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Science in focus

Chain Reaction against Zika, malaria and Co.

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The gene-bomb

chain reaction against Zika, malaria and Co.

Mosquitoes are the worst enemies of humanity. They transmit diseases like malaria, Zika, dengue or yellow fever and kill as indirectly each year about half a million people. The release of genetically modified animals brought so far not given the expected results, but that could change now.

By Michael Long

Maybe mosquito-transmitted virus epidemics by CRISPR / Cas could be prevented. But the social consequences of the new genetic engineering are practically incalculable (picture alliance / dpa / NNS / Landov)

Everything green. Everywhere overgrown nature. My story begins in Cuyabeno nature reserve in Ecuador, a tropical paradise. In the giant trees colorful birds and countless insects. Were it not for the wet heat that bothers me, and those damn mosquitoes. I know: Some transfer of malaria, yellow fever, dengue and recently Zika. I could well do without them. The world would be better off without them.

Omar Akbari, University of California Riverside

Original German text: [Google](#)[Drucken](#)[Contribute a better translation](#)

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Genetic chain reaction

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A surefire way against mosquitoes

Manipulated mosquitoes

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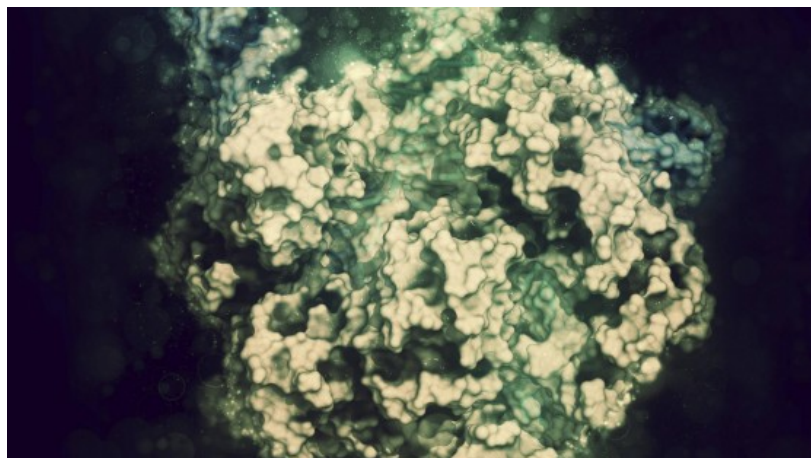
the world, for example, *Aedes aegypti*, the Zika supercarrier, this is now possible. A new technique turns off vital genes of the mosquito and spreads itself in a way. . chain reaction. Sometime breaks the whole population together - and you have eradicated this way ".

It sounds tempting, but also threatening. Man gets a new tool with which it can control the evolution. He can decide which types he wants and what not prefer. Whole ecosystems can be transformed from now on.

I flew from Ecuador to California. Here, researchers, which could make my wish come true. On the campus of the University of Riverside, the dry heat is unbearable. Until the Mojave Desert, one of the hottest places in the world, it is not far. Mosquitoes live only in one place - tucked away in the laboratory of the young professor Omar Akbari. He is building on his team and has a modern Insectarium furnishings:

"As you can see, we have installed two self-closing doors and now enter the first room. The doors are made of stainless steel and are completely sealed so that no insects out or come in."

CRISPR / Cas could exterminate all mosquito species



The new CRISPR / Cas9 technique, entire insect populations are genetically manipulated (imago stock & people)

Behind the second door lurks one of the greatest enemies of humanity: *Aedes aegypti*. Loosely translated: The Unpleasant from Egypt. Called also yellow fever mosquito, dengue mosquito or Egyptian tiger mosquito. Easily recognizable by the bright stripes. Akbari:

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With genetic engineering against malaria

Beautiful new Genetic
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Should we wipe mosquitoes off the face of the earth?
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t8we-wipe-mosquitoes-off-the-face-of-the-earth&usg=ALkJrhgZtKNIHvaTtHt8N51TyyL], The Guardian

Editing to end malaria
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t8an-end-to-malaria&usg=ALkJrhgC4KfxGOHPWBsscl8], Harvard Magazine

