

CAPSULE



New evidence

Based on research at White Pond near Elgin, South Carolina, archaeologists present new evidence of a controversial theory – The Younger Dryas Impact Hypothesis – that suggests an extraterrestrial body crashing to Earth almost 13,000 years ago caused the extinction of many large animals and a probable population decline in early humans.



Super vaccine

A team of researchers has found an antibody that protects mice against a wide range of potentially lethal influenza viruses. This has led to the advancement of efforts to design of a universal vaccine that could either treat or protect people against all strains of the virus, including pandemics.

How cotton leaf worm responds to the defence mechanisms of plants

Plant volatiles that attract predatory wasps could be boosting the worm's immunity levels

SHUBASHREE DESIKAN

A new side to the triangular story of interactions among plant, pest and predatory insect emerges as a result of a study carried out by researchers from the National Centre for Biological Sciences, Bengaluru. The team finds a link between the boosting of immunity levels in pest (cotton leaf worm, *Spodoptera litura*) and exposure to plant volatiles, which are aromatic vapours released by the plant when the worm chews the leaves. "This is the first study showing the impact of plant volatiles on cellular immunity of the worm [*S. litura*], causing elevated defense against natural enemies," says Radhika Venkatesan, in whose lab the work was carried out.

Natural triad

Take the example of the trio: cotton plant, the worm and the predator wasp *Bracon brevicornis*. When the worm feeds on the cotton plant's leaves, the leaves release aromatic and volatile vapours into the air. These volatiles waft in the air and attract the



wasps, which harm the cotton leaf worm. Though the adult wasp is an independent entity, the wasp lays its eggs on the skin of the worm, and when the eggs hatch, the larvae feed on the worm itself, thereby ending up killing it. In order to make this possible, the wasp first injects a toxic substance into the worm which immobilises it, so that the wasp can take time to lay its eggs on the skin of the worm.

Another example of such a triangle is the Cabbage worm *Plutella xylostella*, and the wasp *Cotesia vestalis*. In this

case, the wasp injects the eggs into the body of the worm and the eggs hatch inside and feed on the worm as they grow.

The experiment consisted of spraying the cotton leaf worm with plant volatiles and observing its change in immunity levels. "We exposed the [worm] to various plant volatiles for different time durations, then we collected the blood for immunological assays," says Enakshi Ghosh who is a postdoctoral fellow at NCBS and first author of the paper published in *Journal of Chemical Ecology*.

"As we observed that specific volatiles could modulate their immune status, we challenged the cotton leaf worm with its natural enemies – pathogen and parasitoid," explains Dr Ghosh.

Induced immunity

Six plant volatiles such as beta-cimene and linalool were used in the experiment and each had different effects on the immune system of the cotton leaf worm. "In the case of beta-cimene treatment, immune functions were enhanced that helped the worm combat wasp bet-

ter," says Dr. Ghosh. That is, being immune, the worm is not immobilised by the wasp's sting. This prevents the wasp from laying its eggs on the worm. "In the case of linalool exposure, the worms survived better against bacteria," she adds.

"It is interesting that beta-cimene mediated immunomodulation helped the herbivore [worm] survive better against parasitoid-like stress only, while linalool exposure caused increased survival against pathogen," says Dr. Venkatesan. "The elevated defense caused trade-offs like reduced pupal size and adult life-span in these primed larvae compared to controls," she adds.

Some of the questions that are raised by this study include - what happens when the worms are exposed to a mixture of plant volatiles, and whether this immunomodulation is specific to *Spodoptera litura*. "It would be interesting to see if, in the race of co-evolution, there is any mechanism the parasitoids are building to combat heightened herbivore immunity," says Dr Venkatesan.

Stimulating white blood cells helps clear TB bacteria

Potency of TB drugs improved many times when two receptors of the immune cells were activated

R. PRASAD

Instead of using drugs to directly kill TB bacteria, researchers at the Indian Institute of Technology (IIT) Ropar have directly stimulated the immune system to kill the bacteria. This was achieved by using small molecules (ligands) to stimulate two specific receptors (CLEC4E and TLR4) found on the surface of white blood cells (macrophages) to kill the bacteria. The two receptors are copiously expressed on the surface of the macrophages, and activating them help regulate the cell function.

