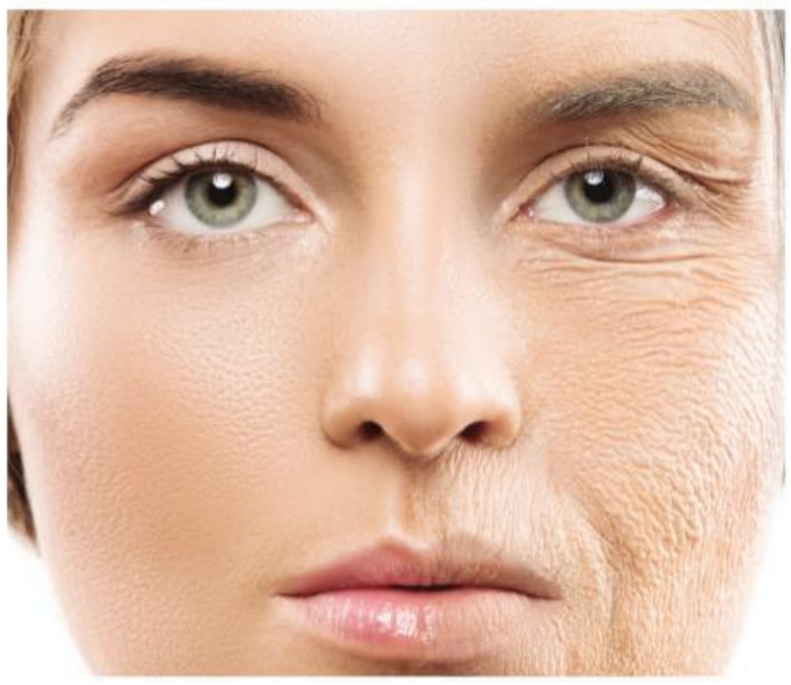
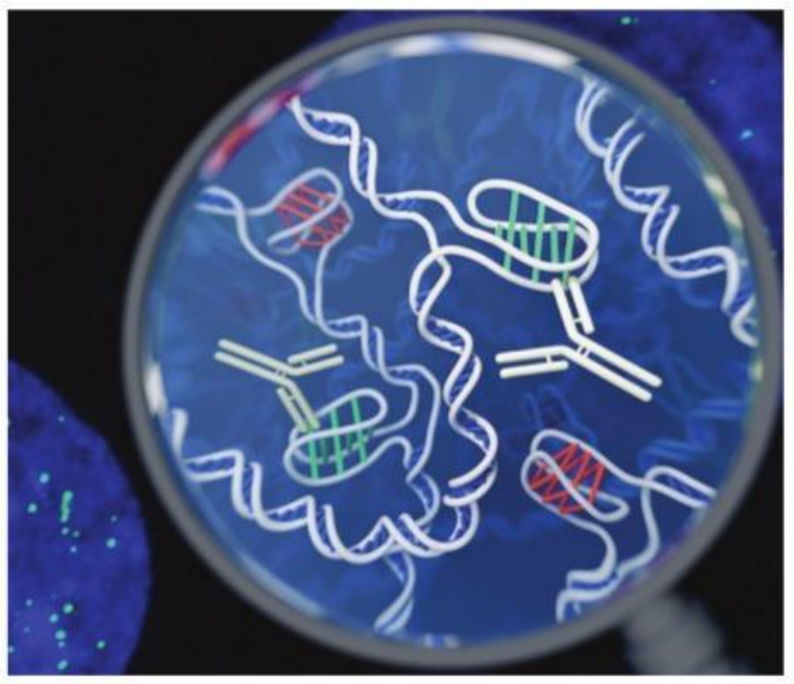
The 'Peter Pan' protein

Scientists have reported a step forward in their understanding of how cells age and it might help find a way for extending human life

S ANANTHANARAYANAN





It is the process of change, and growing old, that makes us aware of the passage of time. And without the awareness of time, human development, science, art and civilisation would have been different.

In a paper in the Proceedings of the National Academy of Sciences, Jiarui Song, Dhenugen Logeswaran, Claudia Castillo-González, Yang Li, Sreyashree Bose, Behailu Aklilu, Zeyang Ma, Alexander Polkhovskiy, Julian JL Chen, and Dorothy E Shippen, from A&M University, Texas, Arizona State University, China Agricultural University, Beijing and Skolkovo Institute of Science and Technology, Moscow, report a step forward in understanding the mechanism of aging of living things.

