INTERNATIONAL

'Climate proof' crops

New rice and green bean plants are now being rolled out to help farmers grow more of these staple foods despite higher temperatures caused by climate change. These new 'climate proof' crop varieties were developed as part of a five-year project aimed at helping countries to improve food security and adapt to changing climate conditions. The project specifically addressed the improvement of tolerance of rice and bean plants to high temperatures in drought-prone areas.

To help protect crop-based food sources, a group of plant breeders, plant physiologists, agronomists and plant biotechnologists and experts from the IAEA, in cooperation with the Food and Agriculture Organization of the United Nations (FAO), teamed up to develop new 'climate proof' crop varieties through a five-year IAEA coordinated research project.

The team began by studying how rice and common bean plants react to normal and aberrant – meaning any climate condition to which a variety of crop is not normally adapted to – climate conditions, and identifying genes related to heat tolerance and higher yields. With this information, they targeted plants with desired traits and bred for these traits using irradiation to speed up the natural process of mutation in plants. This breeding process increases diversity of plants' traits, allowing scientists to more quickly test and select plants with the desired characteristics. The result was a series of 'climate proof' rice and common bean plants that can tolerate high temperature conditions better while producing higher yields compared to local varieties.

One of these new rice varieties called 'Guillemar', which is drought tolerant, is now being used in Cuba and has boosted crop yields by 10 per cent. Other countries such as India, Pakistan, the Philippines, Tanzania and Senegal, are also preparing to release new, high-yielding rice varieties suited to each countries' temperature conditions, while experts in Colombia and Cuba have had success with new varieties of heat-tolerant, higher yielding common bean and tepary bean plants, which they expect to release to farmers by 2020-2021.

Over the course of this five-year project, the team created methods for screening the physiological, genetic and molecular components of plants as well as for accurately assessing the plants' genetic makeup to identify, select and breed plants with desired traits. A pre-field screening technique, for example, was refined to help plant breeders accelerate the evaluation of plant varieties in controlled conditions such as a greenhouse or growth chamber. This approach allows them to effectively narrow down the number of possible plants for further field tests from a few thousand to less than 100. By slimming down the options, it can reduce research and development time from around three to five years to one year, which means new plant varieties can reach farmers more quickly to help them stay ahead of climate change and prevent food insecurity.

Many of the team's methods and techniques are now being made accessible to other researchers to research further. They are being made available through IAEA coordinated research and technical cooperation projects with other teams of scientists, as well as through more than 40 publications, including a recently published open-access guidebook on Pre-Field Screening Protocols for Heat Tolerant Mutants in Rice.

https://www.iaea.org

ASIA-PACIFIC

AUSTRALIA

Test to detect all types of cancer

Researchers from the University of Queensland have developed an inexpensive test that can detect traces of cancer in the bloodstream in as few as 10 minutes. "This new discovery could be a game-changer in the field of point of care cancer diagnostics," Dr. Abu Sina, a member of research team, said. The Queensland scientists discovered that the DNA released by cancer cells sticks to metal differently than DNA from healthy cells, according to a report by the Guardian. The research results were published in the journal Nature Communications.

The DNA is put into water with gold nanoparticles. Even though it's gold, the water looks pink. If cancer DNA is added, the water remains pink. If it's healthy DNA, the water turns blue. "This happens in one drop of fluid," said chemistry professor Matt Trau, who led the research team. "You can detect it by eye, it's as simple as that."

The test has been used to detect breast, prostate and colon cancer and lymphoma. According to a news release from the university, the technology has been up to 90 percent accurate in tests involving 200 human cancer samples and normal DNA. "Virtually every piece of cancerous DNA we examined had this highly predictable pattern," Trau said. "It seems to be a general feature for all cancer. It's a startling discovery."

https://weather.com

CHINA

Decoding cell-specific DNA methylation

Scientists in China have developed an algorithm that can link epigenetic modifications to specific cell types with 90 percent sensitivity. In a study published in Nature Methods, researchers in China have developed a statistical algorithm for identifying sites of DNA methylation (DNAm) in genomes. DNAm is a covalent modification of DNA which can regulate gene activity, with implications on health and disease. Identifying changes in DNAm that correlate with disease risk is the main aim of epigenome-wide association studies (EWAS) in large numbers of individuals.

