

CAPSULE



Living on poison
Arsenic is known to be poisonous, but recently, researchers have identified micro-organisms in the Pacific ocean that breathe arsenic. In the study, the team analysed DNA from the seawater, noting two pathways to gain energy from arsenic-based molecules. Biologists think this is remnant from Earth's early history. The study was published in *PNAS*.



Violent birth
A violent collision of two neutron stars took place 4.6 billion years ago and may have been the source of several heavy elements on Earth such as gold, platinum and uranium, a new study finds. According to the study, published in *Nature*, nearly 0.3% of such elements were created in this collision. The study adds to existing knowledge on origin of our solar system

IIT Kanpur identifies novel molecule to control hyper inflammation

Hyper inflammation compromises pathogen-clearing ability, also destroys the tissues surrounding the inflamed area

R. PRASAD

Researchers at the Indian Institute of Technology (IIT) Kanpur have identified and characterised a novel small protein molecule that can effectively control inflammation leading to better treatment outcomes. In contrast, inflammation control by molecules that are undergoing clinical trials may not be optimal due to inherent drawbacks. The work was done in collaboration with the University of Queensland.

Hyper inflammation
While some amount of inflammation at the site of infection is required for effective clearance of pathogens, too much inflammation compromises pathogen-clearing ability. Hyper inflammation also destroys the tissues surrounding the inflamed area leading to inflammation disorders such as sepsis, inflammatory bowel syndrome, rheumatoid arthritis and psoriasis. A small protein (C5a) that is a part of the innate immunity (immediate defence against pathogens that have never been encountered before) gets activated when a pathogen enters the body. The C5a



Multitasking molecule: Unlike the molecules now being tested, our peptide molecule also reduces the amount of IL-6 being released, say Arun Shukla (right) and Shubhi Pandey.

protein then binds to a particular receptor (C5aR1) found on the surface of certain cells such as macrophages and neutrophils to begin the process of inflammation and pathogen clearance. Neutrophils are already present in the body and circulate in the blood. Once the small protein binds to the C5aR1 receptor found on neutrophils, there is increased

migration towards the site of infection leading to hyper inflammation. At the same time, binding of the small protein to the receptor on macrophages reduces the amount of a pro-inflammatory cytokine called interleukin-6 (IL-6) that is released, which is desirable to overcome inflammatory symptoms. Therapeutic agents now under-

going clinical testing prevent the C5a protein from binding to the receptor found on neutrophils leading to reduced migration of neutrophils to the site of infection. Hyper inflammation is thus prevented. However, it has the opposite effect on interleukin-6 release. Unlike the C5a protein, the drug candidate molecules do not reduce the amount of IL-6 being released thereby causing more inflammation.

Role of IL-6
“There is more inflammation when the amount of IL-6 at the site of infection is more. So it is desirable to reduce the amount of IL-6 being released to overcome the inflammatory symptoms,” says Arun Shukla from the institute's Department of Biological Sciences and Bioengineering. He is one of the corresponding authors of a paper published in the *Journal of Biological Chemistry*. The small protein molecule identified by IIT Kanpur researchers addresses the shortcomings seen with the drug molecules now undergoing clinical testing. The drug molecule that IIT Kanpur team used for this study is already known to bind to the C5aR1 recep-

tor. But its effects were not characterised in term of IL-6 release and neutrophil migration. “Our peptide molecule binds to the C5aR1 receptor found on neutrophils and reduces their migration to the site of infection. And unlike the molecules now being tested, our peptide molecule also reduces the amount of IL-6 being released,” says Prof. Shukla. Under *in vitro* conditions, the combined effect may lead to reduced inflammation. “The molecule only reduces and not blocks neutrophil migration. There should be sufficient inflammation at the infection site to clear the pathogens,” says Shubhi Pandey from IIT Kanpur and first author of the paper. The peptide molecule identified by the team is smaller than the C5a protein so the binding to the receptor is weak. “So we have to use higher concentration of our synthetic peptide to achieve better results. Future work would be to increase the strength of binding by improving the molecule so that less concentration is needed,” Prof. Shukla says. The team plans to carry out animal studies in future to measure the therapeutic potential of the molecule.

Why is northeast India drying up rapidly?

Decreasing monsoon rainfall is associated with natural changes in the subtropical Pacific Ocean

ASWATHI PACHA

Northeast India, one of the wettest places on the Earth has been experiencing rapid drying, especially in the last 30 years. Some places which used to get as high as 3,000 mm of rain during the monsoon season have seen a drop of about 25-30%.