The step is about a component of the DNA of cells, which plays a role in making it possible for cells of living things to divide and renew themselves. This component was first discovered in algae in stagnant water and has been found to be there in the DNA of most living things. And the team writing in PNAS has unravelled a part of how it works in the case of plants. As the longest lived things on the planet are plants, the understanding may help find a way to extend human life too.

Growth and reproduction happen as a result of cell division, where a living cell splits, to become two cells that are just like the original one. The copying takes place thanks to the DNA molecule in the nucleus of the cell, a long, chain molecule, which carries both the blueprint for the construction of the cell and a means by which it can replicate itself. The replication is possible because the DNA consists of a pair of complementary strands. When the two strands separate, each one can draw the elements of its partner strand from the surroundings and regenerate the original.

A problem with the affinity of the parts of the DNA strands to form chemical combinations, which enables replication, is that the strands could get elongated, or that a DNA could form a link with another DNA. The result of such events would be that there could be no viable daughter cell and division would not work. The DNA has thus evolved to have a specific form at its extremities, to mark and announce the end of the molecule, and the DNA itself contains the machinery for the generation of the extremity form.

The extremity form, called the telomere, is a series of repeats of the units of which the DNA is built. And the telomere is formed with the help of an enzyme, or an agent that promotes the chemistry in living things, called telomerase, which contains the template to build the series of units in the telomere.

An early discovery about the nature of aging, however, was that there is a limit to the number of times a cell could replicate itself. The reason was later found to be that at each replication, the daughter DNA was not the same as the parent DNA, but there was a shortening of the telomere. After a series of replications, the telomere ceased to be effective and so was the process of cell division. Cell growth was hence retarded, functions of the organism began to fail and the organism was said to be aging.

Fortunately, Blackburn, Greider and Szostak, who made the discovery in the 1980s (and received the Nobel Prize in 2009), also discovered an enzyme, telomerase, which has the capacity or retard, or even reverse the breakdown of telomere. Telomerase contains the template that enables the synthesis, from the surroundings, of the specific DNA segments that make up the telomere. Alternately, telomerase provides a platform that allows the enzymes that promote the building of the DNA to copy the full length, without missing the end portion, and hence maintain the health of the reproducing cell.

The action of telomere and telomerase are now seen as central to the processes of cell death or cell proliferation. As the large part of an organism's cells does not replicate a great many times, most cells are not affected by telomere attrition. This, however, is not true of stem cells, which replace cells that are destroyed, continuously, by injury or disease. These become less effective with increasing age and the organism is less capable of recovering from injury or illness. In fact there are a number of diseases like anemia, diseases of the skin and respi-ration, which are caused by defects of telomerase.

While finding ways to promote telomerase may thus appear like a solution to the problems of aging, it is seen that enhanced levels of telomerase can have the reverse effect of allowing cancerous cells to replicate without hindrance. Understanding the mechanism of telomerase action is thus important to design therapies that can work without adverse side-effects.

The authors of the paper in PNAS note that although the telomerase function is the same over most living species, this is not true of the operative component of telomerase, the part, which helps DNA synthesise the telomere during cell division. Discovering the nature of this component, called the telomerase RNA, or TR, has been challenging, the authors say, as the structure and working of TR differs widely over the species, ranging from single-celled creatures in ponds to vertebrates.

The team went about the quest by experiment and analysis of telomerase in cells of the plant, *Arabidopsis thaliana*, a model plant species. The study, the paper says, revealed that despite the variability of the TR molecule, there were two specific structures within TR molecules which remained the same over species. The current study has improved over earlier studies and identified a form of TR, in *Ara-bidopsis thaliana*, which can help maintain telomere and also combine with a subunit of telomerase to reconstitute telomerase activity.

The study has also revealed comparable features in the TR in plant cells with that of single-celled pond scum and of vertebrates. These suggest an evolutionary route that was followed in the progress from single-celled creatures to plants to more complex life forms. This could be traced for greater understanding of how persistence of telomere could be promoted or blocked.

The process of telomere attrition, which is necessary to prevent uncontrolled cell proliferation, is the reason that living things must age and die. Animal lifetimes are thus rarely longer than a few decades. Bristlecone pines and the Yew trees, on the other hand, live for thousands of years. Understanding how the plant world deals with aging may show us a way to extend the human lifetime, or the quality of life, at any rate.