Once activated, the ability of the macrophages to reduce the TB load and eliminate the bacteria gets enhanced through increased autophagy. Autophagy is the body's way of cleaning out damaged cells, in order to regenerate newer, healthier cells.

Through *in vitro* studies,



Effective: Just two doses of rifampicin, along with the small molecules cleared the TB bacteria, says Javed Agrewala

the team led by Javed N. Agrewala from the Biomedical Engineering Department at IIT Ropar first tested the ability of the two receptors to activate the macrophages to kill the bacteria. The macrophages were first infected with TB bacteria and stimulated for 48 hours by activating the receptors using the small molecules. Compared with controls, the stimulated macrophages exhibited increased bactericidal activity.

The enhanced bactericidal activity was confirmed using animal models.

Many firsts

Similarly, the enhanced expression of autophagy-related genes in macrophages was first observed in the lab and confirmed in animal models by IIT Ropar researchers in collaboration with CSIR-Institute of Microbial Technology (IMTECH), Chandigarh.

The specificity of the receptors to regulate macrophage function was tested using inhibitors which block the functioning of the receptors. There was increased survival of the bacteria in the macrophages on inhibiting the receptors.

To reconfirm the role of the receptors in inducing autophagy, the researchers abrogated the autophagy in macrophages and tested the ability of the activated receptors to clear the bacteria in mice models. "The ability to clear the bacteria was absent when autophagy was inhibited. This helped confirm that receptor-mediated elimination of TB bacteria in macrophages was through autophagy," says Prof. Agrewala.

Besides *in vitro* studies and mice models, the activated receptors were found to reduce the TB burden when tested on human macrophages too. The results were published in the journal *Autophagy*.

Compared with controls, the potency of anti-TB drugs – isoniazid and rifampicin – to kill the bacteria dramatically improved when the two receptors were also activated. With rifampicin, the ability to kill the bacteria was seen even at one-tenth of the dose. Greater effectiveness at reduced dosage was seen only when rifampicin was used along small molecules that activated the receptors. Also, the ability to clear the bacteria was achieved with just two doses of rifampicin.

Enhanced action

The enhanced potency of anti-TB drugs when used along with the small molecules that stimulate the receptors was seen in animal models, too. In mice, there was significant reduction in bacteria load in the lungs, liver and spleen compared with controls. The number of granulomas in the lung too decreased.

Even in Guinea pigs, there was significant decrease in

bacterial load and increased efficacy of the drugs to kill the microbes. The lungs and spleen of Guinea pigs treated with small molecules and TB drugs exhibited nearly normal morphology compared with controls.

"The activating the receptors have an immunomodulatory role in reducing both the dose and duration of treatment using anti-TB drugs," says Prof. Agrewala. "Since the receptors only activate the macrophages and do not directly act on the bacteria, there are fewer chances of emergence of drug-resistant strains of TB bacteria."

In mouse and Guinea pig models, there was proliferation of certain T cells that offer protection against TB bacteria. Also, there was significant increase in the number of memory T cells that provide long-lasting protection against TB bacteria thus signifying protection from subsequent infection with TB bacteria.

Astrosat views star formation in jellyfish galaxies

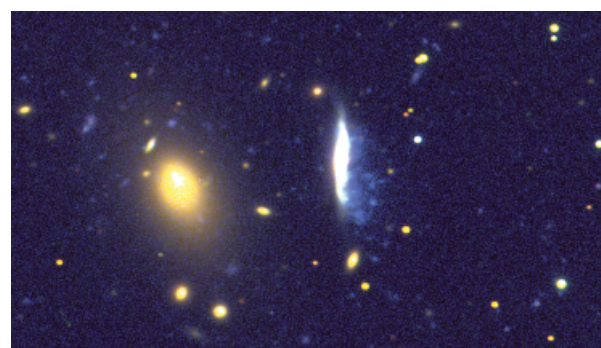
The images were composed using data collected from many telescopes

SHUBASHREE DESIKAN

Observations of a jelly fish galaxy, JW100, by Astrosat using its Ultraviolet Imaging Telescope have thrown up interesting puzzles. These puzzles involve star formation in hostile environments containing X-ray-emitting hot plasma. JW100 is located far away in the galaxy cluster Abell 2626. A recent work describes this analysis and poses the puzzle, vouching for the power of multiwavelength astronomy. The measurements made by the UVIT have been crucial for this work which is to be published in *The Astrophysical Journal*.