Panel Endorses 'Gene Drive' Technology That Can Age Entire Species
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t8academies-sciences-gene-drive-technology.html&usg=ALkJrhgmbmMIQ_OF], New York Times

The genes that I called (Turbo for evolution)
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t8ins-erbgut-die-gene-die-ich-rief-1.2867148&usg=ALkJrhMu2ppS7dpyTGT1C], Süddeutsche Zeitung

Emerging Technology: Concerning RNA-guided gene drives for the alteration of wild populations
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t85J17xB6Qq6QJ], elife Sciences

A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector *Anopheles gambiae*
[https://translate.googleusercontent.com/translate_c?act=url&depth=1&hl=en&ie=UTF8&prev=t8], Nature Biotechnology

The mutagenic chain reaction: A method for converting heterozygous

"I blow a little CO2 in this case inside. Just a little. And then come the mosquitoes in driving.

Can you see it? The females look for a blood meal. They react to the CO2 in the air we breathe. They want my blood. "

A mosquito has left the box. Somehow it has passed through the surrounding network in the space. For such cases Omar Akbari has a mosquito zapper - a sort of mini-tennis racket with electric stringing:

"If a mosquito flying around the room, she receives by zapping an electric shock. So now she's dead and lying on the floor."

A total of nine larger boxes has built in his insectarium Omar Akbari. Therein hundreds of mosquitoes. Here the scientists testing a new superweapon. He injected under the microscope genes in the tiny eggs of the mosquitoes. They are just visible to the naked eye just.

New note when he genetically engineered a mosquito, it shall supply heredity further in the reproduction of the entire generation. Not only from and common to randomly as in nature, but always. Later in well air-conditioned small office with a large mug of tea told me Omar Akbari the principle:

"It's a technology that we outsmart the Mendelian rules. In sexual reproduction, a gene normally inherited half of the offspring. Many genes disappear there again. Gene Drive ensures But that all children receive this particular gene. heredity spread so explosively from around the way. We can thus destroy one species or give this species a desired genetic trait. "

Gene Drive means as much as "gene-drive" or "gene-swing". A German word for it, there is not. I like best the term "gene-Turbo". Because genes Drive gives genes extra strength and ensures that they spread quickly and thoroughly. Almost explosively. One could also say martial: There is a "gene-bomb".

Because the possible implications are enormous. Gene Drive could be used so that the females gradually become extinct and only surviving male. If millions of males fall on fewer and fewer females, the population eventually collapses. Other concepts put on in the fertility of the animals. If the reproduction is disturbed, the animals are doomed.

to homozygous mutations
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 , Science

Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi
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Safeguarding genetic drive experiments in the laboratory
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 , Science

Opinion of the Central Commission for Biological Safety (CCBS)
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 for classifying genetic engineering for the production and use of higher organisms with recombinant genes-Drive systems

The Gene-drive idea is not new. For decades, researchers have tried to start the Turbo or to detonate the bomb. But the methods were complicated, the successes meager and unconvincing. Only after 2012, everything changed with a new genetic engineering techniques called CRISPR / Cas9 says Akbari:

"Today we speak quite differently about Gene Drive. CRISPR / Cas lets us see the concept with fresh eyes. So far lacked the tools. But now we can easily install a photocopier for genetic material in living organisms and implement as many previously failed ideas. We not change more individual creatures but entire populations. "

The new technique works: CRISPR is a kind of viewfinder consisting of the biomolecule RNA that tracks every site in the genome targeted. The enzyme Cas9 works like scissors. It cuts the genetic material exactly where it leads CRISPR. Nearly every day genetic engineering lab uses these CRISPR / Cas toolbox, Omar Akbari.

By changing its mosquitoes with CRISPR / Cas, it starts the gen Turbo. He manipulates the eggs of mosquitoes, and then it starts:

"After fertilization, the following occurs: The manipulated ovum produced the first tools The CRISPR Finder performs Cas9 scissors to a particular site in the genetic material of another nucleus, in this case, the sperm cell, where the DNA double strand is cut and thus.. natural gene destroyed. For example, a female fertility gene.

