnology and breeding – she and other scientists from the DynaMo Center have found an original

solution to this problem. The scientists from the DynaMo Center have invented a technology that can keep the bitter defense compounds out of the seeds while maintaining them in the rest of the plant so that the plant can defend itself against herbivores and pathogens.

The Danish scientists have shown that the technology works in a model plant, while scientists from Bayer CropScience have implemented the technology in the fields and performed large field trials with the optimized mustard plants.

<https://www.sciencedaily.com>

GERMANY

New malaria vaccine

University of Tübingen researchers in collaboration with the biotech company Sanaria Inc. have demonstrated in a clinical trial that a new vaccine for malaria called Sanaria® PfSPZ-CVac has been up to 100 percent effective when assessed at 10 weeks after last dose of vaccine. For the trial, Professor Peter Kremsner and Dr. Benjamin Mordmüller of the Institute of Tropical Medicine and the German Center for Infection Research (DZIF) used malaria parasites provided by Sanaria. The vaccine incorporated fully viable – not weakened or otherwise inactivated – malaria pathogens together with the medication to combat them. Their research results have been published in the latest edition of *Nature*.

The Tuebingen study involved 67 healthy adult test persons, none of whom had previously had malaria. The best immune response was shown in a group of nine test persons who received the highest dose of the vaccine three times at four-week intervals. At the end of the trial, all nine of these individuals had 100 percent protection from the disease.

"That protection was probably caused by specific T-lymphocytes and antibody responses to the parasites in the liver," Professor Peter Kremsner explained. The researchers analyzed the bodies' immune reactions and identified protein patterns which will make it possible to further improve malaria vaccines, Kremsner added.

The researchers injected live malaria parasites into the test subjects, at the same time preventing the development of the disease by adding chloroquine – which has been used to treat malaria for many years. This enabled the researchers to exploit the behavior of the parasites and the properties of chloroquine.

"By vaccinating with a live, fully active pathogen, it seems clear that we were able to set off a very strong immune response," said study leader Benjamin Mordmüller, "Additionally, all the data we have so far indicate that what we have here is relatively stable, long-lasting protection." In the group of test persons who demonstrated 100 percent protection after receiving a high dose three times, Mordmüller said, the protection was reliably still in place after ten weeks – and remained measurable for even longer. He added that the new vaccine showed no adverse effects on the test persons. The next step is to further test the vaccine's effectiveness over several years in a clinical study in Gabon funded by DZIF. Malaria is one of the biggest health threats in the African nation. The University of Tuebingen has worked with the Albert Schweitzer Hospital in the Gabonese town of Lambaréné and with the neighboring research institute, the Centre de Recherches Médicales de Lambaréné, for many years.

<https://www.sciencedaily.com>

SPAIN

New virus to selectively attack tumor cells

Researchers from Barcelona have developed a new genetically engineered oncolytic virus, which can selectively infect and kill tumor cells. Eneko Villanueva and colleagues from the IDIBAPS Biomedical Research Institute and the Institute for Research in Biomedicine (IRB Barcelona) have engineered a virus that infects tumor cells without affecting healthy tissues. Their new cancer therapy approach is based on "oncolytic viruses", which can differentiate between cancer cells and normal cells based on the expression of so called CPEB proteins.

CPEB is a family of four RNA binding proteins that can control the expression of hundreds of genes by binding to their RNA. In cancer, the balance of different CPEB proteins is often disturbed, contributing to malignant gene expression of these cells. The researchers have shown that many cancer cells overexpress CPEB4, which seems to be necessary for tumor growth. On the other hand, the cancer cells lose the expression of CPEB1, which is highly expressed in normal tissues.

To make the viruses specific towards high CPEB4/low CPEB1, the researchers have inserted sequences into the genome of an adenovirus, which recognize CPEB proteins. With this strategy, they achieved attenuated viral activity in normal cells, while in tumor cells, the virus potency was maintained or even increased. Once the virus infects a cancer cell, it will destroy the cell and release even more viral particles. Oncolytic viruses make up a very promising therapeutic strategy and there are several biotech companies developing such viruses for cancer therapy. Recently, Bristol-Myers Squibb signed a €850M (\$886M) deal for the exclusive worldwide rights of NG-348, a next-generation oncolytic virus developed by PsiOxus. The virus is currently in preclinical development.

