Eliminate message, not messenger


Credit:Muhammad Mahdi Karim - GNU Free Documentation License, Version 1.2

Dengue fever may now be stopped in the mosquito gut before it can be transmitted to humans

S ANANTHANARAYANAN

Antibodies against many pathogens, which affect humans, are grown in animals and then transferred to humans. We now have a case of antibodies that arise in humans, and are transferred to mosquitoes to keep mosquitoes free of the dengue virus.

Anna Buchman, Stephanie Gamezi, Ming Li, Igor Antoshechkin, Hsing-Han Li, Hsin-Wei Wang, Chun-Hong Chen, Melissa J Klein, Jean-Bernard Duchemini, James E. Crowe Jr, Prasad N Paradkar, Omar S Akbari, from the University of California and Tata Institute for Genetics and Society, San Diego, California, Institute of Technology, Pasadena, National Tsing Hua University and National Health Research Institutes, Zhunan, Taiwan, Australian Animal Health Laboratory, Geelong, VIC, Australia and Vanderbilt University Medical Center, Nashville, Tennessee, describe in the journal, *PLOS-Pathogens,* their work of modifying the mosquito genome to make mosquitoes resistant to all four variations of the dengue virus. A small number of these dengue-resistant mosquitoes could then transform the mosquito population, worldwide, to be dengue-resistant, say the authors.

The interest, of course, is not the health of the mosquitoes. The interest is human health, for mosquitoes are not affected by dengue, they are the carriers of dengue. And very effective carriers at that, as 50 per cent of the world's human population is now at risk. There are 390 million documented cases of dengue fever in a year, the paper says, and the estimated economic losses amount to 40 billion USD. There are no specific methods of treatment or prevention and the sole commercially available vaccine, which is only partially effec-tive, often cannot be used because it increases rather than mitigate the risk with some groups of people.

The main carrier of the dengue virus is *Aedes aegypti*, or the yellow fever mosquito, and it is the vector that transmits dengue fever, chikungunya, Zika fever, Mayaro and yellow fever viruses, and other disease agents. The mosquito originated in Africa but has spread out, and is now found in tropical, subtropical and temperate regions throughout the world.

It is difficult to control its breeding, as it develops resistance to insecticides and adopts evasive behaviour, the paper says. There is hence need to think of other means, particularly genetic engineering, either to reduce mosquito populations or to reduce their ability to carry dengue. There has been some success in developing such strains of mosquitoes, but for them to be effective, it is necessary to release the strains in large numbers and frequently. This is laborious and expensive, the paper says.

Researchers have therefore sought methods where the genetic modification of a few mosquitoes can rapidly spread into an entire population. This is achieved through a genetic engineering device known as a gene drive, where the probability of a gene in an organism being inherited by its offspring is altered. Usually, a gene is present in two versions in the pair of chromosomes and either one has a 50 per cent chance of being inherited by the descendent.

The gene drive technique is an insertion that cuts the chromosome at a specific place, and in the process of repair of the cut, the gene drive version, which consists of the drive and the altered gene, is copied. The cell then has two copies of the gene drive sequence, and the altered gene as well as the gene drive will occur in every descendent. The result is very rapid replication and the altered gene is soon present in a whole population.

While the gene drive is an effective way to spread a useful modified feature through most of the infecting population of mosquitoes, the work done so far has been able to target only one, or two, of the four major strains of the dengue virus, the paper says. As dengue epidemics affect large numbers and infection by one strain followed by infection by another can result in severe disease, it is necessary that the genetically altered mosquitoes block all kinds of the dengue virus.

Finding a broad-spectrum antibody, one that acts against all forms of dengue, in the mosquito, would thus be promising. Such an antibody has been synthetically developed for the mosquito to resist the parasite that causes malaria, the paper says, but not one that targets a virus. Nevertheless, antibodies against the dengue virus have been isolated in humans infected with dengue. Laboratory studies have shown that these antibodies were able to deal with the four versions of the dengue virus and were effective against two of the versions when used in a mouse model.

In the current study, the paper says, the human antibody has been engineered for the yellow fever mosquito to express a genetic feature, based on the human dengue antibody, which is effective against all four versions of the dengue virus. The female of the yellow fever mosquito ingests the virus when she targets an infected human for blood, to sustain her protein needs for reproduction. The virus then multiplies and enters the body of the next human that the mosquito bites. When the mosquito expresses the engineered antibody, however, the antibody gets active as the dengue virus enters, and can block its reproduction. The virus is thus prevented from reaching all parts of the mosquito, particularly the mosquito saliva, which it injects into human subjects while feeding. The mosquito is hence prevented from transmitting dengue to humans when she bites again.