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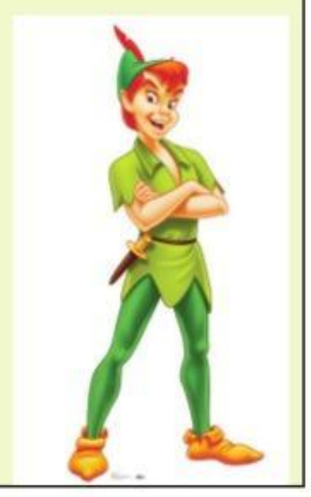
IF AGING WERE OVERCOME



Peter Pan, a character created by the Scottish playwright JM Barrie, is an impish, young boy who has the gift of flight and never grows old. His adventures take place in Never Never Land, a name that implies that things are timeless.

But many aspects of our world would change if such a thing were possible. The need to overcome and discover; the nature of relationships and property, the fabric of society as we know it, depends on the fact that things age and people die. Also the need to procreate, the wonder of renovation and the hopefulness of a second chance.

It would appear that immortality is contrary to nature's laws!

PLUS POINTS

'Redesigning' photosynthesis

Scientists have solved the structure of one of the key components of photosynthesis, a discovery that could lead to photosynthesis being "redesigned" to achieve higher yields and meet urgent food security needs. The study, published today in the journal *Nature*, reveals the structure of cytochrome b6f — the protein complex that significantly influences plant growth via photosynthesis.

Photosynthesis is the foundation of life on Earth providing the food, oxygen and energy that sustains the biosphere and human civilisation. Using a high-resolution structural model, the team found that the protein complex provides the electrical connection between the two light-powered chlorophyll-proteins (Photosystems I and II) found in the plant cell chloroplast, which convert sunlight into chemical energy.

Lorna Malone, the first author of the study and a PhD student in the University of Sheffield's department of molecular biology and biotechnology, said, "Our study provides important new insights into how cytochrome b6f utilises the electrical current passing through it to power up a 'proton battery'. This stored energy can then be then used to make ATP, the energy currency of living cells. Ultimately this reaction provides the energy that plants need to turn carbon dioxide into the carbohydrates and biomass that sustain the global food chain."

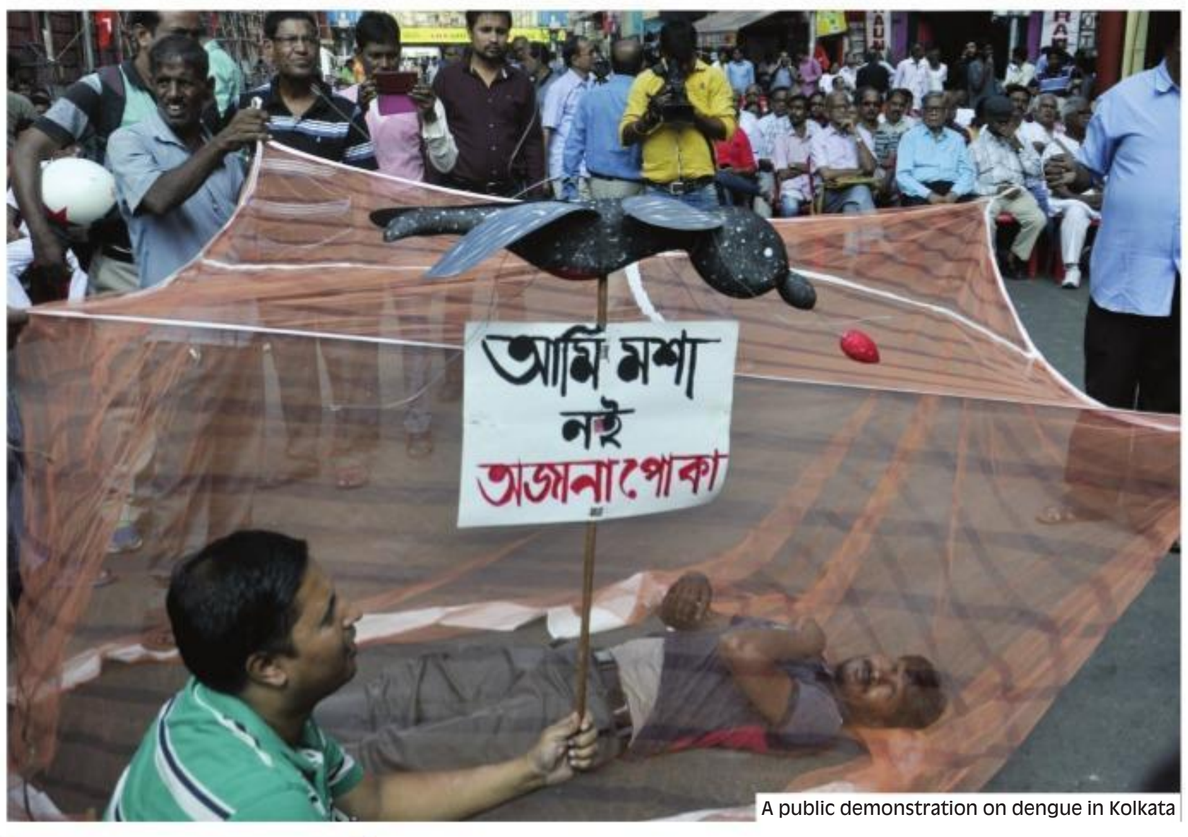
The high-resolution structural model, determined using single-particle cryo-electron microscopy, reveals new details of the additional role of cytochrome b6f as a sensor to tune photosynthetic efficiency in response to ever-changing environmental conditions. This response mechanism protects the plant from damage during exposure to harsh conditions such as drought or excess light.

