ASIA-PACIFIC

CHINA

New drug to inhibit cancer stem cells

Chinese researchers have developed a new drug that can inhibit the growth and spread of cancer stem cells. Researchers from Wuhan and Shanghai announced that a molecular targeted synthetic drug called WYC-209 could kill or inhibit the proliferation of stem cells of melanoma and lung, ovarian, and breast cancers.

Through experiments on mice, researchers found that the drug can also prevent metastasis of lung cancer in 87.5 percent of cases. The research, led by Wang Ning, professor at Huazhong University of Science and Technology, and Yu Biao, researcher at Shanghai Institute of Organic Chemistry under the Chinese Academy of Sciences, was published in the journal *Nature* Communications on April 11.

The cancer stem cell therapy is a current strategy for cancer treatment. Inhibiting cancer stem cells can decrease the chances of new tumors. Wang and Yu started cooperating on synthesizing the new drug in 2014. According to researchers, animal experiments show that the new drug can treat malignant tumors with low toxicity.

http://www.xinhuanet.com

New medicines for lung cancer

Chinese researchers have developed two new medicines that may prolong the lives of lung cancer patients, the China Daily reported. Researchers from Shanghai Chest Hospital conducted clinical trials showing that using a small molecular, multi-targeted drug, called anlotinib hydrochloride, can inhibit the growth of tumors and the development of surrounding blood vessels.

The treatment could prolong the lives of lung cancer patients an average of 50 percent over patients receiving placebos. They survived another 3.3 months on average, said Han Baohui, who led the clinical trials involving 437 patients at 34 health centers and hospitals nationwide. "One headache for doctors around the world is that there is no guide for how to prescribe medicines for late-stage patients who build up tolerance to various medicines after taking them for long periods," said Han, also the director of respiratory medicine at the hospital.

The new treatment "may become a standard in our country as a viable prescription for these patients," Han added. According to Han, the treatment will be available to the public this year, and the cost is estimated at around 10,000 yuan (1,600 U.S. dollars) per month. Another drug, fruquintinib, that can also inhibit vascular development around tumors will soon be used in final stage clinical trials, said Lu Shun, director of oncology at Shanghai Chest Hospital. Clinical trials showed that the three- and six-month survival rates of those who took the medicine were 90 percent and 67 percent, respectively, compared with 73 percent and 58 percent among those who received placebos.

The research was published in *Journal of Clinical Oncology* in the United States in March.

http://www.xinhuanet.com

Tomatoes with enhanced antioxidant properties

The School of Biological Sciences, Faculty of Science, the University of Hong Kong (HKU), in collaboration with the Institut de Biologie Moléculaire des Plantes (CNRS, Strasbourg, France), has identified a new strategy to simultaneously enhance health-promoting vitamin E by ~6-fold and double both provitamin A and lycopene contents in tomatoes, to significantly boost antioxidant properties.

The research group manipulated the plant isoprenoid pathway through the utilization of a variant of 3-hydroxy-3-methylglutaryl-coenzyme A synthase (HMGS). The overexpression of HMGS in tomatoes increased not only phytosterols, squalene, provitamin A and lycopene, but also vitamin E (α-tocopherol) by 494%.

The HMGS DNA used in these experiments originated from a food crop, Brassica juncea (Indian mustard), that yields edible leaves, stems and seeds, the latter used in vegetable oil production. Earlier, this research group reported that the recombinant HMGS variant S359A (in which amino acid residue "serine" at position 359 was switched to "alanine") exhibits 10-fold higher enzyme activity. The introduction of S359A in the model plant Arabidopsis increased phytosterol content.

Now, the research group has introduced the S359A into tomatoes, a crop plant. Although there were no differences in the appearance and size of the transformed tomato fruits, total carotenoids including provitamin A and lycopene increased drastically by 169% and 111%, respectively, as observed by a deeper colour of carotenoid extracts in S359A tomatoes over the control. Furthermore, these carotenoid extracts exhibited 89.5-96.5% higher antioxidant activity than the control. Besides carotenoids, the transformed tomatoes displayed elevations in vitamin E (α-tocopherol, 494%), squalene (210%), and phytosterols (94%). These observations were attributed to the increased expression of genes in the isoprenoid pathway.

