Oxitec's GM Mosquitoes - The Solution Against Dengue?

Biology Term Paper

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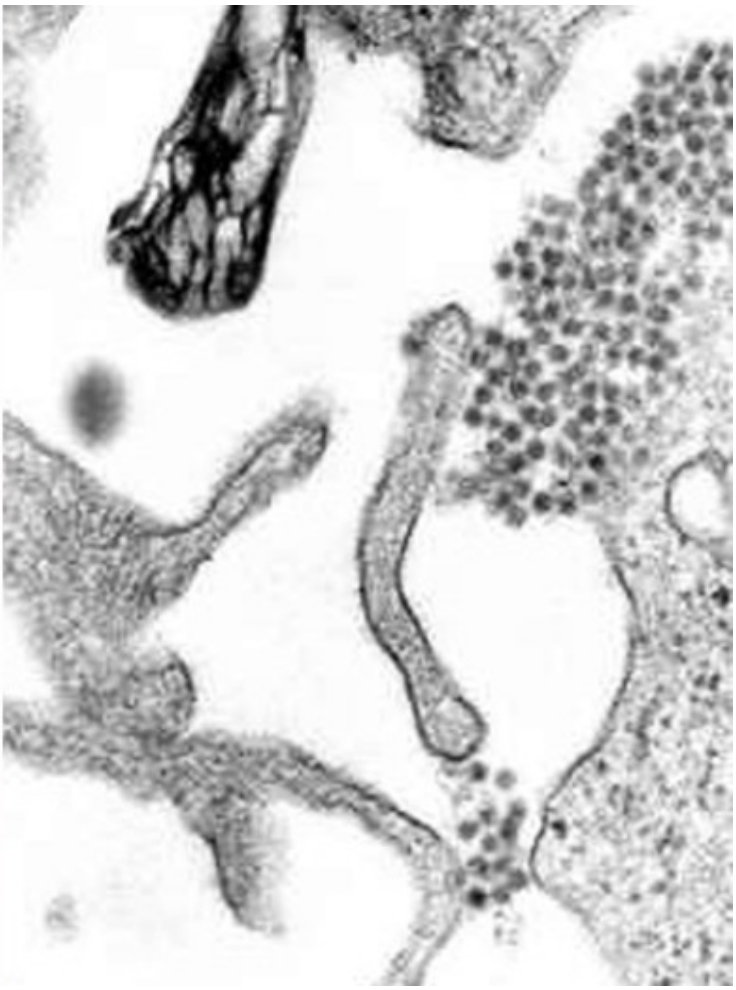

November 2014 – February 2015, Class 4G, P. Ruggle, Gymnasium Kirschgarten

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1. Preface

1.1 What was our motivation to work on the topic?

Dengue fever is a serious worldwide problem, especially in Brazil and the rest of South America. Every year 50 to 100 million people get infected and about 20'000 die.[1]

One of the big problems with dengue fever is that there is no medication against it, and so far there is no vaccination against it.

While searching for a suitable topic we stumbled across the fight against dengue fever in Brazil with genetically modified mosquitoes which represents a totally new way to approach the problem. Instead of using very strong chemicals which affect humans and environment negatively, this could be the beginning of a completely new method to fight diseases around the world, in particular dengue fever.

1.2 What is especially interesting?

The attraction of this subject is definitely its up-to-datedness. This project of Oxitec to fight dengue fever with genetically engineered mosquitoes is presently running and it is currently being discussed whether to establish it in other countries like the United States.

Furthermore, we found it interesting that this method to fight a disease with genetic engineered mosquitoes is completely new. Prior to this project dengue fever had never been fought effectively.

Even though not as featured as, for example, Ebola, which killed nearly 9000 people in 2014 mainly in West Africa, dengue kills about 20 000 per year and 40% of the world's population lives in dengue risk areas! This shows how important it is to fight dengue fever.

1.3 Our questions with respect to the topic

- What is dengue fever and how does it affect the body?
- How is dengue fever spread?
- How are the mosquitoes genetically changed?
- How do the genetically engineered mosquitoes fight the wild type?
- What are the advantages and disadvantages of this process?
- Are there any possible consequences?
- What are possible alternatives to Oxitec's GM mosquitoes?