However, tissues profiled in EWAS are complex mixtures of many different cell types, each with its own characteristic DNAm profile, which can confound analyses. In the present study, researchers led by Professor Andrew Teschendorff at the Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, developed

a statistical algorithm called 'CellDMC,' which allows researchers to pinpoint not only the specific genomic sites that have undergone DNAm, but also the cell types in which these DNAm alterations occur. They demonstrated that their algorithm can identify DNAm changes with over 90 percent sensitivity.

Using CellDMC, the researchers were able to show that many DNAm changes associated with rheumatoid arthritis occur in one particular subtype of immune cells, the B-cells. Applied to the analysis of samples from patients who smoked tobacco, their algorithm could identify epigenetic pathways linking smoking to lung cancer. The researchers propose that CellDMC will allow researchers in the EWAS community to identify the relevant cell types altered in disease, without the need for laborious cell sorting or generating single-cell methylomes, both of which are expensive and time-consuming procedures. Their technology could facilitate the identification and development of epigenetic disease risk biomarker assays, paving the way for personalized medicine.

https://www.asianscientist.com

INDIA

Transgenic rice with reduced arsenic accumulation

Arsenic accumulation in rice grains is one of the serious agricultural issues in India. To address this, researchers at Lucknow-based CSIR-National Botanical Research Institute have developed transgenic rice by inserting a novel fungal gene, which results in reduced arsenic accumulation in rice grain.

In their latest study, researchers have cloned Arsenic methyltransferase (WaarsM) gene from a soil fungus, Westerdykellaaurantiaca, and inserted the same into the rice genome with the help of Agrobacterium tumefaciens, a soil bacterium which has natural ability to alter the plant's genetic makeup. The newly developed transgenic rice along with normal rice was then treated with arsenic. Comparison of transgenic and non-transgenic rice showed that transgenic plants accumulated less arsenic in root as well as shoot as compared to non-transgenic lines.

Researchers found that the resulting transgenic plant acquired the potential for methylating inorganic arsenic to a variety of harmless organic species, including volatile arsenicals. This could be potential strategy for developing transgenic rice capable of low arsenic accumulation not only in grain but also in straw and feed which are used for livestock.

Now the team is focusing on food safety test and field trials, subject to regulatory approvals. In addition, researchers are also looking for gaps in arsenic metabolism in rice which will ultimately lead to understand arsenic uptake and metabolism in rice. The recent research results have been published in *Journal of Hazardous Materials.*

https://www.downtoearth.org.in

Fighting drug-resistant bacteria in biofilms

Researchers at Indian Institute of Technology, Roorkee (IIT-Roorkee) have developed a new eco-friendly nanocomposite that promises to help fight the problem of such antibiotic resistance more effectively. The newly synthesized nanocomposite is capable of penetrating these biofilms and kill microbes. The new compound has been developed by combining silver particles with κ-Carrageenan, a polymer derived from red sea weed. The polymer is conventionally used in food products as a gelling, thickening and emulsifying agent.

Silver nanoparticles are already known to have the ability to kill microbes but they are instable and have a short shelf life. Researchers used κ-Carrageenan to increase stability and shelf life of silver nanoparticles. They made a solution of κ-Carrageenan with silver nitrate and irradiated it in a microwave synthesizer. The nanocomposite thus obtained was found to be very stable and having a long shelf life, while being effective against both Gram-positive and Gram-negative bacteria.

