CAPSULE

Timing eruptions
A group from Cambridge University has estimated that magma can be stored from hundreds to a thousand years at the crust-mantle boundary before being let out in a volcanic eruption. Researchers used diffusion of chromium and aluminium atoms to estimate this. The discovery can help forecast volcanic eruptions.

Similar species
The brain circuitry involved in the sense of smell is similar across six different mammal species from mice to cats. The relative sizes of three components of the olfactory neural network – nose, olfactory bulb and piriform cortex – are preserved across the six species studied, finds a study published in *Currrent Biology*.

Mind of the mosquito
Researchers from University of Washington, U.S., have figured out how female mosquitoes integrate various sensory cues to decide how and where to find their next blood meal. After the mosquito senses chemical cues with her olfactory system, she looks around to scan the area for shapes and integrating these inputs decides where to fly.

Fossil mammal
A 165-million-year-old fossil of *Microdocodon gracilis*, a shrew-like mammal, found in China in 2014, was examined recently. Researchers find in it the earliest evidence of tiny hyoid bones that link the back of the mouth, the pharynx, to the openings of the oesophagus and larynx. The tiny animal must have weighed 5 to 9 grams.

NCBS: How micro RNAs regulate the colour of fruits, leaves

Engineered plants can produce anthocyanin and flavonol which have medicinal uses, the team finds

SHUBASHREE DESIKAN

A team from the National Centre for Biological Sciences (NCBS), Bengaluru, has found that the rich colour in fruits and leaves of plants are indirectly controlled by specific micro RNAs – miR828 and miR858.

Grape plants bear fruits having colours that can be deep purple or green. This colour is due to compounds called anthocyanins and flavonols, both of which are present in grape fruits.

When the grape plant has a high amount of anthocyanin as compared to flavonol, the fruits are deep purple. When the reverse is true, the grapes are not brightly coloured. The relative abundance of anthocyanin and flavonol is controlled by genes known as the MYB transcription factors. Also referred to as activators, when present in large amounts, they result in dark purple grape, as in the Bangalore Blue variety, and absence correlates with lack of bright colour but high incidence of flavonols as in the Dilkhush grape variety.

Transgenic: Plants grown from infected "ex-plants" had reddish leaves and abundant anthocyanin, says (from left) Varsha Tirumalai, Ashwin Nair and P V Shivaprasad.

Repressor target

"Researchers knew microRNAs can regulate MYBs, but they did not know why such a regulation takes place. They were mostly working with *Arabidopsis* model where one might not see coloured fruits," says P V Shivaprasad of the Epigenetics lab in NCBS, where the work was done.

The team found that the microRNAs miR828 and miR858 were also found in abundance when the grapes had dark colour. Hence they figured out that there must be an intermediary repressor which was what the miRNA targeted.

"The microRNA was targeting something that is competing with the activator MYB. This [competing factor] is a repressor of the anthocyanin pathways," says Varsha Tirumalai, PhD student at NCBS and first author of the paper published in the *Journal of Experimental Botany*.

Micro RNAs are regulators of gene expression, acting like switches. They decide which protein should be made and how much in a given cell or tissue or an organism. They are tiny, having some 20 to 22 digits of RNA. The miRNA inhibit target RNAs by cutting them into two bits in plants. The miRNAs partner with a protein called Argonaute to do this regulation.

Two experiments

The researchers did two sets of experiments with tobacco plants *(Nicotiana tabacum)*. First, they injected through the stomata in the leaves of the plants, an *Agrobacterium* culture by which overexpression of the gene in question was achieved. This method of feeding the culture led to a local effect in the particular leaf only. Also the cells in the leaves were not damaged as the injection was done through the stomata. The leaves also overexpressed the gene and changed colour to a reddish shade.

They also did another experiment in which instead of pushing the culture through the stomata they infected an "ex plant"– a scientific term for a piece of the plant from which the whole plant can be grown. They found that the plants grown in this manner had reddish leaves and abundant anthocyanin.

"This was very interesting. I have never seen red-leaved tobacco plants earlier. Abundant flavonols were not produced in tobacco earlier," says Varsha.