[1] http://www.spiegel.de/wissenschaft/mensch/dengue-fieber-tropenkrankheit-verbreitet-sich-schnell-a-833829.html (last visited 19.01.15)

2. Introduction (Background)

2.1 The context of our topic

Dengue fever and our goals

Dengue Fever, a virus spread by mosquitoes, is a big topic worldwide and there are no effective and environmentally friendly ways to fight it, yet. But now Oxitec, a British biotech company has found a new way to combat the mosquitoes that spread it. In the following pages we want to clarify this type of genetic engineering, and evaluate its pros and cons. While working on the topic and doing research about it we noticed that a lot of background knowledge is needed to understand the whole situation and we therefore included quite a bit. One example for this is *Stegomyia albopicta.* While we primarily only intended to write about *Aedes aegypti,* we found out that it makes little sense to only write about one of the species. This is why our paper has turned out a bit longer than expected, but it is also more complete.

What is Oxitec and what do they do?

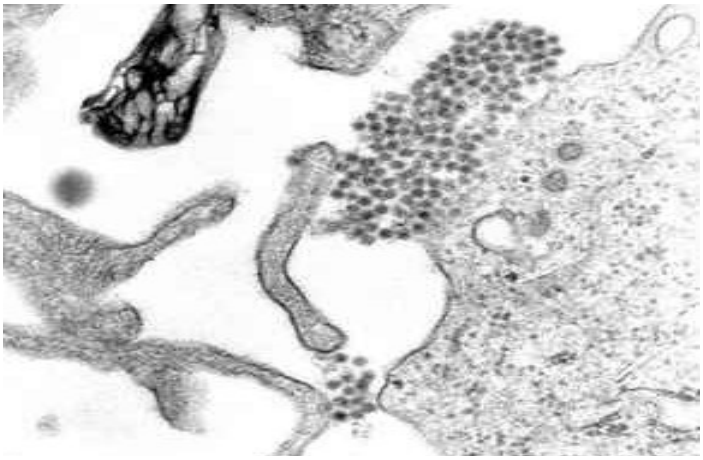
Oxitec is a British biotech company pioneering new approaches to fight insect pests. Therefore the name Oxitec, it means as much as Oxford insect technologies. They do this to fight disease spreading insects such as mosquitoes as well as insects that are agricultural pests. They call their system “self-limiting”. By releasing male insects with a lethal a gene into the wild, (to mate with wild females), they partly wipe out the local population. As they have a lethal gene, their offspring die in the larvae stadium. Doing this reduces insect numbers very effectively but does not extirpate them.

2.2 What is Dengue Fever? Where does it occur?

Dengue fever, also called break bone fever, is a tropical disease transmitted by the mosquitoes *A. aegypti* and *Stegomyia albopict*. It is caused by the dengue virus. In the majority of cases the symptoms occur 3-7 days after the bite of an infected mosquito. In 90 % of the cases the symptoms are mild and the dengue fever passes after approximately 10 days. But in 10 % of the cases the symptoms are severe with high fever, skin rash as well as muscle and joint pains.

The occurrence of the dengue virus is clearly connected to the occurrence of *A. aegypti* and *Stegomyia albopicta*. They are usually found around the equator, but due to global warming as well as globalization they are spreading quickly. This is the reason why dengue fever has been on the rise since the Second World War, and especially in the last few years.