"Capping of silver nanocomposites with κ-carrageenan imparts it stability and shelf life up to six 6months, which is one of the essential features of therapeutic formulations. The nanocompositeshows excellent antimicrobial activity against S.aureus and P.aeruginosa bacterial biofilms," researchers said. Ascarrageenan has been widely studied for its antifungal, anti-viral, anti-cancerous andimmunomodulatory properties, the nanocomposite based on it can have huge potential in biomedical applications.

The new nanocomposite also has potential applications in food packaging industry as microbial films spoil food products. "We are currently devising cost-effective anti-bacterial wound dressing materials and food packaging materials using the new nanocomposite. We plan to study its efficacy as potent anti-fungal and anti-viral agents too," said Dr. Krishna Mohan Poluri, a member of the research team, while speaking to India Science Wire. The research results have been published in *Journal Carbohydrate Polymers.*

https://www.downtoearth.org.in

Transgenic rice for high salinity and drought conditions

A group of researchers from Jawaharlal Nehru University (JNU), International Centre for Genetic Engineering and Biotechnology (ICGEB) and University of Illinois have developed transgenic rice that promises to generate high yields even under conditions of high salinity, high temperature and drought. The scientists hit upon the idea while studying a wild rice variety, Pokkali, grown in coastal regions of Kerala. When they tried to figure out its ability to survive and thrive in highly saline environment, it emerged that it had very high level of a gene, OsIF.

Tests showed that the plant expressed the gene four times more than in traditional plants. Using this insight, researchers raised another rice plant, IR 64, with OsIF over-expressed in it. They did so by using a promoter derived from cauliflower mosaic virus (CaMV). It was found that over-expression of OsIF improved the growth and yield of this plant significantly in adverse conditions of high salinity, high tempera-

ture and drought. This plant had a yield of 20 per cent more than a normal one.

Further studies showed that over-expression helped by stabilising the process of photosynthesis in the plant. The OsIF gene encodes a protein in rice for cell components called intermediate filaments (IFs). These filaments protect cells from external forces, besides participating in cell adhesion and tissue integrity. They also act as a molecular scaffold that controls intracellular organisation and contribute to signalling events in response to cell stress. The research results have been published *Journal Scientific Reports.*

https://www.thehindubusinessline.com

Hybrid corn variety high in vitamin A

Researchers at the Indian Agricultural Research Institute (IARI) have developed a maize variety which is rich in both Vitamin A and essential amino acids through the process of plant breeding. … The hybrid varieties of maize currently grown in India, though rich in essential amino acids – lysine and tryptophan – are poor in vitamin A. Scientists have developed a new hybrid variety of maize by crossing. It contains natural variations of three genes – beta-Carotene Hydroxylase, Lycopene-eta-Cyclase and Opaque2 – required for production of high amount of vitamin A and the two essential amino acids. The new hybrids, thus produced, have 4.5 folds more vitamin A content and similar amounts of lysine and tryptophan as earlier varieties.

In addition, the grain yield of new hybrids has been found to be similar to existing varieties, as evaluated by growing both varieties at two different locations in India. Researchers believe that bio-fortified high-yielding maize hybrid could help address micronutrient malnutrition.

https://geneticliteracyproject.org

ISRAEL

Bacteria to cure fungal infections

Researchers in the Technion-Israel Institute of Technology's Faculty of Biotechnology and Food Engineering have cured fungal infections using a soil-dwelling bacteria. The findings of the research led by Assistant Professor Boaz Mizrahi and conducted by his student Maayan Lupton and Dr. Ayelet Orbach were published recently in *Advanced Functional Materials.*

Fungal infections are common among various animals, including humans. One of the primary sources of such infections is Candida – a yeast regularly found in our bodies. Candida exploits abnormal functioning in the organism to spread and harm the host. Most people will experience a fungal infection at least once in their lifetime, in some part of their body – on the skin, in the digestive system or genitals.

The frequency of fungal infections is constantly on the rise due to the aging population and possibly global warming. Additional reasons include use of drugs, which suppress the immune system, and the increased use of broad-spectrum antibiotics, which indirectly enhance the proliferation of Candida by disrupting the bacteria balance in the body.