Professor Chye Mee-len who led this research said: "Increasing health-promoting components in crops is an important research area that aligns with the aspirations of Dr Wilson and Mrs Amelia Wong on the use of plant biotechnology for a sustainable future. The accumulation of the healthy components in food crops would provide added-value to fruits and vegetables in the human diet, as well as enrich feed for livestock and aquaculture." Dr Wang Mingfu added: "Extracts with enriched phytosterols, vitamin E and carotenoids can be used in the production of anti-ageing cream and sun-care lotion. These compounds show excellent anti-inflammatory and antioxidant activity."

https://phys.org

INDIA

Nanotech-based novel cancer drug delivery system

A path-breaking drug delivery system using nanotechnology, developed by a team of scientists at Regional Centre for Biotechnology (RCB) at Faridabad, would radically upgrade cancer therapy in the country and may dramatically boost the

number of potent therapeutic agents. The groundbreaking discovery – a new ray of hope for millions of cancer patients in India -- is validated at laboratory stage and ready to be transferred to the industry for commercial application.

"It's a vehicle for delivery of predominantly anti-cancer drugs either in encapsulated or conjugated pattern in nanoparticle forms. Unlike the drug delivery systems currently available in the market, this technology ensures a fourfold enhancement in bioavailability, which means three times higher drug concentration at tumor site. And all this is achieved with lesser toxicity owing to low drug concentration in circulation," Dr Avinash Bajaj, Associate Professor at RCB and a prominent member of the team that developed the system, told Pharmabiz. The innovative system is highly effective in the treatment of cancers affecting stomach, breast, lungs, prostrate and neck.

RCB has handed over the know-how to Biotech Consortium India Limited (BCIL), a public sector company promoted by the Department of Biotechnology, to facilitate its speedy commercialisation. According to sources, a handful of companies have already evinced interest in it and talks with BCIL for technology transfer are at an advanced stage.

The inventors have exploited the potential of nanotechnology to develop a delivery system that can substantially reduce drug toxicity in chemotherapy patients. The lipid-based nanoparticle-drug formulation is aggregated in supra-molecular form to attain different structural assemblies which is useful in target specific drug delivery. While doing so, the researchers have overcome the problem of delivery, toxic nature and insufficient retention time of hydrophobic and hydrophilic cancer drugs using a lipid-based formulation. Enhanced drug entrapment is achieved in less than an hour through a simple and single step without any special equipment for synthesis.

"We have conducted numerous animal studies to check the validity of the invention. It was checked in mice, rabbits and rhesus monkeys. In fact, this is the first time in India that a drug delivery system's efficacy is tested in monkeys. The results were extremely impressive," Dr Bajaj, who has done is post-doctoral work at the University of Massachusetts, pointed out. According to inventors, the nanotechnology-based system's uses are not restricted to cancer treatment alone. It can be used for the treatment of bacterial and fungal infections, diabetes and many inflammatory ailments.

Established by the Department of Biotechnology under the auspices of UNESCO, RCB focuses on shared biotechnology growth in the Asia-Pacific region. It is part of the Biotech Science Cluster and operates in synergy with the other institutions in the Cluster.

http://www.pharmabiz.com

Scientists edit gene to kill cervical cancer cells

In a recent study, scientists at the Cancer Research Program, Rajiv Gandhi Centre for Biotechnology (RGCB) in Kerala, have devised a new approach that can edit genetic sequences, in cervical cancer cells that can knock out the cancer-causing gene and thus, serve as an alternative therapeutic approach in treating cervical cancer.

Human Papilloma Virus (HPV) is one of causative agents of cervical cancer in women. While most infections caused by HPV clear up on their own, many women, with persistent HPV infections, gradually develop cervical cancer. According to a study, India accounts for one-third of the cervical cancer deaths globally. Among the two genetic sequences (genotypes) of the virus – HPV-16 and HPV-18 – that cause cancer, HPV-16 is the most prevalent gene in India. The recent study, published in Nature's journal Scientific Reports, the researchers have used a gene editing molecule that can edit the protein producing gene E7, found in HPV, and has a role in causing cervical cancer and making it malignant.