PsiOxus' lead viral candidate Enadenotucirev, which selectively kills cancer cells and at the same time triggers the immune system, is already in Phase I clinical trials. Amgen's IMLYGIC was the first oncolytic virus to be approved by the FDA in 2015 for the treatment of refractory melanoma. Although there are already some viruses in the pipeline, the new virus developed by the researchers in Barcelona may be a promising addition to this young and developing market.

<http://labiotech.eu>

UK

TB drug developed from soil bacteria

A new treatment for tuberculosis (TB) is set to be developed using compounds derived from bacteria that live in soil – according to an international collaboration of research-

ers, including the University of Warwick. The research partnership – involving the University of Warwick, and spanning institutions from Australia, Canada and the USA – has discovered a compound that could translate into a new drug lead for TB.

The group looked at soil bacteria compounds, known to effectively prevent other bacteria growing around them. Using synthetic chemistry, the researchers were able to recreate these compounds with structural variations, turning them into more potent chemical analogues. When tested in a containment laboratory, these analogues proved to be effective killers of *Mycobacterium tuberculosis* – the bacterium that causes TB. These chemicals target an enzyme in *Mycobacterium tuberculosis* called *MraY*, which catalyses a crucial step in building the cell wall around a bacterium. Attacking this part – a potential “Achilles’ heel” of the bacterium – provided an essential pathway for the antibacterial compounds to attack and destroy TB strains.

Key reagents and expertise in antimicrobial resistance from the research groups of Dr David Roper, Professor Chris Dowson and Professor Tim Bugg at the University of Warwick played a crucial role in successfully targeting TB bacteria with the new compounds.

The research is published in *Nature Communications*.

<https://www.sciencedaily.com>

Increasing crop yields without genetic modification

A team of scientists has developed a chemical that increases the starch content of wheat crops. The new product could significantly increase wheat yields without the use of genetic modification. The details are in a paper that was just published in the journal *Nature*. Researchers from Oxford University and Rothamsted Research focused their attention on a molecule called trehalose-6-phosphate (T6P). T6P regulates the amount of sucrose used by plants. In wheat, this means that extra T6P would result in starchier wheat grains. The research team used this information to test a number of synthetic versions of T6P.

The team developed a modified version of T6P that could be sprayed onto wheat plants. The plants would absorb the extra T6P, which would become active when the wheat was exposed to sunlight. This results in wheat grains with extra starch and could increase wheat crop yields by up to 20% after simple applications of the modified T6P. Furthermore, the modified chemical helped protect plants from drought stress, solving another major problem.

The team's findings show that a simple T6P spray, a modified version of a naturally occurring chemical, could improve wheat crop yields by up to 20%. The spray encourages the plant to produce more starch and also reduces drought-induced stress. The authors point out that T6P pathways are common in plants and their method could be adapted for use in other crops. This would significantly help the global food shortage while also providing a possible solution for the record droughts occurring throughout the world.

<http://naturalsciencenews.com>

New strains of staple crops

By developing enriched versions of staple crops, researchers aim to produce foods that can meet the nutritional requirements for a healthy diet. “We need sustainable agriculture to feed the growing population with adequate nutrients, besides just enough calories,” said Dr Swati Puranik, of the Institute of Biological, Environmental and Rural Sciences at Aberystwyth University in the UK. She aims to develop calcium-rich finger millet – a staple for millions of people around the world, including some of the poorest in Asia and Africa. The hardy cereal grows in areas of low rainfall where many other grains would fail.

Using finger millet germplasm, Dr Puranik has identified more than a million genetic variations, known as single-nucleotide polymorphism markers, that she is assessing to see if they are linked with higher calcium content. She is also checking the markers for correlations with iron and zinc, as well as “antinutrient” compounds such as phytate and oxalate, which interfere with the body's absorption and use of micronutrients.

Where markers indicate higher levels of micronutrients, Dr Puranik and her col-

laborators in Kenya and India aim to use conventional genomics-based breeding to come up with varieties of finger millet that contain higher levels of calcium and vitamins, without using genetic engineering. She is also assessing if her research can help improve rice and wheat.