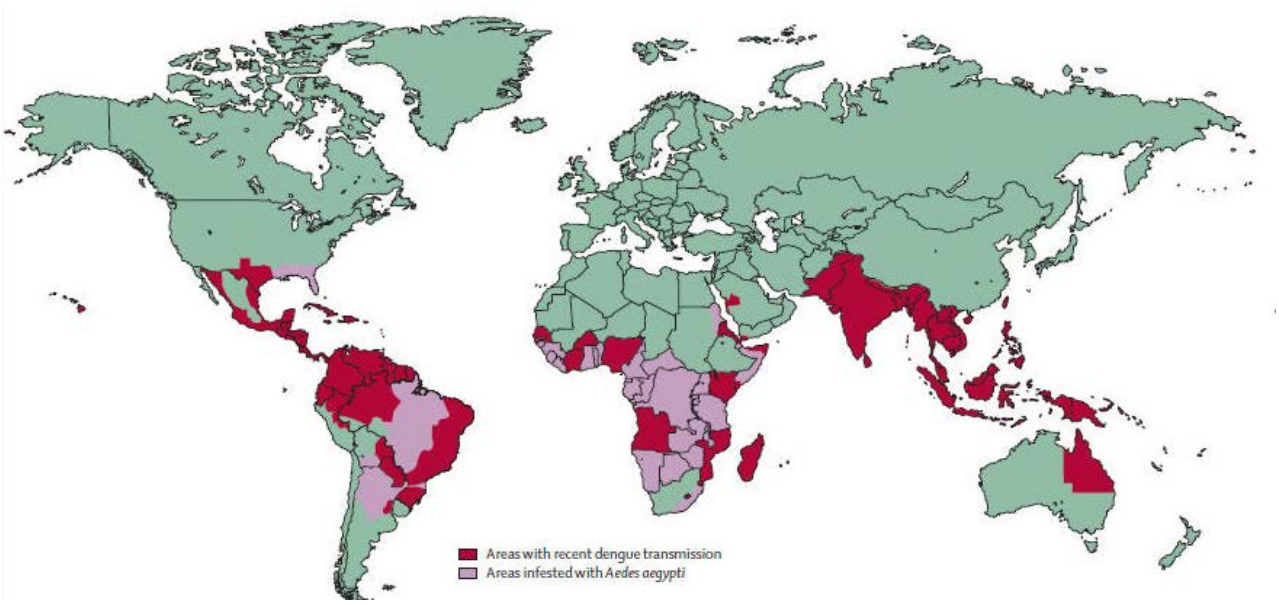
Picture 1: Aedes Aegypti



Picture 2: A micrograph showing Dengue virions (the cluster of dark dots near the centre)

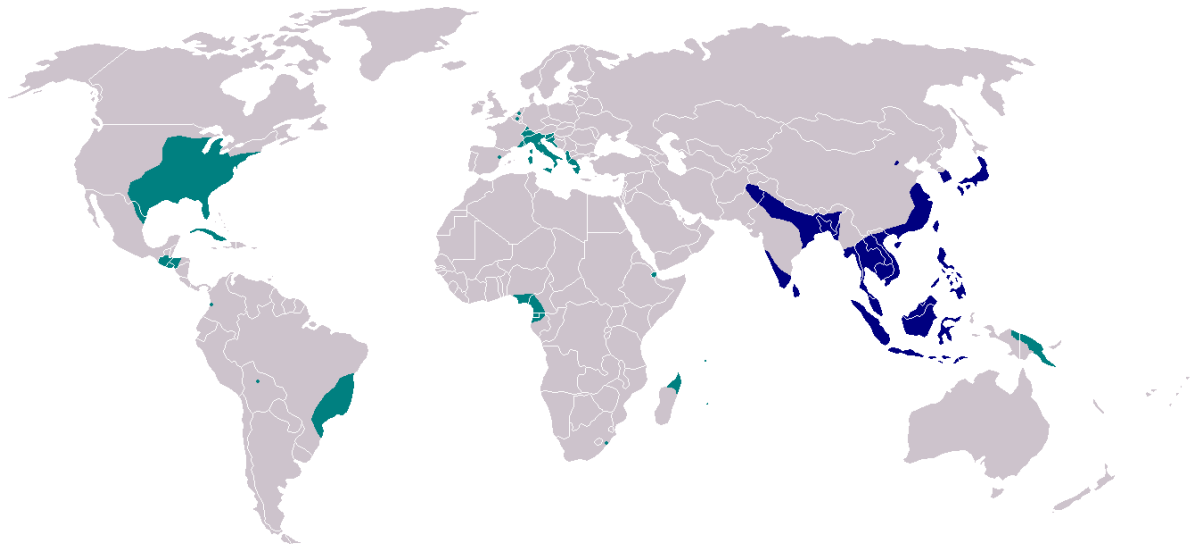
The distribution of the disease extends from the Caribbean to South America, the Pacific Rim, Southeast Asia, China, Africa and the eastern Mediterranean area. In Europe there are sporadic infections, too.