Matt Johnson, reader in biochemistry at the University of Sheffield and one of the supervisors of the study said, "Previous studies have shown that by manipulating the levels of this complex we can grow bigger and better plants. With the new insights we have obtained from our structure, we can hope to rationally redesign photosynthesis in crop plants to achieve the higher yields we urgently need to sustain a projected global population of nine to 10 billion by 2050".

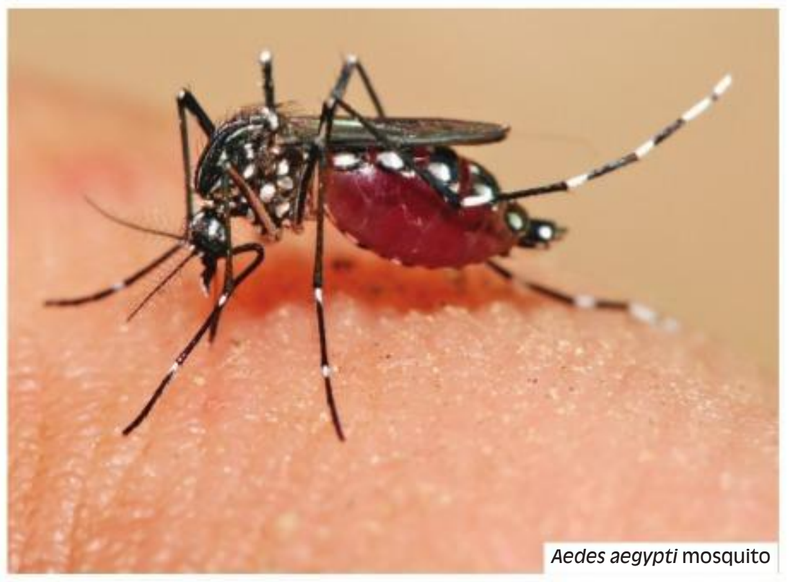
Researchers now aim to establish how cytochrome b6f is controlled by a myriad of regulatory proteins and how these regulators affect the function of this complex.

A civic challenge

Here's the science behind how dengue fever affects the human body



A public demonstration on dengue in Kolkata



Aedes aegypti mosquito

TAPAN KUMAR MAITRA

The viral nature of dengue fever was ascertained in 1907 by P Ashburn and C Craig. The virus measures from 30 to 40nm. After adaptation to the body of mice by successive intra-cerebral passages, it grows readily in a chicken embryo *in vitro*. Two types of viruses have been discovered. The virus contains thermostable and thermolabile antigens. The latter causes a group complement-fixation reaction with the viruses of yellow fever and Japanese and West Nile encephalitides.