Vitamin and mineral supplements can help overcome dietary deficiencies, but Dr Puranik believes that improving nutrition right from the farmer's field may have the strongest impact. "Developing improved food crops has benefits for farmers and their families, both economic and nutritional," she said. "And ultimately these calcium-rich products should have an impact in lowering rates of osteoporosis and calcium malnutrition in children or pregnant and lactating women."

Her EU-funded project, CaMILLET, targets conventional breeding methods, but other research has shown the strong potential of genetic modification in improving the nutritional quality of food crops.

<https://horizon-magazine.eu>

NORTH AMERICA

USA

Chikungunya vaccine from virus

Researchers have developed the first vaccine for chikungunya fever made from an insect-specific virus that doesn't have any effect on people, making the vaccine safe and effective. The newly developed vaccine quickly produces a strong immune defense and completely protects mice and nonhuman primates from disease when exposed to the chikungunya virus.

Researchers from The University of Texas Medical Branch at Galveston have developed the first vaccine for chikungunya fever made from an insect-specific virus that doesn't have any effect on people, making the vaccine safe and effective. The newly developed vaccine quickly produces a strong immune defense and completely protects mice and nonhuman primates from disease when exposed to the chikungunya virus. The findings are detailed in *Nature Medicine*. "This vaccine offers efficient, safe and affordable protection against chikungunya and builds the foundation for using viruses that only infect insects to develop vaccines against other insect-borne diseases," said UTMB professor Scott Weaver, senior author of this paper.

The researchers used the Eilat virus as a vaccine platform since it only infects insects and has no impact on people. The UTMB researchers used an Eilat virus clone to design a hybrid virus-based vaccine containing chikungunya structural proteins. The Eilat/Chikungunya vaccine was found to be structurally identical to natural chikungunya virus. The difference is that although the hybrid virus replicates very well in mosquito cells, it cannot replicate in mammals.

Within four days of a single dose, the Eilat/Chikungunya candidate vaccine induced neutralizing antibodies that lasted for more than 290 days. The antibodies provided complete protection against chikungunya in two different mouse models. In nonhuman primates, Eilat/Chikungunya elicited rapid and robust immunity – there was neither evidence of the virus in the blood nor signs of illness such as fever after chikungunya virus infection.

<https://www.sciencedaily.com>

Scientists engineer sugarcane to produce biodiesel

A multi-institutional team led by the University of Illinois have proven sugarcane can be genetically engineered to produce oil in its leaves and stems for biodiesel production. Surprisingly, the modified sugarcane plants also produced more sugar, which could be used for ethanol production. The dual-purpose bioenergy crops are predicted to be more than five times profitable per acre than soybeans and two times more profitable than corn. More importantly, sugarcane can be grown on marginal land in the Gulf Coast region that does not support good corn or soybean yields.

Published in *Biocatalysis and Agricultural Biotechnology*, this paper analyzes the project's first genetically modified sugarcane varieties. Using a juicer, the researchers extracted about 90% of the sugar and 60% of the oil from the plant; the juice was fermented to produce ethanol and later treated with organic solvents to recover the oil. The team has patented the method used to separate the oil and sugar. "The oil composition is comparable to that obtained from other feedstocks like seaweed or algae that are being engineered to produce oil," said co-author Vijay Singh, Director of the Integrated Bioprocessing Research Laboratory at Illinois.

To date, PETROSS has engineered sugarcane with 13 percent oil, 8 percent of which is the oil that can be converted into biodiesel. According to the project's economic analyses, plants with just 5 percent oil would produce an extra 123 gallons of biodiesel per acre than soybeans and 350 more gallons of ethanol per acre than corn.

<https://www.sciencedaily.com>

Global Innovation Index 2017

The Global Innovation Index provides detailed metrics about the innovation performance of 127 countries and economies around the world. Its 81 indicators explore a broad vision of innovation, including political environment, education, infrastructure and business sophistication. This year's report reviews the state of innovation in agriculture and food systems across sectors and geographies.

For more information, access:

<http://www.wipo.int>