The study showed the total silencing of E7. Even in a HeLa cell line, a type of immortal cell line used in scientific research, the researchers observed 10% editing activity and total elimination of E7 proteins produced by the gene.

But, suppressing the activity of E7 genes is not without consequences. It results in cell death. Biologically, our cells die in two ways. One is a programmed cell death, which is a relatively 'cleaner' death, where all the cell contents are promptly recycled. The second, also called 'necrotic death', is a messier affair. Here the dead cell bursts out spewing its contents all around it. Usually, genes when edited by TALENs, result in a programmed cell death. However, in this study, the researchers report a cell death by necrosis when TALENs were used to target genes that produce E7 in cervical cancer cells. The advantage of necrotic cell death is that with the cancer cell contents now all spilled outside, the immune system can easily pick this up. Once our immune system knows the presence of these foreign bodies, it triggers pro-inflammatory cytokines – small proteins helping in cell signaling — leading to tumor-specific immunity. This could, in turn, destroy other malignant cells including those that have been resistant to natural cell death.

https://researchmatters.in

Diarrhoea vaccine

The World Health Organisation (WHO) has awarded pre-qualification to the developing world's first rotavirus diarrhoea vaccine, ROTAVAC, developed by Hyderabad-based Bharat Biotech. The recognition will allow UN agencies and Gavi, the global vaccine alliance, to purchase the vaccine from Bharat Biotech at significantly lower prices than those sourced from global pharmaceutical majors and make it available in other developing regions including Africa where diarrhoea kills thousands of children every year.

"Not only will ROTAVAC have a market in Gavi-supported countries where it will be priced much lower than similar vaccines supplied by companies such as GSK and Merck, there is also a huge market in non-Gavi countries such as South Africa where the vaccine is now available at a very high price," Duncan Steele from The Bill & Melinda Gates Foundation told BusinessLine.

The 2015 rotavirus weighted average price for Gavi was $ 4.80 per course, with the price for Rotarix (produced by GSK) at $ 4.17 per course and the price for RotaTeq (produced by Merck) at $ 10.50 per course, as per Gavi's web-site. Bharat Biotech plans to supply ROTOVAC for Gavi countries at $ 1 per vaccine which would add up to $3 per course. "In a non-Gavi country such as South Africa,

one course of rotavirus can be priced up to $ 20. If the Indian company can work out an arrangement with such countries at even a price as high as $5 per course, there could be a big demand," Steele said.

In India, ROTAVAC, the vaccine to prevent infant deaths and hospitalisations due to rotavirus diarrhoea, was launched in March 2015 and introduced into the universal immunisation programme. At present, the programme has been introduced in nine states including Odisha, Andhra Pradesh, Haryana, Himachal Pradesh, Assam, Tripura, Tamil Nadu, Madhya Pradesh and Rajasthan. Jharkhand, too, would soon get included.

ROTAVAC was developed as a result of a multi-country and multi partner collaborative model for over two decades, Ella said. The partnership included the Department of Biotechnology, the Indian Council of Medical Research, the Indian Institute of Science, the All India Institute of Medical Science, the Christian Medical College, King Edwards Memorial Hospital, the Translational Health Sciences and Technology Institute, the Society for Applied Studies, the US National Institutes of Health, the US Centres for Disease Control and Prevention, Johns Hopkins University and PATH.

https://www.thehindubusinessline.com

REPUBLIC OF KOREA

Anti-diabetics using microbial enzyme

The Ministry of Science and ICT announced on January 16 that a research team led by Professor Oh Deok-kun of Konkuk University developed a substance similar to lipid regulating agents in human body using microbial enzyme and confirmed the potential as a drug for diabetes.

The research team successfully compounded substances, such as hepoxilin and trioxilin which are lipid regulating agents that control glucose metabolism with a minute amount of them existing in human body. Lipid regulating agents is a substance that is involved in various biological activities in the body, including immunity, anti-inflammatory and controlling glucose and fat metabolism. Since only a small amount of substances are created in the body and they are dissolved very quickly, it has been impossible to secure the substance until now.