Jelly fish galaxies

Jellyfish galaxies are called so because they are shaped like discs that have many tentacle-like arms streaming away from the disc. They are formed when a disc-shaped galaxy rams into a galaxy cluster, which is a dense region containing many hundreds or thousands of galaxies packed into a small region. This can happen when the galaxy is attracted by the gravitational attraction of the cluster. As the individual galaxy rams into the galaxy cluster, the cold gas in its disc interacts with the hot plasma in the cluster. Acting like a strong wind, the plasma in the cluster strips away



Colour composite: This JW100 image is created by combining three images. The red, green, blue colour scheme is assigned to image taken at each wavelength. • KOSHY GEORGE

the cold molecular gas of the disc, causing it to stream behind like tentacles. Unlike usual galaxies that have stars forming in the disc, the jellyfish galaxies have star formation in the tentacles also.

The European Southern Observatory has an international programme led by Bianca Poggianti of Padova Observatory, Italy, to observe 100 such gas-stripping jellyfish candidates using the MUSE Integral Field Spectrograph. This programme is called GASP (Gas Stripping Phenomena in galaxies with MUSE).

Astrosat joins this effort by contributing data from its Ultraviolet Imaging Telescope (UVIT) instrument. "We have already acquired data of many jellyfish galaxies with UVIT and the quality of UV images are amazing," says Koshy George who is work-

ing on UVIT data. Dr. George is currently with Ludwig-Maximilians-University, Munich, Germany and has been working on this since his post-doctoral term at Indian Institute of Astrophysics, Bengaluru.

The jellyfish galaxies' tentacles contain a very hostile environment as they interact with the galaxy clusters that are rich in X-ray emitting hot plasma. "What triggers star formation in these environments is a puzzle," says Dr George.

Multiwavelength study

The jellyfish galaxies are being observed by various telescopes each sensitive to different parts of the electromagnetic spectrum. The star formation in JW100 was gauged using observations of the visible (H-alpha) spectrum using the MUSE in-

strument of the Very Large Telescope in Chile and the ultraviolet imaging using the UVIT instrument of Astrosat.

Puzzling behaviour

One of the jellyfish galaxies that UVIT has collected data about is JW100. This galaxy is unusual because of its orientation. We see it edge-on so that the gas stripping can be seen perpendicular to our field of vision. It is also different from other jellyfish galaxies. In other jellyfish galaxies, star formation is estimated by the H-alpha observations matches with that calculated from ultraviolet observations.

In JW100, there is higher contribution from H-alpha but much less from ultraviolet in the tail. This could mean that other mechanisms such as shocks or thermal conduction from the hot plasma of the galaxy cluster is contributing to H-alpha emission from these regions. "Jellyfish galaxies experience several mechanisms at the same time. Many of these happen over various timescales. The paper attempts to throw light on some of these mechanisms in JW100, using data which trace various components," says Annapurni Subramaniam, director of Indian Institute of Astrophysics who was not involved in this work.

Now, machine learning-based model can determine if skin cancer has spread

Six machine learning models were used to validate the genomic signatures

R. PRASAD

Using the expression of 17 key genes (messenger RNAs) it is now possible to distinguish primary and metastatic cutaneous melanoma, which is the most common type of skin cancer. While 11 of the 17 genes have already been reported by other studies for cutaneous melanoma, it is for the first time that the potential role of remaining six genomic signatures in classifying samples as either primary or metastatic skin cutaneous cancer has been made.

The 17 genomic signatures, which were identified by a team led by Prof. Gajendra P.S. Raghava from the Indraprastha Institute of Information Technology (IIIT), New Delhi, have high accuracy – over 89% – in discriminating metastatic from primary skin melanoma. These signatures also have high sensitivity (in case tumour is metastatic), and high specificity (in case the tumour is primary). The results were published in the journal *Scientific Reports*.