The researchers assessed the possibility of treating Candida via the bacillus subtilis bacterium, which naturally produces and secretes substances that inhibit Candida growth. This mechanism evolved in the bacteria as part of its competition with Candida over common growth substrates.

"Our first challenge," said Assistant Professor Mizrahi, "was to develop a transport system that would enable application of the live bacteria on the infected lesion without impairing their ability to proliferate and secrete their therapeutic substances in the target site."

To do so, the researchers developed a unique gel that is in liquid form in the refrigerator and at room temperature (enabling easy application on the skin), but which hardens within seconds after being applied to the skin. Beside the thermo-responsive polymers, the gel contains food substances, which ensure maintained bacterial viability on the skin, where they can "treat" the infection. The researchers applied the gel on the skin of mice suffering from a fungal infection, after marking it (the gel) with a fluorescent substance that would allow for monitoring. The formulation penetrated deep into the skin but not into the underlying blood vessels, implying that the effect of the formula is limited to the diseased area. Later, the clinical efficacy of the bacterial formulation was demonstrated on mice suffering from Candida infection. In the control groups – treated with bacteria-free gel or not treated at all – the infection continued to develop, but the group treated with the Technion-developed bacterial gel showed rapid skin healing. Moreover, comparison of the novel treatment to the commonly used ketoconazole demonstrated the superiority of the Technion gel both from the clinically and the safety point of views.

The researchers noted that aside from development of the unique gel, a new therapeutic treatment model was demonstrated here: a miniscule factory, which after its penetration into the target, begins to produce the active substance. This is in contrast to the standard pharmaceutical model, in which the drug passes through the entire body and portions of it may be broken down in the process. The researchers hope that their novel model will be used in the future to treat a range of diseases, including psoriasis, acne, various inflammations and even cancer.

https://phys.org

REPUBLIC OF KOREA

Antimalarial substance

Republic of Korean scientists have discovered a substance that could be used as a new malaria treatment in a rare native microorganism found on the East Sea island of Ulleung, a state-run research center said. The Korea Research Institute of Bioscience and Biotechnology (KRIBB) said its scientists found the anti-malaria substance in actinomycete, a rare microorganism that lives in the soil of Ulleung Island. Actinomycetes are bacteria that live in various environments such as soil, plants, animals, rivers and seawater. They have been used as important biological resources for the development of new drugs

for decades.

KRIBB researchers selectively isolated very slowly growing bacteria from Ulleung Island soil and then examined liquid extracted from them. They discovered four kinds of new compounds that showed inhibitory activity against Plasmodium falciparum, one of the protozoans that cause malaria, without cytotoxicity.

"The successful isolation of the rare microorganism and secondary substances indicates the possibility of utilizing Ulleung Island soil as an important domestic resource," said a researcher at the KRIBB. The KRIBB's paper on the Ulleung Island achievements was published in the November issue of *Organic Letters*.

https://en.yna.co.kr

Biosensor to produce microbial cell factories

A research group at Korea Advanced Institute of Science and Technology (KAIST) presented a novel biosensor which can produce diverse, high-level microbial cell factories. The biosensor monitors the concentration of products and even intermediates when new strains are being developed. This strategy provides a new platform for manufacturing diverse natural products from renewable resources. The team succeeded in creating four natural products of high-level pharmaceutical importance with this strategy.

Malonyl-CoA is a major building block for many value-added chemicals including diverse natural products with pharmaceutical importance. However, due to the low availability of malonyl-CoA in bacteria, many malonyl-CoA-derived natural products have been produced by chemical synthesis or extraction from natural resources that are harmful to the environment and are unsustainable. For the sustainable biological production of malonyl-CoA-derived natural products, increasing the intracellular malonyl-CoA pool is necessary. To this end, the development of a robust and efficient malonyl-CoA biosensor was required to monitor the concentration of intracellular malonyl-CoA abundance as new strains are developed.