A team of researchers from the Indian Institute of Tropical Meteorology, Pune, and Assam University set out to understand whether this decline is caused by anthropogenic activity or is it part of natural changes. The results published recently in *JGR-Atmospheres* show that the decreasing monsoon rainfall is associated with natural changes in the subtropical Pacific Ocean.

Pattern of fluctuations
“We found that changes in the Pacific decadal oscillation (PDO) – a pattern of fluctuations in the ocean, particularly over the north Pacific basin – are mainly associated with this declined rainfall,” explains Abida Choudhury, a Ph.D. scholar at Assam University and the first author of the paper. “Just like El Nino/La Nina in the tropical Pacific, PDO has a signature for a longer time (on the decadal scale) in the sea surface temperatures and its interaction



Root cause: Rainfall reduction over the last 36 years is associated with natural phenomena. *S.S. KUMAR

with the atmosphere, which in turn affects the northeast Indian summer monsoon.”
Natural and manmade
The team used observed rainfall and sea surface temperature data for the period 1901-2014 for the study. The results show out that the reduction in rainfall during a major part of the last 114 years may be associated with global man-made factors, while the trend during the last 36 years is associated with natural phenomena. “Only about 7% of the rainfall in this region is associated with local moisture recycling, which means that anthropogenic activities can affect only this small percentage. So we concluded that the recent rapid drying is a part of interdecadal variability of monsoonal rainfall which is strongly associated with the PDO,” says

Subodh Kumar Saha from IITM, Pune. The researchers note that this study can be used to predict the monsoon rainfall over the northeast region on a decadal time scale using Pacific Ocean region data. Previous studies have found that a dry spell may be preceded by a wet spell, so the researchers warn that “change in land cover and deforestation could potentially result in more natural disasters, for example, flash flood, landslides from torrential rains, and damage to crops and biodiversity”. “Policymakers should take these long-term predictions into account while planning construction of dams, power plants, etc. to prevent loss of property,” adds Mahen Konwar, the corresponding author of the study from IITM, Pune.

IIT Delhi 3D prints human skin

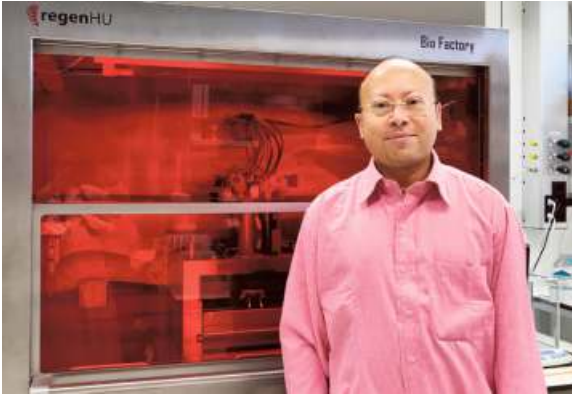
The model can reduce and even replace testing cosmetics on animals

R. PRASAD

Researchers at the Indian Institute of Technology (IIT) Delhi have successfully 3D bioprinted human skin models that have certain anatomically relevant structural, mechanical and biochemical features similar to native human skin. The bioprinted skin produced in the lab by the team is already being used by ITC Ltd for experiments.

The bioprinted skin model will have wide applications in testing cosmetics. It can also reduce and probably even replace testing on animals. It can also be used for testing dermatology drugs on human skin and at a future date even help in testing drugs for personalised medicine.

Testing on animals
The European Commission has prohibited testing finished cosmetic products and cosmetic ingredients on animals. It even prohibits marketing of finished cosmetic products and ingredients in the European Union. The skin is composed of two important layers – the inner dermis (made of fibroblasts) and the outer epidermis (keratinocytes, melanocytes). The junction between the two layers is not flat but is undulatory or wavy. The undulatory morphology is important as it provides biochemical cues



Commercialised: The bioprinted skin produced in the lab by the team is already being used by ITC Ltd for experiments, says Sourabh Ghosh

and mechanical support to the epidermis layer, provides structural stability to the skin by making the two layers adhere to each other, and not allow cells to cross the junction. Unlike the currently available tissue-engineered skin equivalents, the team led by Sourabh Ghosh from the institute's Department of Textile Technology was successful in creating this wavy junction in the bioprinted skin model. The results were published in the journal *Bioprinting*. The study was funded by ITC Ltd. The undulatory junction was designed using 3D CAD and 10 layers of dermis were constructed through bioprinting followed by eight layers of epidermis. “We designed the pattern so that both layers fit and the interface had a wavy pattern,” says Prof. Ghosh.