The virus persists for a period of five years at -70°C and in a dried state and remains viable for 2 months in a patient's serum at room tempera-ture. It dies very quickly on exposure to light and is non-resistant to heating. Weak bile dilutions inactivate it in five minutes whereas ultraviolet rays and a 0.05 per cent formalin solution destroy it.

The virus is poorly pathogenic for laboratory animals. Adapted strains cause paralysis and death in albino mice and virusaemia in guinea pigs. Infection of Macaca rhesus monkeys results in a mild form of the disease.

The virus possesses toxic activity. It affects the neurons in the cerebrum and spinal cord and causes degenerative changes in the cells of the liver, kidneys, and heart. It produces haemorrhagic lesions in the endocardium, pericardium, gastric and intestinal mucosa, peritoneum, central nervous system, muscles and skin. Deep disorders are revealed in the small blood vessels (swelling of the endothelium, perivascular oedema, and infiltration by mononuclear cells).

The sources of infection are sick people. The virus appears in the patient's blood during the latter 24 hours of the incubation period and remains there for three or four days of the febrile period. Infection occurs through the bite of *Aedes aegypti*, *Aedes allopictus*, and *Aedes scutellaris* mosquitoes. At a temperature of 22°C, the mosquito becomes capable of transmitting the virus in eight to 12 days after a meal of the patient's blood. At 16°C the causative agent does not develop within the mosquito's body. The mosquito remains infective for a period of 174 days.

The incubation period in dengue fever varies in duration from 2.5 to 15 days, lasting five to eight days on average. Quite frequently the disease has a sudden onset with chills, headache, severe pains in the joints, muscles and eyeballs and a high fever (39-41°C). Erythema may be observed in some patients. A remission occurs in one to four days. The temperature drops and the body becomes covered with profuse perspiration. This is followed by a second attack, which is characterised by an elevation of temperature and the presence of the same symptoms as in the first attack. A maculopapular or scarlatina-like eruption appears on the body, lasting not longer than three or four days. The duration of the disease is four or five days.

During epidemics, mild and severe forms of the disease are encountered along with the typical form. They are marked by coma, delirium, convulsions, and mucopurulent diarrhoea. The mortality rate is low and the patient usually recovers. The disease leaves an immunity, which lasts from two to six months.

Diagnosis rests on clinical, epidemiological, and laboratory findings. The virus is isolated from the blood in the first days of the disease by intracerebral inoculation of mouse sucklings (not over three days of age), and the complement-fixation reaction and the neutralisation test are performed.

There is no specific therapy. Symptomatic remedies are used — large amounts of liquid are given to drink, a 10 per cent glucose solution is in-jected intravenously, and amidopyrine, acetylsalicylic acid, preparations of iron, and vitamins C, B1, and B2 are given.

Dengue fever occurs as an endemic disease in regions with a tropical and subtropical climate. Prophylaxis comprises isolation of patients, prevention of access of the vectors to them, extermination of mosquitoes, and protection from their bites. Quarantine measures are enforced to prevent the spread of the infection to countries free from the disease. Measures of specific prophylaxis are still being elaborated.

The writer is associate professor and head, department of botany, Ananda Mohan College, Kolkata

First ever 'cyborg'

British scientist Peter Scott-Morgan refused to accept his fate after being diagnosed with motor neurone disease in 2017 and decided to extend his existence using technology. The 61-year-old announced he was planning to upgrade both his body and brain to become "the most advanced human cybernetic organism ever created in 13.8 billion years".

And last week the roboticist emerged from 24 days in intensive care to reveal that "Peter 2.0 is now online". "All medical procedures now complete and a huge success," he told his followers online. "My mini-ventilator keeping me breathing is a LOT quieter than Darth Vader's. All speech is synthetic but at last sounds like me again. Long research road ahead but in great spirits. (sic)"

The process has included a series of operations to insert a feeding tube directly into his stomach, a catheter directly into his bladder and a colostomy bag directly on to his colon, to allow him to deal with feeding and toilet problems. He also underwent a laryngectomy to avoid the added danger of saliva potentially entering his lungs — which he described as trading his natural voice for "potentially decades of life".

Scott-Morgan now relies on synthetic speech and has developed a life-like avatar of his face, designed to respond using artificially intelligent body language. He has also explored eye-tracking technology to enable him to control multiple computers, undergoing laser eye surgery to give him perfect vision at 70cm — the distance from his computer screen.

The independent