The paper describes how the human antibody, which is capable of neutralising all four version of the dengue virus, was modified so that it was compatible with mosquitoes and retained its effectiveness against dengue. Experiments were then carried out to verify that blood meals of infected blood did not lead to midgut infection of the mosquitoes, and that the procedure was effective with all four variations of the dengue virus.

The next assay was to see what effect the engineered antibody had on the fitness of the mosquito. This was to ensure that the genetically altered mosquitoes would be able to reproduce and spread their genetic content to progeny, for dissemination in the mosquito population. They assessed several parameters, like the time for development from the larva stage, male and female fecundity and fertility, male mating success and longevity. The results were that there was no significant effect on fitness and the ability to confer dengue resistance to progeny in good numbers.

"The strategy we describe here provides an efficient 'cargo' gene that can be coupled with a gene-drive system to reduce or eliminate the risk of dengue transmission by mosquitoes," the paper says. There is even a feature where the mosquito would keep in step with evolution of the dengue virus in reaction to being blocked by resistant mosquitoes. The paper goes on to say that the same methods, of synthesising genetic solutions, coupled with gene-drive systems, could render mosquitoes resistant to other viruses, like those that cause Zika and chikungunya.

The writer can be contacted at response@simplescience.in

What is dengue?

- Dengue is a mosquito-borne viral infection.
- There are four types of the virus, which means that it is possible to be infected four times.
- The global incidence has grown dramatically. About half of the world's population is now at risk.
- Dengue is a leading cause of serious illness and death in some Asian and Latin American countries.
- There is no specific treatment for dengue/severe dengue. Early detection and access to proper medical care lowers fatality rates to below one per cent.
- Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.
- The mosquito vectors of dengue breed in and around human habitation. Their eggs can remain dry for months and hatch when in contact with water.
- Dengue prevention and control depends on effective vector control and sustained community involvement.

Extinction on the cards?

Bushfires have reshaped life on Earth before and they could do it again

MIKE LEE

The catastrophic bushfires raging across much of Australia have not only taken a huge human and economic toll, but also delivered heavy blows to biodiversity and ecosystem function.

Already, scientists are warning of catastrophic extinctions of animals and plants.

Humans have seldom if ever seen fires like these, but we do know that wildfires have driven mass extinctions and reshaped life on Earth at least once before — when the asteroid strike that led to the demise of the dinosaurs sparked deadly global firestorms.

Australian biodiversity

Australia is one of only 17 "megadiverse" countries. Much of the species richness is concentrated in areas torched by the current bushfires.

While some mammals and birds face elevated extinction risk, things will be even worse for small, less mobile invertebrates (which make up the bulk of animal biodiversity).

For example, the Gondwana Rainforests of New South Wales and Queensland have been badly affected by the fires. These World Heritage listed forests are home to a rich diversity of insects and a huge range of land snails, some restricted to tiny patches.

The bushfires have been rightly described as unprecedented, and extinctions can play out over an extended period. The full gravity of the impending catastrophe is not yet clear.

Fire has driven extinctions before

There have been greater burnings in the deep past, as we can see from the fossil record. They provide strong and disturbing evidence of how fire drove widespread extinctions that completely reshaped life on Earth.

Around 66 million years ago, a mass die-off called the Cretaceous-Paleogene extinction event famously put an end to the reign of dinosaurs (sparing only birds). The event erased 75 per cent of the planet's species.

Scientists agree these extinctions were primarily caused by an asteroid about 10 kilometres wide crashing into present-day Mexico, blasting a huge crater the size of Tasmania.

A nuclear winter followed the impact, as fine particles thrown up into the atmosphere blocked sunlight for years. The extended frozen darkness killed ecosystems from plants and phytoplankton upwards.