In addition, the research team studied an enzyme and metabolic pathway involving in biosynthesis of lipid regulating agents from germs. They found proteinlike in microorganism, which has the same function of lipoxidase and hydroxy fatty acid enzyme that compound lipid regulating agents in the body, and use them to biologically synthesize numerous lipid regulating agents.

Professor Oh Deok-kun said, "We succeeded in mass developing and producing lipid regulating agents that only a minute amount of them can be found in human body, by making use of microorganism. We will be able to biologically synthesize various lipid regulating agents that can treat diabetes and infection in the future."

The latest findings were published in the international journal *Nature Communications.*

http://www.businesskorea.co.kr

AI program for effective gene editing

Yonsei University Medical School professor Kim Hyung-bum and Seoul National University engineering professor Yoon Sung-ro announced on January 30 that their joint research team developed an AI program choosing the most effective gene scissors for cutting different target parts.

Gene scissors can be defined as artificial enzymes cutting certain DNA parts by coupling with animal and plant genes. Each of the enzymes is divided into a cleavage enzyme for DNA cutting and a guide RNA functioning as a cleavage enzyme carrier. One of the most important parts for effective gene editing is attachment of a selected enzyme to a target DNA sequence. These days, researchers around the world are studying which guide RNAs can be most effective for different target DNA sequences. Although there have been some computer simulation programs for predicting the effects of gene scissors, the predictions have not been accurate due to the shortage of data.

The team used deep learning as their solution to the limitation. Earlier, professor Kim Hyung-bum came up with the gene editing effects of CRISPR-Cpf1 with 15,000 guide RNAs based on an analysis method for measuring the activities of genetic scissors. Professor Yoon Sung-ro combined the data with deep leaning so that the most effective gene scissors can be presented in different conditions.

The newly developed AI program has a correlation coefficient of 0.87 whereas existing simulation programs' range from 0.5 to 0.6. Details of the research are available in the *Nature Biotechnology* journal.

http://www.businesskorea.co.kr

EUROPE

SWITZERLAND

Artificial skin implant to detect cancer

An implant which detects cancer in the body and causes a small artificial mole to appear on the skin as an early warning sign has been developed by scientists. The tiny patch lies under the skin and is made of a network of cells which constantly monitor calcium levels in the body.

Swiss scientists from the university ETH Zurich say the device can recognise the four most common types of cancer - prostate, lung, colon and breast cancer - at a very early stage of tumour development.

Cancer patients are far more likely to survive if the disease is picked up early. For example, nearly all women with stage one breast cancer survive for five years, but by stage four, survival falls to just 22 per cent. Martin Fussenegger, Professor at the Department of Biosystems Science and Engineering at ETH Zurich, said the implant could be available within a decade. "Nowadays, people generally go to the doctor only when the tumour begins to cause problems. Unfortunately, by that point it is often too late. "Early detection increases the chance of survival significantly." An implant carrier should see a doctor for further evaluation after the mole appears. The mole does not mean that the person is likely to die soon."

https://www.telegraph.co.uk

UK

Synthetic, bacteria-killing virus

Researchers at University College London on Wednesday announced they have developed a laboratory-built virus that kills unwanted bacteria on contact. The breakthrough, detailed in a study published in the journal *Nature Communications,* comes from researchers at UCL, as well as Britain's National Physical Laboratory. They created a synthetic hollow shell 20 nanometers wide, or less than 0.0000008 inch, which emulates naturally occurring viruses. The artificial viruses recognize and then destroy the membranes of bacteria.

The discovery demonstrates a new approach to treating infectious and antibiotic-resistant diseases, the researchers said. "We used high-resolution and real-time imaging to see the impact of the synthetic viruses on bacterial model membranes and found that they are extremely destructive," Hasan Alkassem, a doctoral student at UCL and co-author on the study, said in a press release.

"Seconds after landing on the surface, the synthetic viruses disassemble and form rapidly expanding holes in the membrane, causing it to leak. Experiments on intact bacteria then showed that this caused the bacteria to die."