In its place, the copying machine builds a copy of their own blueprint. Now both sets of chromosomes in the embryo possess - that of the mother and from the father -. The gene Turbo The inheritance rate for the turbo is not 50 but more than 99 percent. Impressive."

Slowly I understand: A genetic copying machine that copies itself. And always in the same place. A position in the genome that occurs in every individual of a particular species. There destroys or alters a natural Gen. Gene Drive spreads itself with every reproduction and weakens both the biological species in which it multiplies. Brilliant.

On the idea of the young Professor Omar Akbari came by an article in the journal Science. There reported developmental biologists from San Diego on a genetic chain reaction in flies. Omar Akbari had his research topic found.

The mutagenic chain reaction the genetic material of all offspring can be manipulated

Behind the journal article put the group of Ethan beer. His research at the University of California at San Diego - Located just two hours' drive from Riverside. Towards the Pacific. My next goal. I meet Ethan beer in his small office with a cockatoo on his shoulder.

The Cunning fellow has already picked a decent hole in the shirt of the professor. A wayward bird.

Ethan Beer is an animal lover. Birds he likes rather than insects. As a research object he has selected a small fruit fly "Drosophila melanogaster". To German: The tauliebende Schwarzbäuchige:

"Little guy. The kind flies that you find in the supermarket on a pineapple."

In the laboratory, there are only dead flies or ova. The animals reproduce elsewhere: In a secured special building. For me banned. Because there have some fly a genetic Turbo. A fly, leaving the space could conquer the world with their genes:

"We use plastic tubes in a box in a box in a box. And the stand in a high-security building on the other side of the campus. You have to five secured doors to get in there. A very safe place."

The team led by Ethan Bier had nothing with Gene Drive in mind. The discovery was accidental, and how it happened: As in many other laboratories in the world tried Ethan beer graduate student Valentino Gantz 2014 new genetic engineering modular CRISPR / Cas9 from reports beer:

"Valentino had the idea to change the genetic makeup of the fly so that always wear both partners chromosomes, the maternal and the paternal, the same genetic mutation. Thus, each gene mutation is in the genome before twice and comes in living things always to the fore. The facilitates research when both chromosomes always have the same state. "

What was previously impossible or difficult, managed easily with CRISPR / Cas9. Soon both partners chromosomes contributed thus the same genetic information. That in one fell swoop, all descendants of the flies were manipulated was the researchers clear only later. When they

saw that all the flies after a few weeks had red eyes in the chest, their mouths hung open. They called this process: mutagens chain reaction. Almost like the nuclear chain reaction, I think. Once triggered, unstoppable. With the chain reaction in the nuclear reactor that had nothing to do, appeased Ethan Bier, but Saki, the Kakadu is all excited:

"The mutagenic chain reaction is named after the polymerase chain reaction PCR. A laboratory method with which DNA can reproduce any size. And now we have built a genetic copier in living organisms. So after PCR now MCR, that was the idea."

The term "genes Drive" unused Valentino Gantz and Ethan beer first. But they soon became clear: They had an idea realized that haunted other researchers for decades:

"If a blonde person marries a dark-haired, then usually all children are dark-haired, because the gene for dark hair is dominant. Only in the next generation reappear single blond children. This does show the Mendelian rules. The chain reaction are suddenly all descendants blond, in the first generation, in the second and so on. All blond. forever. "

Gene Drive gives genes momentum. Individual genes are powerful and eliminate the genetic diversity of nature. Once released, they are unstoppable.

"Even if people do not like mosquitoes, they are a form of life on Earth"



*Helper of WHO in São Paulo after the outbreak of the epidemic in February 2016.
Zika For WHO it comes in controlling epidemics transmitted by mosquitoes by no less than the future of the world.*

(Imago / Xinhua)

My thoughts digress. I imagine how hundreds of mosquitoes - released from a box on the shore - buzz on the Cuyabeno River. In its interior a time bomb. Your heredity spread from generation to generation like a plague, conquer the region, the country, the continent and ultimately the world. Chain reaction. And then: Buff. The end of the species, inevitable.