"Anthocyanins and flavonols remove reactive oxygen species that damage DNA, RNA and proteins. Reactive oxygen species are involved in most human diseases," explains Dr Shivaprasad.

Biofortification

Plants having anthocyanin and flavonol can be generated by controlling the microRNAs affecting them. "We can make more of them in tobacco, which can be extracted easily and used as supplements," he adds. The genes identified here can be used in biofortification.

The group is trying to patent flavonol engineering. Their next step is to find out how the MYB transcription factor works to make the specific enzymes needed to make flavonols.

A new 'clutch' to engage the immune cell 'gear'

Two adaptor proteins act like a clutch, help protein condensates get into the correct slot

ASWATHI PACHA

A unique summer institute held at the Woods Hole Marine Biological Laboratory in the U.S. (during 2013-2018) helped unlock a few mysteries of the immune system. A team of leading biologists and biochemists identified a molecular 'clutch' which helps move clusters of proteins inside the immune cells.

Microscopic mystery: If the clutch is not active in the immune cells, they are unable to respond to the information from the outside, says Satyajit Mayor (right).

Signalling machinery

The main aim of the study was to understand how the T-cell receptors, which play a main role in our immunity, form a signalling complex and how they build a signalling machinery that picks up information from the outside and use it to activate the immune mechanism.

The team identified two adaptor proteins which act as clutch and help protein condensates get into the correct slot.

Protein condensates are a form of a macromolecular assembly formed by multivalent proteins coming together to create a region that is highly concentrated. It is in the form of a phase separated patch, like oil droplets that form a distinct patch on water.

The recruitment of these adaptor proteins to the condensates was found to be influenced by where the T-cell receptor clusters are located.

"When a T-cell receptor binds to an antigen, the T-cell undergoes a global reorganisation forming a signalling centre at the site of the antigen-bound receptor. The continuous transport of the studied protein condensates towards this signalling centre is important for maintaining the signalling output which is part of the immune response," adds Prof. Darius Vasco Köster from the Marine Biological Laboratory at Woods Hole, U.S. in an email to *The Hindu*. He is one of the authors of the work published in the journal *eLife*.

The adaptor proteins also promoted association of the protein condensates with actin present inside the cell.

Crucial role

Actin plays a crucial role in cellular processes required for normal immune function. "We fully don't know the implications of the function of these proteins, but we know that if the clutch is not active in the immune cells, they are unable to respond to the information from the outside. These adaptors are also quite general, they go and adapt to other processes as well," says Prof. Satyajit Mayor, from the National Centre for Biological Sciences, Bengaluru, and one of the authors.

Understanding the cascade of events that take place in the immune cells can help develop new vaccines and treatment regimens.

Ebola vaccine tested during epidemic saves lives in Congo

Preliminary data from vaccination in Congo suggest the vaccine has 97.5% efficacy in preventing Ebola

R. PRASAD

The 2014-2015 Ebola epidemic mainly in the three western African countries of Guinea, Liberia and Sierra Leone has been the most deadly one since the virus became known in 1976. It caused disease in 28,616 people and killed 11,310 others. But what stands out as a remarkable scientific and public health achievement has been the conduct of a large clinical trial in Guinea to test the efficacy of an Ebola vaccine in the midst of the epidemic.

The phase-3 clinical trial involving thousands of volunteers tested the efficacy of Merck's vaccine (VSV-EBOV) to protect vaccinated individuals from getting infected with Ebola virus.

The phase-1 and phase-2 clinical trials involving fewer volunteers were carried out in Europe and Africa in 2014-2015 and consequently used in Guinea in 2015 during vaccination campaigns even when it was being tested in the phase-3 trial.

Prevention: A woman getting vaccinated in Conakry, Guinea, on March 10, 2015, during the first clinical trials of Merck's vaccine. ▪ AFP

Clinical trials

During the trial, the vaccine was administered to 2,119 individuals who had come in contact with a person infected with or died due to Ebola virus and 2,041 people who had come in contact with the primary contacts (known as contacts of contacts). In July 2015, an interim analysis revealed that the vaccine had 100% efficacy. The final results of the trial, too, showed the same result. The duration of protection is not known, though a few studies suggest protection up to one year.