Unlike in the case of primary skin melanoma, people with metastatic cutaneous melanoma have reduced survival rate and higher mortality rates. It therefore becomes important to be



Discriminative: The messenger RNA expression profile was the strongest predictor of metastasis, says Harpreet Kaur.

able to identify and classify skin cutaneous melanoma as either primary or metastatic so correct therapeutic strategies can be chalked out and survival rates improved in patients.

Messenger RNA

Six machine learning models were used to study and validate the genomic signatures. They used expression profile of messenger RNA, micro RNA and methylation profile for discriminating tumour as primary or metastatic. "We found the messenger RNA expression profile was the strongest predictor of metastasis. The mRNA expression profile performed better than micro RNA and methylation



Preventable: Controlling hypertension, diabetes could have halved the number getting stroke, heart attack. • GETTY IMAGES

Heart disease risk high in rural area near Chennai

Two-thirds of people in the rural area who developed cardiovascular disease died

SPECIAL CORRESPONDENT

Contrary to the general notion, cardiovascular disease is becoming an important preventable cause of events (heart attacks and stroke) and death even among the rural population in India, a study shows. The study involved 5,641 adults aged 25-64 years living in a rural area near Chennai and followed up for nearly eight years. There were 96 deaths – 79 from heart attacks and 17 from stroke. There were 59 adults who suffered but did not die from heart attack and stroke.

The study, which began in 2005, was carried out in five villages in Tiruvallur district near Chennai. While baseline data were collected in 2005 and two follow-up surveys were carried out in 2008-2009 and 2013-2015.

The study was carried out by a team led by Dr. Prabhdeep Kaur from the Chennai-based National Institute of Epidemiology (ICMR-NIE). The results were published in the journal *BMJ Open*.

Hypertension, which is a huge risk factor for cardiovascular disease, was prevalent in 21.6% of men and women, while tobacco use was high both among men (nearly 35% smokers) and women (43% smokeless tobacco). Central obesity was also high both among men (20.2%) and women (26.4%). Alcohol use was high among men (28.6%), while diabetes, which was self-reported, was 4% in both men and women.

"Two-thirds of people who developed cardiovascular disease died. This could have been prevent-

ed. The risk factors were causing two times or more risk of cardiovascular disease," says Dr. Kaur. "Reducing tobacco use and treating hypertension and diabetes and keeping them under control could have halved the number of people getting stroke or heart attack."

Hypertension was a risk factor for both men and women. In the case of men, smoking turned out to be a big risk factor while it was central obesity and diabetes that were risk factors for women.

"With cardiovascular disease becoming an important preventable cause of death in rural areas, there is a compulsion to focus our attention on rural areas too," says Dr. Kaur. "Early diagnosis, treatment and regular follow-up to ensure control of hypertension and blood sugar will help people through their lifetime."

Dr. Kaur does agree that getting people to achieve control of hypertension and blood sugar is a huge challenge. With an estimated burden of 200 million people in India, hypertension is the most important noncommunicable disease risk factor. Many studies have shown that reducing hypertension by 20 mm mercury in people aged 4-69 years can help achieve a 50% reduction in coronary heart disease.

However, as per a May 2019 study published in *PLOS Medicine*, in India, only about 45% of people with hypertension were even aware of their diagnosis, hardly 13% were under medication and a paltry 8% had hypertension under control.

goring different stages of metastasis. For instance, it can tell if the tumour has spread to lymphatic nodes, which is an early stage of metastasis. Also, it can tell if the cancer has spread to distant parts of the body, which is a late stage of metastasis, says Dr. Sherry Bhalla from IIT Delhi and the other first author.

Six machine learning models were tested and used for classifying the tumour as either primary or metastatic. Of the six models, one model – Support Vector Classification with Weight (SVC-W) – has an accuracy of nearly 89.5%. The researchers have further integrated the major prediction models in the webserver called CancerSPP that will help clinicians in classifying cutaneous melanoma as primary or metastatic using RNA sequence data, microRNA and methylation expression data. "It will also help in knowing the different states of metastatic samples," says Kaur. "The analysis module in the CancerSPP webserver will provide information on the role of each of the important genes in various stages of metastasis and whether the expression of a gene is up-regulated or down-regulated."