Metabolic engineering researchers at KAIST addressed this issue. This research reports the development of a simple and robust malonyl-CoA biosensor by repurposing a type III polyketide synthase (also known as RppA), which produces flaviolin, a colorimetric indicator of malonyl-CoA. Subsequently, the RppA biosensor was used for the rapid and efficient colorimetric screening of gene manipulation targets enabling enhanced malonyl-CoA abundance. The screened beneficial gene targets were employed for the high-level production of four representative natural products derived from malonyl-CoA. Compared with the previous strategies, which were expensive and time-consuming, the new biosensor could be easily applied to industrially relevant bacteria including Escherichia coli, Pseudomonas putida, and Corynebacterium glutamicum to enable a one-step process.

The study employs synthetic small regulatory RNA (sRNA) technology to rapidly and efficiently reduce endogenous target gene expression for improved malonyl-CoA production. The researchers constructed an E. coli genome-scale synthetic sRNA library targeting 1,858 genes covering all major metabolic genes in E. coli. This library was employed with the RppA biosensor to screen for gene targets which are believed to be beneficial for enhancing malonyl-CoA accumulation upon their expression knockdown.

From this colorimetric screening, 14 gene targets were selected, all of which were successful at significantly increasing the production of four natural products (6-methylsalicylic acid, aloesone, resveratrol, and naringenin). Although specific examples are demonstrated in E. coli as a host, the researchers showed that the biosensor is also functional in P. putida and C. glutamicum, industrially important representative gram-negative and gram-positive bacteria, respectively. The malonyl-CoA biosensor developed in this research will serve as an efficient platform for the rapid development of strains capable of producing natural products crucial for the pharmaceutical, chemical, cosmetics, and food industries.

An important aspect of this work is that the high-performance strains constructed in this research were developed rapidly and easily by utilizing the simple approach of colorimetric screening, without involving extensive metabolic engineering approaches. 6-Methylsalicylic acid (an antibiotic) could be produced to the highest titer reported for E. coli, and the microbial production of aloesone (a precursor of aloesin, an anti-inflammatory agent/whitening agent) was achieved for the first time.

https://www.eurekalert.org

EUROPE

FINLAND

Turning skin cells into pluripotent stem cells

Professor Timo Otonkoski at the University of Helsinki and Professor Juha Kere at Karolinska Institutet and King's College London, with their teams of researchers, have now for the first time succeeded in converting skin cells into pluripotent stem cells by activating the cell's own genes. This was achieved by using gene editing technology - called CRISPRa - that can be directed to activate genes. The method utilizes a blunted version of the Cas9 'gene scissors' that does not cut DNA and can therefore be used to activate gene expression without mutating the genome.

"CRISPR/Cas9 can be used to activate genes. This is an attractive possibility for cellular reprogramming because multiple genes can be targeted at the same time. Reprogramming based on activation of endogenous genes rather than overexpression of transgenes is also theoretically a more physiological way of controlling cell fate and may result in more normal cells. In this study, we show that it is possible to engineer a CRISPR activator system that allows robust reprogramming of iPSC", tells Professor Otonkoski.

An important key for the success was also activating a critical genetic element that was earlier found to regulate the earliest steps of human embryo development after fertilization. "Using this technology, pluripotent stem cells were obtained that

resembled very closely typical early embryonal cells", Professor Kere says.

The discovery also suggests that it might be possible to improve many other reprogramming tasks by addressing genetic elements typical of the intended target cell type.

"The technology may find practical use in bio banking and many other tissue technology applications", says PhD student, MSc Jere Weltner, the first author of the article published in *Nature Communications*. "In addition, the study opens up new insights into the mechanisms controlling early embryonic gene activation."

https://www.eurekalert.org

SPAIN

Antifungal proteins in plants

Researchers from the Spanish Research Council (CSIC) at the Centre for Research in Agricultural Genomics (CRAG) and the Institute for Plant Molecular and Cellular Biology (IBMCP), in collaboration with the IATA, have developed a biotechnological tool to produce, in a very efficient manner, antifungal proteins in plants. The results of this research, that could impact the agri-food and pharmaceutical sectors, have been published this week in the *Plant Biotechnology Journal*.