So when Ebola struck the Democratic Republic of Congo on August 1, 2018, the decision to use Merck's vaccine, which has not been licensed in any country for clinical use, was taken without much thought as it was the only vaccine that been tested in phase-3 trials. Also, the World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) had in March 2017, recommended that in the absence of a licensed vaccine for Ebola, the investigational vaccine could be used during an outbreak caused by the Zaire strain of the virus.

The vaccine was developed by the Public Health Agency of Canada and licensed to NewLink Genetics. In November 2014, Merck entered into a licensing agreement with NewLink Genetics to research, develop, manufacture and distribute the vaccine.

The vaccine was administered to nearly 29,000 health-care workers and about 94,000 primary contacts and contacts of contacts in Congo under "compassionate use". The vaccination began a week after the outbreak was officially declared.

Efficacious vaccine

Putting to rest the debate on the extent of efficacy during the phase-3 trial, the WHO noted that the preliminary data suggest that the vaccine used during the current outbreaks in Congo was 97.5% efficacious in preventing Ebola infection.

Of the 94,000 people who were vaccinated during the current outbreaks, only 71 developed the disease. Of the 71, only 15 developed symptoms 10 or more days after vaccination. The majority – 57 individuals – displayed symptoms within nine days of vaccination, before the vaccine could fully protect them. It had become clear during the trials that the vaccine needed 10 days to fully protect vaccinated individuals.

There were only nine deaths among the 57 people who developed the disease before the vaccine could be fully protective. In comparison, no deaths were reported among people who developed the disease more than 10 days post vaccination.

More importantly, 54 of the 71 Ebola cases were in high-risk contacts, and only two cases were among the contacts of contacts, thus underlining the effectiveness of the ring vaccination strategy in preventing the spread of the disease. In the ring vaccination strategy, the spread of the virus is curtailed by creating protective rings by vaccinating people based on the risk of infection. The first ring of protection is created by vaccinating everyone who has come in contact with infected persons or their bodies, or has lived in the same house. The second ring – contacts of contacts – comprises neighbours and family members of all contacts.

As a result of delay in detecting and isolating cases and tracing the contacts, the virus continues to spread, and about 80 new cases are reported each week, the WHO said on July 17. The hotspots have been shifting and new cases are being reported from areas that were previously cleared. In May 2019, SAGE cautioned that virus transmission continues to occur in areas where there is difficulty in implementing ring vaccination and that new cases are being reported among unknown contacts.

Third ring

In order to cut the transmission chain, SAGE recommended the inclusion of a third ring of contacts to be vaccinated. Currently available evidence does not support mass immunisation of the population.

There are indications that the epidemic is not going to end anytime soon, and the number of people who need to be vaccinated is bound increase. To avoid any diversion of critical human resources and being in the thick of an epidemic, the Congo health minister has ruled out a clinical trial using Johnson & Johnson's experimental vaccine. This would mean that more Merck vaccines would be needed to end this epidemic. Though Merck intends to double the supply by 2020, vaccine supplies are currently insufficient. The only way to stretch supplies of the vaccine to meet the ever-increasing demand is to use smaller doses.

In May 2019, SAGE recommended that the currently administered dose (1 ml) can be halved to match the dose tested in phase-3 trial in Guinea to protect health-care workers, contacts and contacts of contacts. People in the third ring could be given one-fifth the current dose. Instead of 10, it would take 28 days for the vaccine to confer protection when one-fifth of the current dose is used. But it would provide a "reasonable risk-benefit trade-off for protection," SAGE noted.

Yes we can, indeed we must, restore forests

An outstanding example of reforestation is Philippines

SPEAKING OF SCIENCE

D. BALASUBRAMANIAN

Global warming, largely caused by industrial development and consumer demands, has been causing havoc across the world. Temperatures are shooting up, floods have been ravaging South China and Northeast India, unseasonal rains and, ironically, delayed and poor monsoon rains are experienced. A major solution to mitigate such climate changes is to reduce the levels of greenhouse gases, particularly carbon dioxide, which cause this warming. In an effort to try and limit this warming, many countries across the world are gathering together and agreeing to make efforts to limit the rise in temperature to no higher than 1.5 degrees by the year 2050.