The synthetic viruses do not affect living human cells but can enter cells in the same way that natural viruses can. The researchers say the capability suggests their lab-built viruses can also be involved in gene editing and delivery, as well as in synthetic biology. "We have a potential strategy to treat infectious diseases, and we also understand how it works," said Bart Hoogenboom, a professor at the UCL London Center for Nanotechnology, UCL Physics and Astronomy, and UCL Institute of Structural and Molecular Biology.

https://www.upi.com

NORTH AMERICA

USA

Mutant enzyme that eats plastic

Scientists have developed an enzyme which is able to "digest" some of the planet's most commonly polluting plastics. Undertaken by teams at the U.S. Department of Energy's National Renewable Energy Laboratory (NREL) and the U.K.'s University of Portsmouth, the research could potentially lead to a "recycling solution" for plastic bottles made from polyethylene terephthalate (PET), which lingers in the environment for hundreds of years.

The researchers were initially examining the crystal structure of PETase, an enzyme that can digest PET, in order to understand how it works. But during their research, the scientists managed to engineer an enzyme that was more effective at "degrading" the plastic than the naturally occurring one, which was recently discovered in the soil of a Japanese recycling plant.

"Serendipity often plays a significant role in fundamental scientific research and our discovery here is no exception," John McGeehan, director of the Institute of Biological and Biomedical Sciences in the School of Biological Sciences at Portsmouth, said in a statement Monday.

"Although the improvement is modest, this unanticipated discovery suggests that there is room to further improve these enzymes, moving us closer to a recycling solution for the ever-growing mountain of discarded plastics," McGeehan added. The University of Portsmouth said that the "mutant" enzyme was also able to degrade polyethylene furandicarboxylate, which is a bio-based substitute for PET plastics.

https://www.cnbc.com

CRISPR-carrying nanoparticles edit the genome

Nanoparticles that allow for CRISPR genome-editing in adult animals have now been developed by researchers. Using a new nanoparticle-based, nonviral delivery technique, the researchers were able to cut out a disease-causing gene in about 80 percent of liver cells, and permanently lower cholesterol in mice.

In a new study, MIT researchers have developed nanoparticles that can deliver the CRISPR genome-editing system and specifically modify genes in mice. The team used nanoparticles to carry the CRISPR components, eliminating the need to use viruses for delivery. Using the new delivery technique, the researchers were able to cut out certain genes in about 80 percent of liver cells, the best success rate ever achieved with CRISPR in adult animals.

"What's really exciting here is that we've shown you can make a nanoparticle that can be used to permanently and specifically edit the DNA in the liver of an adult animal," says Daniel Anderson, an associate professor in MIT's Department of Chemical Engineering and a member of MIT's Koch Institute for Integrative Cancer Research and Institute for Medical Engineering and Science (IMES).

One of the genes targeted in this study, known as Pcsk9, regulates cholesterol levels. Mutations in the human version of the gene are associated with a rare disorder called dominant familial hypercholesterolemia, and the FDA recently approved two antibody drugs that inhibit Pcsk9. However, these antibodies need to be taken regularly, and for the rest of the patient's life, to provide therapy. The new nanoparticles permanently edit the gene following a single treatment, and the technique also offers promise for treating other liver disorders, according to the MIT team.

Anderson is the senior author of the study, which appears in the Nov. 13 issue of *Nature Biotechnology*. The paper's lead author is Koch Institute research scientist Hao Yin. Other authors include David H. Koch Institute Professor Robert Langer of MIT, professors Victor Koteliansky and Timofei Zatsepin of the Skolkovo Institute of Science and Technology, and Professor Wen Xue of the University of Massachusetts Medical School.

In the new Nature Biotechnology paper, the researchers came up with a system that delivers both Cas9 and the RNA guide using nanoparticles, with no need for viruses. To deliver the guide RNAs, they first had to chemically modify the RNA to protect it from enzymes in the body that would normally break it down before it could reach its destination.

The researchers analyzed the structure of the complex formed by Cas9 and the RNA

guide, or sgRNA, to figure out which sections of the guide RNA strand could be chemically modified without interfering with the binding of the two molecules. Based on this analysis, they created and tested many possible combinations of modifications. "We used the structure of the Cas9 and sgRNA complex as a guide and did tests to figure out we can modify as much as 70 percent of the guide RNA," Yin says. "We could heavily modify it and not affect the binding of sgRNA and Cas9, and this enhanced modification really enhances activity."