Disease-causing fungi that infect plants, animals and humans pose a serious threat to human and animal health, food security and ecosystem resilience. More people die every year from fungal infections than from malaria. Furthermore, fungal infections can have fatal consequences for at-risk immunocompromised patients with HIV/AIDS and organ transplantation, among others. In addition, fungi are a challenge to food security because they destroy major crops globally and contaminate food and feed with mycotoxins that are detrimental to animal and human health.

Maria Coca, researcher at CRAG and one of the senior authors of the study, explains that "only a few classes of antifungal agents are available today, and even these are not fully effective due to the development of resistance, host toxicity, and undesirable side effects. Many of these compounds do not even comply with the regulations, and therefore they cannot be used. Thus, there is an urgent need to develop novel antifungals, whose properties and mechanisms of action represent improvements on the existing ones, and which can be applied in diverse fields, including crop and postharvest protection, preservation in cosmetics, materials and food, and animal and human health." Coca's research group, in collaboration with the IATA's researcher Jose F. Marcos, aims to develop new antifungal compounds based on the antifungal proteins (AFPs) secreted by filamentous fungi. The problem is that the synthesis of these compounds is extremely complex; hence their exploitation requires efficient, sustainable and safe production systems.

The CSIC researcher at the IBMCP José Antonio Daros is an expert in viruses that infect plants. Through genetic engineering, Daros and his team in Valencia managed to modify the tobacco mosaic virus (TMV) so that, instead of producing its own pathogenic proteins, it produced other proteins of interest. In Barcelona, the team led by Maria Coca implemented this tool to produce antifungal proteins in leaves of the Nicotiana benthamiana plant -a plant from the tobacco family widely used in research- discovering that these leaves produced large quantities of these new antifungals.

In addition, the researchers demonstrated that extracts recovered from the N. benthamiana plants are active against pathogenic fungi, being able to protect the tomato plant from the infection by the fungus Botrytis cinerea, better known as grey mould. The work of the CRAG, IBMCP and IATA researchers shows that the plants can be used as biofactories of antifungal proteins for commercial purposes.

https://www.news-medical.net

UK

Technology to highlight cancer area for biopsies

A research team at University College London (UCL) has developed a new technology that could pinpoint the potential cancer area in the prostate gland, allowing better biopsies and disease detection.

The new technology, deployed through the SmartTarget system, creates a 3D model of the prostate and cancer from MRI scans of each patient by leveraging image processing and machine learning algorithms. While performing a biopsy, the 3D model can be integrated with ultrasound images to pinpoint the area of concern in order to guide surgeons in detecting the cancer quickly. The researchers said that the technology has enabled surgeons to identify clinically relevant cancers that were missed with existing visual detection techniques. They believe that a combination of both techniques would be the best approach.

During a study, the team performed two biopsies in 129 people with suspected prostate cancer using the SmartTarget system and visual MRI scan review. The combination of the two methods identified 93 clinically significant prostate cancers, while each of them detected 80 and missed 13 that the other technique picked up.

UCL Medical Physics & Biomedical Engineering researcher Dr Dean Barratt said: "We developed the SmartTarget system to equip surgeons with vital information about the size, shape and location of prostate tumours during a biopsy that is otherwise invisible on ultrasound images. "The software provides them with a clear target. As MRI-targeted biopsies require a very high degree of expertise and experience, we hope that the imagery displayed by SmartTarget will help to bring high accuracy prostate cancer diagnosis to a much wider range of patients and hospitals."