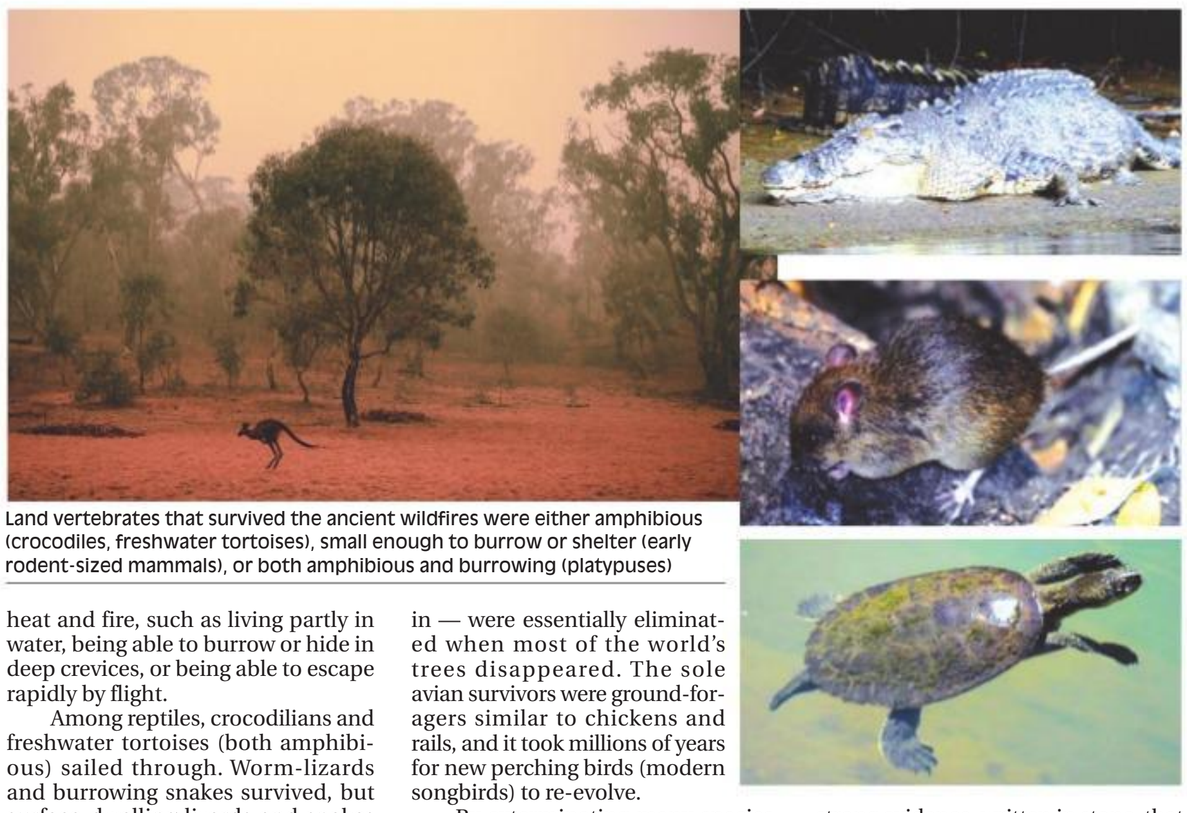
Recent research shows that global wildfires were likely also an important driver of extinctions, at least for life on land.

The asteroid blasted flaming debris across the atmosphere. Massive deposits of soot found in the fossil record at this precise time suggest most of the Earth's forests went up in smoke, though these cataclysmic calculations remain controversial.

Only animals that could escape fire survived

The fossil record of land-dwelling animals — especially reptiles, birds and mammals — attests to the deadly efficiency of what has been dubbed the dinosaur firestorm. The nature of the victims and survivors is very relevant to current events.

The land animals that made it through the extinction all lived in ways that could confer resilience to heat and fire, such as living partly in water, being able to burrow or hide in deep crevices, or being able to escape rapidly by flight.


Land vertebrates that survived the ancient wildfires were either amphibious (crocodiles, freshwater tortoises), small enough to burrow or shelter (early rodent-sized mammals), or both amphibious and burrowing (platypuses)

Among reptiles, crocodilians and freshwater tortoises (both amphibious) sailed through. Worm-lizards and burrowing snakes survived, but surface-dwelling lizards and snakes were hard hit.

Among mammals, platypus-like monotremes (aquatic and burrowing) clung on, as did tiny rodent-like placental mammals (able to burrow, or hide in deep crevices), but all large placental mammals died. And while at least some birds survived, all their large, earth-bound, dinosaurian relatives perished.

In fact, it appears that every land-dwelling animal species larger than a domestic cat was ultimately doomed, unless it could swim, burrow or fly.

Even these abilities did not guarantee survival: they merely gave creatures a slightly better chance. For instance, pterosaurs could fly well, but still went extinct, along with most bird species.