The researchers packaged these modified RNA guides (which they call enhanced sgRNA) into lipid nanoparticles, which they had previously used to deliver other types of RNA to the liver, and injected them into mice along with nanoparticles containing mRNA that encodes Cas9. They experimented with knocking out a few different genes expressed by hepatocytes, but focused most of their attention on the cholesterol-regulating Pcsk9 gene. The researchers were able to eliminate this gene in more than 80 percent of liver cells, and the Pcsk9 protein was undetectable in these mice. They also found a 35 percent drop in the total cholesterol levels of the treated mice. The researchers are now working on identifying other liver diseases that might benefit from this approach, and advancing these approaches toward use in patients.

https://www.sciencedaily.com

New method to improve crops

A team of University of Georgia researchers has developed a new way to breed plants with better traits. By introducing a human protein into the model plant species *Arabidopsis thaliana*, researchers found that they could selectively activate silenced genes already present within the plant. Using this method to increase diversity among plant populations could serve to create varieties that are able to withstand drought or disease in crops or other plant populations, and the researchers have already begun testing the technique on maize, soy and rice. They published their findings in *Nature Communications*.

The research project was led by Lexiang Ji, a doctoral student in bioinformatics, and William Jordan, a doctoral student in genetics. The new method they explored, known as epimutagenesis, will make it possible to breed diverse plants in a way that isn't possible with traditional techniques. "In the past this has been done with traditional breeding. You take a plant, breed it with another plant that has another characteristic you want to create another plant," said Jordan. "The problem with that is getting an individual that has all of the characteristics you want and none of the characteristics that you don't want. It's kind of difficult. With our new technique, you can modify how the genes are turned on and off in that plant without having to introduce a whole other set of genes from another parent."

The idea for the method evolved originally from working in the lab with department of genetics professor Robert Schmitz, the corresponding author on the study. In his lab, researchers were studying DNA methylation, which controls expressed genetic traits, and creating maps of where DNA methylation is located in many plant species, including crops. When DNA methylation is removed, researchers found that they could selectively turn on previously silenced genes in the underlying genome of the plant.

"We saw repeatedly that lots of genes are silenced by DNA methylation and thought it was kind of curious," said Schmitz. "There are lots of discussions you can have about why these exist, but the reality is that they are there. So we wondered, how can we leverage them? Let's use the plant already in the field and reawaken some of those silenced genes to generate trait variation."

To turn these dormant or silenced genes on, researchers introduced a human enzyme, known as a ten-eleven translocation enzyme, to plant seedlings using specially modified bacteria as a delivery vector. Introducing this human protein allows researchers to remove DNA methylation and thereby turn on previously silenced genes.

Figuring out the best way to introduce the protein to the plant species has been a trial and error process. With Ji's expertise in bioinformatics, researchers are able to look at large sets of data about their experiment and make decisions on how to best proceed with the project. "The data has really helped us brainstorm and coordinate what we should do next," said Ji. "That was particularly important in the beginning of this project because we just didn't know what was going to happen with this new technique."

https://phys.org

Technology Bank for Least Developed Countries

The 2011 Istanbul Programme of Action called for the establishment of a technology bank and a science, technology and innovation supporting mechanism dedicated to least developed countries (the "Technology Bank"), a long-standing priority of the LDCs confirmed in the 2015 Addis Ababa Action Agenda and in Sustainable Development Goal 17. The establishment of the Technology Bank is expected to be the first target of the SDGs to be met. The new Bank is expected to improve the utilization of scientific and technological solutions in the world's poorest countries and promote the integration of least developed countries into the global knowledge-based economy. This will be achieved through improving technology-related policies and facilitating the access to appropriate technologies.

On 22 September 2017 The Technology Bank was operationalized with the signing of the Host Country Agreement and the Contribution Agreement between the Government of Turkey and the United Nations. The Technology Bank will be located in Gebze, Turkey.

For more information, access:
http://unohrlls.org/technologybank/