"Is humanity ready for this responsibility?" asks also Ethan beer. He knows that Gene Drive could help to defeat diseases like malaria and Zika. The chain reaction could save millions of lives. And yet it was not an easy decision for him, he concludes our conversation:

"Even if the people mosquitoes do not like, they are a form of life on earth and I personally see this as follows:.. Although we humans have countless species extinct But that is exactly the shape of the human arrogance with which I have nothing to would have to do. "

Dear Ethan beer would genetically defuse a dangerous for man kind, rather than eradicate. Manipulation takes destruction. Looking for concepts he got in touch with the leading specialists mosquito California: Anthony James. I see him in a laboratory building on the sprawling campus of Irvine, a city on the edge of metropolitan Los Angeles:

"Probably more mosquitoes live in my laboratory than in the whole city."

In fact: Behind the first security door already buzzing around some. The animals there is apparently able to leave their mosquito prisons. Somehow they have passed through the first door into the workspace.

Behind the second door, it's muggy and loud. Thousands mosquitoes - sometimes in empty coffee cups, encircled by fine networks - or in larger former popcorn boxes. Anthony James takes a box from the shelf. The mosquitoes are about five millimeters in size. They belong to the genus "Anopheles". In German: The Useless. Some of them - Anopheles gambiae and Anopheles stephensi - known as malaria vectors. But the animals in the laboratory are guaranteed free of malaria, the Lord of mosquitoes insured:

"If you examine mosquitoes, you will find some groups that transmit the malaria parasite well, and others that do less well. As we explored their genetics, we found genes that greatly affect this ability for disease transmission."

In his scientific colleagues Anthony James enjoys an excellent reputation. For over 30 years he pursued doggedly one goal: the fight against malaria vectors. For a long time it was difficult for him to come to research funds. But he kept going. And he finally succeeded to breed mosquitoes that could not transmit the malaria parasite. In large-scale tests in Mexico he set the animals free. You should displace the disease-carrying counterparts:

"Everything spoke for it. It should have worked. But many proved more complicated than expected. Then came CRISPR / Cas, and we changed our plans. And suddenly it happened very quickly."

James' mosquitoes possessed genes with which they could defend themselves against malaria pathogen. What was missing was a method for reliable distribution of these genes in the mosquito world. With the help of colleagues from San Diego, the anti-malarial genes now receive the necessary impetus:

"We have the system tricked -. And CRISPR / Cas9 programmed to the scissors cuts at a certain point of mosquito DNA and genes Drive installed at this point In addition, we have genes that prevent the transmission of malaria These genes. builds the repair system of the cell is also at this point - on both chromosomes. "

strengthen Through gene modification the defense system of mosquitoes: The alternative to extinction



Transmits heaps diseases: the yellow fever mosquito.

(picture alliance / dpa / James Gathany / CDC)

Anopheles can survive, albeit genetically modified. The new property, the defense system against malaria, is inherited as a chain reaction - transfer rate over 99 percent instead of 50 percent. In the laboratory, it works. Anthony James sees the realization of his life's dream closer. He hopes to prove through his research a service to mankind. An ecologist sees may be different, I think, and going back to Riverside.

On the university campus there is still boiling hot. In the heat of the last days even the aphids had fallen dead from the tree, told me Mark Hoddle at a cup of tea. The zoology professor directs the Center for the Study of invasive species in California:

. "Invasive species are a serious problem for California, we have now determined: Each year, nine new species can be down here, many of them insects 20 percent develop into pests - in agriculture, but also in nature, where man.. does not intervene. "

Only too happy would Mark Hoddle some of immigrant pests off again. And what are aphids in California, are further south - in Central and South America, but also already in Florida - mosquitoes of the genus Anopheles or Aedes.

Originally, these mosquitoes are from Africa. They would not only be human protection, but practiced conservation eradicate in America. In this respect for Mark Hoddle no problem. What prevents him to cheer, is the method of mosquito eradication. Genetic engineering:

"That sounds like a great idea. And in the lab everything is working fine. The problem begins when the genetically modified mosquitoes are released into the environment. Then they are the competition of wild mosquitoes exposed."