Findings from the research have been published in *European Urology*.

https://www.medicaldevice-network.com

NORTH AMERICA

USA

New cancer treatment

Researchers at The University of Texas at Austin have developed a new approach to treating cancer using enzyme therapy. The enzyme, PEG-KYNase, does not directly kill cancer cells but instead empowers the

immune system to eradicate unwanted cells on its own. PEG-KYNase is designed to degrade kynurenine, a metabolite produced by numerous tumors that suppresses the immune system. The UT team's findings were published in a recent issue of Nature Biotechnology.

"Our immune system constantly polices the body and normally recognizes and eliminates cancerous cells," said Everett Stone, research assistant professor in the College of Natural Sciences', Department of Molecular Biosciences and co-author of the study. "Kynurenine acts as a roadblock to immune cells that impedes normal surveillance; our drug removes this obstacle."

Enzymes have been used in specific treatments before, to treat cancers such as leukemia for example, but this is the first time one has been designed to take on the role of immune checkpoint inhibitor. The researchers are confident this approach could prove effective in treating a variety of different cancers.

The team, led by Stone and professor George Georgiou in the Cockrell School of Engineering, developed an enzyme therapy that stimulates a human immune system abnormally suppressed by cancer cells, unleashing the body's power to fight back against the disease. Their next step is to initiate clinical trials to test the safety and efficacy of the enzyme.

https://phys.org

'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.

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. The research was published in the Proceedings of the National Academy of Sciences.

https://www.cnbc.com

Methods to control bacterial factories

Michigan State University scientists have announced a breakthrough in manipulating miniature factories, found in bacteria, that hold much promise in the biotech field. The factories, or bacterial microcompartments, are widespread in nature and do different things depending on the host. For example, in cyanobacteria that harvest energy from the sun, they help to construct high-energy compounds. In our own guts, pathogenic bacteria use the factories – because the processes they perform are inefficient outside of them and sometimes use toxic materials – to outcompete our good bacteria.

Scientists want to retrofit the factories with new machines to perform designed functions. The synthetic versions could sustainably make biofuels, industrial materials and nanoscale medical devices.

In a *Nature Communications* publication, the lab of Cheryl Kerfeld announces new methods to manipulate factories:

- Complementation-based Affinity Purification, or CAP, which quickly screens for the assembly and extraction of the factories
- Encapsulation via Covalent-linkage, or EnCo, which helps to predictably insert custom machinery in the factories
- "Current technologies require many days to prepare and extract a synthetic factory shell," Andrew Hagen, a post-doc in the Kerfeld lab, said. "We also have had limited options to insert custom machinery in it. I wanted to develop better ways to do those two things."

The factory walls are made of proteintiles, shaped like hexagons and pentagons, that snap together to form an enclosure that looks like a soccer ball.

In the lab, scientists rely on chemical mixtures to make synthetic factories. And it is challenging to fish them out once they're completed. The new method shows an easier way to extract the factories:

- The team creates a factory that lacks one of the wall protein tiles.
- They add a tag to the missing tile.
- They add the tile back to the mixture, where it snaps into place when it finds the factories;
- The team extracts the factory with the help of the tagged tile. The team attracts that tag with a system that works like Velcro.

The scientists also report a method to insert custom enzymes inside the factories. It relies on a new technology that works like protein super glue.

"The technology has two entities, SpyTag and SpyCatcher, that are attracted to each other," Andrew said. "We insert a SpyCatcher 'docking site' on the inside of a factory wall. We then add a SpyTag on the machinery. Once in the same environment, the SPY system comes together like glue."

Once 'glued' to a factory, the machinery can't get out. So far, the team has managed to insert 60 copies of a single enzyme into a factory. The team aims to increase that number, as one factory could ideally fit around 200 copies.

The current proof of concept is looking promising. Next is to realize some of the technology's promise. One such application is to produce chemicals that are used in industry. For example, another team member is working on producing the molecule that gets turned into rubber, a process that usually needs fossil fuels. Other ideas include biofuels and medical tools. "We also think other scientists can use these methods with different bacteria and their factories," Andrew said. "There is a good chance they will adopt these new methods widely."

https://msutoday.msu.edu