Silk bioink mixed with fibroblasts was used for growing the dermis, while bioink mixed with keratinocytes and melanocytes was used for growing the epidermis.
No shrinkage
The bioprinted skin also retained the original dimension without any shrinkage for up to three weeks. Traditionally, collagen used for developing skin constructs start shrinking within a few weeks thus affecting the morphology. Testing on such skin constructs therefore cannot be carried out beyond one week. The bioink containing the cells are deposited in a criss-cross pattern leaving gaps in between. “The keratinocytes in the epidermis were seen migrating and filling the pores. This type of migration, which was very clear and striking, and

cellular self-assembly recapitulate wound healing-like situation in native skin,” says Prasad Admane from IIT Delhi and first author of the paper. The keratinocytes in the epidermis differentiate and form into four distinct layers. “We studied three proteins – fibronectin, cytochrome 1 and 14 – that are biomarkers of keratinocyte differentiation. They are produced in the bioprinted skin though the amount was comparatively less than native skin,” he says. Most importantly, gene and protein expression analysis showed 60% similarity in gene expression between bioprinted and native skin. “We identified 56 proteins expressed in bioprinted skin which play an important role in skin development, extracellular matrix organisation and keratinocyte differentiation,” says Abhishak C. Gupta from IIT Delhi and co-author of the paper. “We will now explore the possibility of growing hairs on the bioprinted skin,” says Dr. Gupta. Prof. Ghosh's team has already developed a 3D construct for hair follicle structure in collaboration with ITC Ltd. “Our goal is set up a start-up to focus on developing different diseased skin conditions to test different drug molecules in patient-specific manner,” he says.

Robot from IIT Madras checks pipelines for leakage

Endobot is a low-cost solution to identify faults and stealthy connections

SHUBASHREE DESIKAN

At a time when water scarcity pervades many urban centres, it is important to ensure that water being transported through pipes is not lost through leakages. In an attempt to address this issue, researchers from IIT Madras have developed a robot to check pipelines for leaks and other faults. Named Endobot, this robot is to be marketed by an IIT Madras incubated startup, Solinas Integrity, founded by the researchers. Quite often, pipes that transport water suffer from low maintenance and neglect which causes them to develop leakages. These often go unnoticed except when the water seeps to the surface. Periodically, water pipelines are dug up, and this may bring leaks to notice, but this is left to chance and is a costly process at best. Water is also lost through connections that have not been



Mobile eye: The electrically-powered robot runs on four wheels connected using a conveyor belt and is tethered at one end.

sanctioned officially. Endobot is presented as a solution that can identify these faults and stealthy connections, at a low cost. The electrically-powered robot looks like a small tank, runs within the pipe on four wheels connected using a conveyor belt. It is

tethered to the entry point outside the pipe. This construction allows it to run over tough terrain within the pipe without stalling. “Endobot is about 6 inches high and can study any pipe having a diameter more than 8 inches. Since water pipes typically have

The robot captures videos and transmits a live feed to the base at the entry point. It also uses laser-based techniques to examine the pipes as it moves.

an inner diameter of at least 15 inches, it suits the purpose well,” says Prabhu Rajagopal from the Centre for Nondestructive Evaluation in IIT Madras, where the robot was developed. He is also a non-executive director of the company. “As the robot, which is electrically powered, runs through the pipes at about 15 cm per second, it captures videos and transmits a live feed to the base at the entry point. It also uses laser-based techniques to examine the pipes as it moves,” explains Vishwa Sai Prathyusha, who is the Chief

Technology Officer of the company and alumna of IIT Madras. These feeds are conveyed to the user's computer and may be analysed later using software developed by the team. “Of course, the robot has noteworthy features, but also the software and tools for analysis developed by our team give us a major advantage over competition,” adds Ms Prathyusha.
Additional sensors
Any technology goes through phases of development and Endobot is no exception. “As a next step, we plan to add more sensors - ultrasonic and electromagnetic - which can help us find out whether the pipes develop corrosion or cracks on the outer side,” says Krishnan Balasubramanian, a director of the company. He is a chair professor in the Mechanical Engineering department of IIT Madras and head of the Centre for Nondestructive Evaluation. “As of now, not many people

are working on such small robots,” says Prof. Rajagopal. He acknowledges, however, that there is competition at an international level. “Having small robots is a novelty even there, and open source electronics is driving this here,” he adds. So while such robots may not be out of reach of international companies, they still have not focused on such solutions. “Recently, the Indian government and corporations and municipalities are increasingly looking at outsourcing operation and management of water resources to private players, and we are in a sort of Goldilocks zone,” says Prof. Rajagopal. The team has already completed one set of trials within IIT Madras campus, where many pipes and installations are nearly 40 years old. They are now in talks with various urban corporations to allow them to try out the robot. Some municipalities have expressed interest in pilot studies using the robot.