Because of this increase of infections it is very important to find a remedy for the fight against dengue fever. There are five different types of the virus infection. One of them gives lifelong immunity against the one type and short term immunity against the other four types.



Picture 3: Distribution of dengue fever

Red: Areas with recent Dengue transmission
Purple: Areas infested with *A. aegypti*



Picture 4: Distribution of Stegomyia albopicta

Blue: Native regions
Green: Introduced regions

2.3 What does the disease pattern of dengue fever look like?

Dengue fever has two different disease patterns. The first one is the more harmless one. It is called the normal or the classic dengue fever (DF). The symptoms are the same as if you had the flu or a cold, e.g. an uncomplicated fever. The other possibility is that people are asymptomatic, that means that the patient carries the infection but experiences no symptoms.

The second disease pattern is called viral hemorrhagic dengue fever (DHF) or dengue shock syndrome (DSS). This type of dengue fever can be deadly, because of its symptoms. It is a circulatory shock, in which development the permeability of the blood vessels increases and because of that uncontrollable bleedings and blood plasma leakage can occur. The hemorrhagic dengue fever begins like the "normal" Dengue fever, but the condition of the patient worsens.

2.4 How is dengue fever spread?

As written in 2.2 dengue fever is spread by mosquitoes mainly by A. aegypti but can also be spread by other mosquitoes such as Stegomyia albopicta.

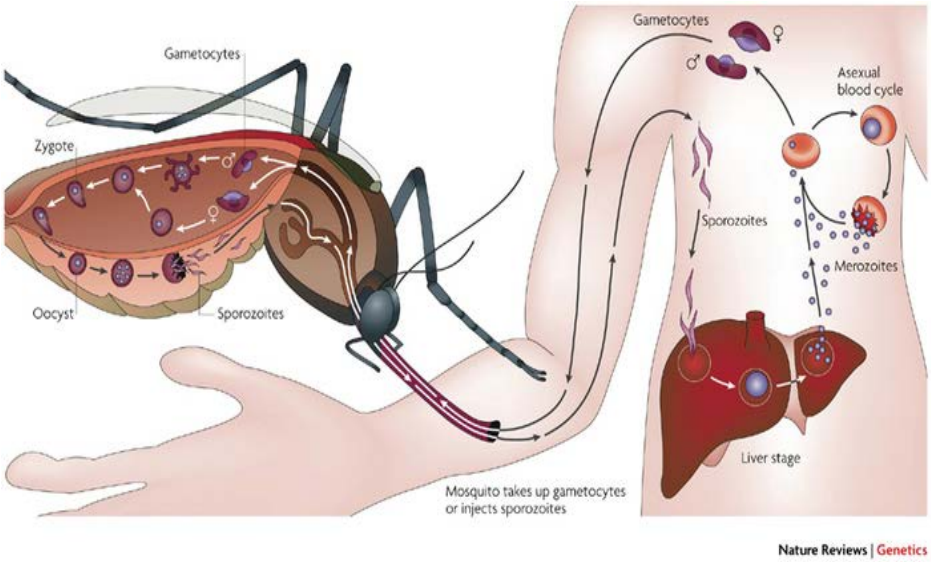
The reason for the wide range spreading of the mosquitoes is not due to their ability to fly, they only fly up to 500 m during their life, but due to globalization. Their eggs are very small and survive almost everywhere. Eggs of Aedes have been found in barrels, tin cans and even in beer bottles.

Even though normally occurring in tropical regions (A. aegypti), or in South East Asia (Stegomyia albopicta), they are extremely adaptive and are able to survive in subtropical climate zones. Those are growing as we speak, due to climate change.

The Dengue Virus cycle in 3 steps:

1. To be able to infect a human the mosquito needs to feed on an infected organism, a human or an ape for example.
2. After an incubation period of about 10 days, the mosquito remains infectious for its whole life from now on, i.e. for about 2-3 weeks.
3. The virus stays in the humans' blood circle for 2-7 days, when bitten by an uninfected mosquito, the mosquito becomes infectious.

Even though there are a lot of mosquitoes in the tropical forest this doesn't automatically mean they are not infected with dengue because there are no humans. As shown in the figure below, primates can also transmit it. Therefore, even if mosquitoes are exterminated in urban areas due to, for example, very strong chemical use, the virus is still able to spread and come back into urban settlements.