Recent research suggests perching birds — which need forests to live in — were essentially eliminated when most of the world's trees disappeared. The sole avian survivors were ground-foragers similar to chickens and rails, and it took millions of years for new perching birds (modern songbirds) to re-evolve.

By exterminating many species, and doing so highly selectively, the global wildfires (alongside other effects of the asteroid impact) totally restructured Earth's biosphere.

What about the current fires?

The recent rampant bushfires are regional rather than global (like in Australia, the Amazon, Canada, California, Siberia), and are burning less land cover than the worst-case dinosaur firestorm scenario.

Yet their long-term extinction effects could also be severe, because our planet has already lost half its forest cover due to humans. These fires are hitting shrunken biodiversity refuges that are simultaneously threatened by an anthropogenic cocktail of pollution, invasive feral species, and climate change.

The ancient catastrophe provides strong evidence, written in stone, that firestorms can contribute to extensive extinctions, even among large vertebrates with large distributions and high mobility.

It also shows certain types of organisms will bear the brunt of the impact. Entire guilds of similar species could vanish, severely impacting ecosystem function.

It took millions of years of regeneration and evolution for our planet's biosphere to recover from the nuclear winter and wildfires of the asteroid impact. When a new world order eventually emerged, it was radically different — the age of dinosaurs gave way to the age of mammals and birds.

The writer is professor in evolutionary biology (jointly appointed with South Australian Museum), Flinders University, Australia. This article first appeared on www.theconversation.com

PLUS POINTS

New embryo

Scientists have created a new embryo they hope will contribute to a return of the near-extinct northern white rhino.

The artificially made embryo is just the third viable example. All three were created *in vitro* by combining frozen sperm taken from male rhinos, before they died, with eggs harvested from one of the two remaining northern whites in the world, which are both female. Sudan, the last known male of his subspecies, died in 2018 aged 45.

Researchers now plan to implant the three embryos they have created into surrogate southern white rhino females, a species which is more numerous. "It's amazing to see that we will be able to reverse the tragic loss of this subspecies through science," said Kenya's wildlife minister, Najib Balala, in a statement released by the Kenya Wildlife Service and conservationists from Kenya, the Czech Republic, Germany and Italy.

The three embryos were made from eggs taken from Fatu, Sudan's granddaughter. Fatu lives at Kenya's Ol Pejeta conservancy with her mother, Najin — under 24-hour armed guard "Now the team will make every effort to achieve the same result for the 30-year-old Najin before it is too late for her," said Thomas Hildebrandt with the Leibniz Institute for Zoo & Wildlife Research in Germany.

Scientists created the first two embryos last autumn. They hope to build a herd of five northern white rhinos that could eventually be returned to the wild, a process likely to take decades. Kenya, which was home to as many as 20,000 rhinos in the 1970s, now has about 650 mostly black rhinos. The northern white subspecies was once found in a number of countries in eastern and central Africa. Conservationists estimate that there are about 18,000 of its southern white cousins left in the world, and 5,000 black rhinos.

Southern whites have already made their own remarkable comeback, thanks to the efforts of rangers dedicated to protecting them. In 1897 there were only about 50 left on the planet. The number rose past 400 in the 1950s and in the mid-1960s the subspecies was upgraded from critically endangered status.

Rhinos are hunted for their horns, which are used as a carving medium and in traditional Chinese remedies, without any evidence for their effectiveness.

The independent

Oldest solid material

Researchers said last week that new techniques have allowed them to identify the oldest solid material ever found on Earth. The stardust, formed five to seven billion years ago, came from a meteorite that fell to Earth 50 years ago in Australia, they said in a paper published in the journal *PNAS*.

It came down in 1969 in Murchison, Victoria state, and scientists from Chicago's Field Museum have possessed a piece of it for five decades. Philipp Heck, curator of meteorites at the museum, examined pre-solar grains, which are bits of stardust that become trapped in meteorites, making them time capsules of the period before the sun was born. "They're solid samples of stars, real stardust," Heck said in a statement.

When the first stars died after two billion years of life they left behind the stardust, which formed into the block, which fell to Earth as the meteorite in Australia. Although researchers first identified the grains in 1987 their age could not be determined. But Heck and other colleagues recently used a new method to date these grains, which are microscopic in size. They are from silicon carbide, the first mineral formed when a star cools.

To separate the ancient grains from the relatively younger ones, scientists crushed fragments of the meteorite into a powder. Then they dissolved it in acid, which left only the pre-solar particles. "It's like burning down the haystack to find the needle," says Heck.

AFP