The major way to do so is to increase the number of plants, trees and forests across the world. They all absorb carbon dioxide from the air, and with the help of sunlight and water, produce food (staple for us) and oxygen (which we breathe). And the wood and timber they offer are used by us in buildings and furniture. They are thus justly named in Sanskrit as Kalpataru – the wish-giving tree.

Yet, we kill them: deforestation has been going on decade after decade across the world, affecting the weather as well as the lives of plants, animals, microbes and the livelihood of human tribes that live in forests. The total surface area of our Earth is 52 billion hectares (Ha), and 31% of this has been forest cover. But the huge Amazon forests of South America are being chopped off for commercial reasons. Peru and Bolivia in the western Amazon region are the worst affected by such deforestation; so are Mexico and its neighbours in Mesoamerica. Russia, with forests occupying 45% of its land area, is chopping off trees. Large scale deforestation this kind has contributed to global warming over the years.

What is a forest?

The Food and Agriculture Organization (FAO) defines a "forest" as a land area of at least 0.5 hectares, covered by at least 10% tree cover, without any agricultural activity or human settlement. Using this definition, a group of Swiss and French ecologists have analysed these 4.4 billion hectares of tree canopy that can exist under the current climate. And, excluding existing trees and agricultural and urban areas, there is room for an extra 0.9 billion hectares. Their analysis using the latest ecological methods, was published two weeks ago (Bastin et al., *Science,* 365 76-79, 5 July 2019). Thus, there is the potential climate change mitigation through global tree restoration. They point out that more than 50% of this restoration potential can be found in six countries (Russia, USA, Canada, Australia, Brazil and China). While it is not clear how much of this land is public or private, they confirm that the calculation of 1 billion hectares (>10% tree cover) is achievable.

Happily enough, several group (and governments) in countries, notably Philippines and State government in India (see the report for the Forest Survey of India, and an analysis by Down to Earth) have moved towards more tree plantations. In India with its 7,08,273 sq km land area, 21.54% has tree cover. And between 2015 and 2018, we have added 6,778 sq km. Madhya Pradesh has the largest forest cover, followed by Chhattisgarh, Odisha and Arunachal Pradesh while Punjab, Haryana, UP and Rajasthan have the least. Andhra Pradesh, Telangana, Karnataka, Kerala and Odisha have improved their forest canopy somewhat (<10%). Private groups, notably The Guru Nanak Sacred Forest in Ludhiana, Punjab, the middle-of-the-town forest in the heart of Raipur, the "Afforest" group of Shubhendu Sharma (The Hindu Business line, 3-12-2018) are some notable non-government initiatives. Readers will surely add more. (On an aside, who can forget the centenarian Salumarde Thimmakka, who has planted 385 banyan trees and 8,000 other trees, or Sunderlal Bahuguna of the Chipko movement of Uttarakhand?)

Leading by example

But the most outstanding example of reforestation is Philippines, an archipelago of 7,100 islands, with a total land area of 3,00,000 sq km and a population of 104 million people. Way back in 1900, about 65% of its land mass was covered in forest canopy. Large-scale commercial deforestation continued after that, so by 1987, it was reduced to 21%. The government thereafter committed itself to steady reforestation, and by 2010, the forest covered 26%. It has now introduced a remarkable programme in which it makes it mandatory for each elementary, high school and college student to plant 10 trees before graduating. The sites where they plant and the location-appropriate plant are advised to them; (see<news.ml.com.ph> of *Manila Bulletin*, July 16, 2019). The mover of this idea, Gary Alejano, stressed on the need to utilise the educational system as an avenue for propagating ethical and sustainable use of natural resources among youth to ensure the cultivation of a socially responsible and conscious citizenry.

Here is an excellent example for our Indian students. Your columnist has recommended this model to be added to the National Education Policy 2019, so that we may demand youngsters to follow and gain from the Filipino experiment.

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