Picture 5: Mosquito transmitted virus cycle

This graphic shows how mosquito transmitted virus attack the human body and are passed on to mosquitoes biting an infected human. Dengue fever is passed on from mosquito to human, by sucking the humans' blood, where sporozoites of the virus are injected. These travel with the blood cycle into organs which they attack, later it reproduces and is passed on to other mosquitoes. When they suck the humans' blood they take up gametocytes and become infective themselves.

2.4.1 Other Virus spread by *A. aegypti* and *Stegomyia albopicta*

When talking about A. aegypti and Stegomyia albopicta, we should not forget that they also transmit Chikungunya fever and yellow fever. While Chikungunya is not deadly, but shows similar symptoms to dengue fever such as muscle and joint pains, yellow fever is. In the most severe cases of Chikungunya, these pains can last for years. As in the case of dengue fever, there is no specific treatment against it.

Much more serious, however, is yellow fever. This hemorrhagic fever is deadly, and while there are an estimated 200 000 cases per year, up to 30 000 people die of it. Around 90% of the infections occur in Africa.

In contrast to Chikungunya and dengue fever, there is a vaccination against yellow fever called 17D.

Although it was developed 60 years ago, it is still very effective, with a single dose lasting for ten years. It has been given to more than 300 million people.

2.5 The recent scientific history concerning dengue fever

Presently there is a lot being undertaken to fight Dengue fever - especially by Oxitec. There are two big projects: One on the Cayman Islands, which took place in 2010, and it is planned to release the GM mosquitoes in Florida this spring.

Grand Cayman project:

In 2010 Oxitec released its GM mosquitoes on the Grand Cayman Island, as a field study. They released around 3.3 million sterile males over 23 days. It was proved that they did mate with the wild females and as an outcome there was a reduction of 80% in the number of mosquitoes, compared to the untreated areas around. There are no environmental damages reported. Since then there have been releases in Brazil and Malaysia.

Florida Keys project:

Very recently Oxitec announced that a similar sized project to the one in the Cayman Islands is planned in the Florida Keys. Chikungunya and Dengue fever both had outbreaks in the last years and are a growing threat to Americans.

However not everyone seems enthusiastic about the project, and it has not yet been approved by the FDA.

Many Americans are afraid of being used as an experiment or simply don't see it as a real threat. This is the reason why the petition with the title "Say No to Genetically Modified Mosquitoes Release in the Florida Keys" has been called into life to stop it from happening.

It needs 150 000 supporters to be sent to various politicians and experts such as the director of Florida Keys mosquito control district management, Michael Doyle.

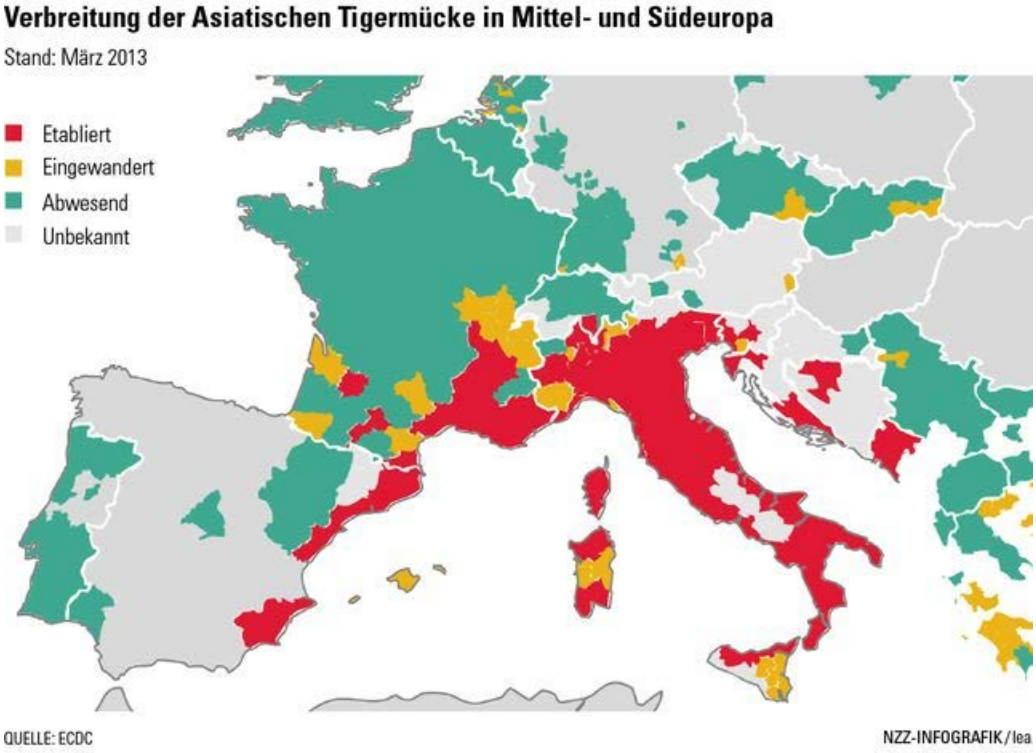
So far the petition has been signed by 145'609 people, which means it only needs another 4'391; it will be interesting to see the result of it in the near future.