In fact, the first field trials with genetically modified mosquitoes brought so far only partial success. Malaria Free mosquitoes for a time spread well, only to be ousted by malaria vectors, and that those from outside the test region again. The GM mosquitoes are simply not competitive. By this will not change anything of the genes Drive, said Mark Hoddle:

"The real test will be in the field instead. Before large field trials have taken place, can not predict what will happen. Only then will show whether the new mosquitoes really can displace wild-type populations."

The gene Turbo supposed to distribute the foreign genes, I object. Each penetrating from the

outside mosquito would also be changed by the chain reaction. I would like to know: What if? As the eradication of individual mosquito species could affect their predators? What if Gene Drive drives foreign genes across the ocean to the mosquito native to Africa? Then a local population would be affected. All questions that Mark Hoddle can not answer or wants. I need to see: Gene Drive is too new. So far, no one has scientifically deals with possible environmental consequences.

it was very similar that went forth before me with Anthony James. He kindly answered all the questions, but speculate disliked James:

"Something Biological might still playing in that could stop the spread of genes, the experiments in the laboratory and the models tell the computer:.... It works very well now we have to make larger and longer experiments from something very small things into something big"

What happens to the Gene-Drive genes in nature, is difficult to predict

What in the laboratory went very quickly, will take years in the field. From small to large boxes. Then too, enclosed with nets outdoor cages. And at some point: The release on a small island, later on a larger island, perhaps Hawaii. Only then you will know the changes in the species composition. If other insects migrate? Are birds, amphibians and fish find new prey? And so on. And another question arises: What happens to the Gene-Drive genes when they skip in other ways? For mosquito specialists Anthony James there are many contingencies to consider. And some of it has been considered:

"If we CRISPR / Cas tailored for a mosquito species and the genes arrive somehow at random into a butterfly. This so-called horizontal gene transfer is really extremely rare. But even if it happens, the butterfly can not do anything with these alien genes, and that is the end of the story. the concern for horizontal transfer are in my view unfounded. "

Anthony James looks thoughtful. He admits that he can not predict everything. Nevertheless, he wants to try it. It's about his life's work, the fight against malaria and other diseases that are transmitted by mosquitoes. Of course, he would like to know as much as possible before getting started. He and other researchers have repeatedly asked the experts for discussion. But it remains still in the research community. Few speak out.

Scientists from Boston and the team from San Diego have now developed concepts into a kind

of reverse-Gene-Drive. The idea: If the chain reaction gets out of control, then it must be another chain reaction that can stop them. An anti-genes-Drive, an antidote. Anthony James is not convinced:

"When my first engagement is not working as expected, then I should make another similar procedure? If then do what I expect? If I do not have the first chain reaction really shows through, I should be careful better no second unleash. Dear and intervene if need with insecticides. Much more important is good preparation. we must not go too fast, if we do not know what's coming. "

Evening in a motel I think back to the nights in the Cuyabeno nature reserve. Absolute darkness. No artificial light. For the forest lies there full of sound. The buzzing of mosquitoes somehow belongs to. A world without mosquitoes would be safer, but also poorer. Nature as a theme park. Wilderness without teeth, I really want this?

With Gene Drive can not make money



The mosquito control by insecticides such as DDT here in South Africa is much more profitable for the industry as a sustainable solution by Gene Drive - independently of any reason to doubt the Genetic Modification (epa / afp / Alexander Joe)

When the first genes Drive occurs in nature for use, is completely open. In addition to researchers from California scientists at Harvard University in Boston and pushing from Imperial College London towards practice.

For Anthony James remain two problems. Firstly: The financing. The industry has no interest in

Gene Drive. This allows not make money - unlike malaria medications or insecticides. Therefore, the scientists negotiated with the World Health Organization. He also needs the consent of the people in the affected areas:

"There are people who say:... It is important to preserve the species in its original form, but if you live in a country where malaria or yellow fever every year thousands of people killed, they would think differently Can we the victims really the technology withheld? this is about a balancing of values. We provide tools, and the local people have. I'll decide not to make that decision for them. "

Who should decide? On the flight home I read the quote of another researcher, Kevin Esvelt of Harvard University. He puts it this way: ". Our company has never been faced with a technology that affects one and all in such an extent"

It said Bernhard Schütz and Karim Cherif
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