2.5.1 Recent events in Europe and Switzerland

The Asian tiger mosquito Stegomyia albopicta is invading Europe. It has been found in several countries and is even established in a few of the southernmost, such as Italy.

It has not only been found in Italy, but also in the Tessin, where is being being fought with insecticides. There have not been many cases of tropical illnesses spread by them in Europe yet, but 2007 there was a Chikungunya outbreak in northern Italy which infected 200 people.

So even though we are quite far away from the tropics, a dengue infected tourist is enough to change the situation entirely. Whether this is possible in Switzerland, is currently being studied by Tobias Suter, a biologist working for the Swiss TPH.



Picture 6: Distribution of Stegomyia albopicta in Central- and South Europe

2.6 Alternative treatments

Option vaccine

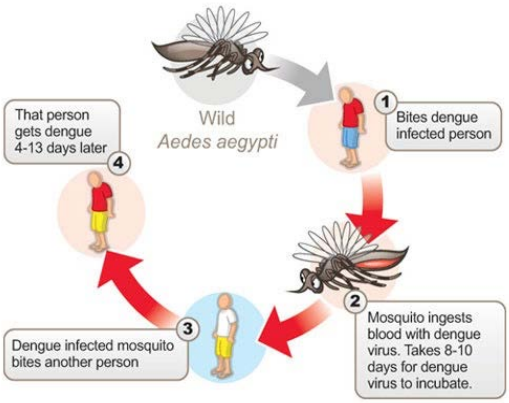
At the moment there is no effective and safe vaccine for dengue fever. There are various reasons for that.

As there are four different, so-called serotypes that can cause Dengue, it is extremely difficult to find a vaccine against all four types of virus. Another problem is the lack of suitable animals to test it on. Even if a vaccine was possible it would be extremely expensive and would have to be able to reach all 2.5 billion people that are at risk.

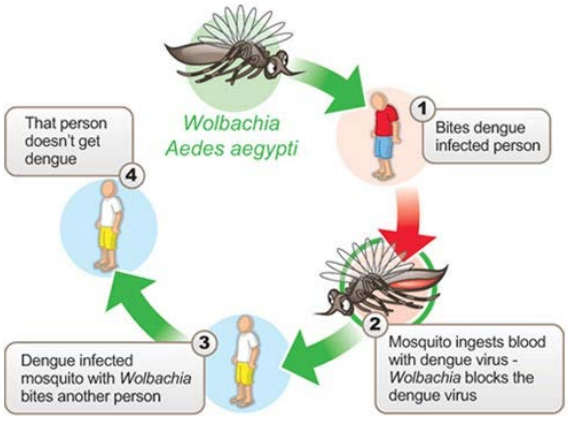
Option Wolbachia

A totally different approach would be to insert Wolbachia, bacteria that occur in around 60% of all insect species into *A. aegypti*. Research has shown that inserting Wolbachia into the mosquitoes it reduces their ability to transmit dengue, Chikungunya, yellow fever and even the parasites that cause malaria. So far many trials are still running, some of them had setbacks when only few of the Wolbachia containing mosquitoes hatched, due to bad weather conditions.

A team consisting of scientists and universities all over the world, led by Professor Scott O'Neill with the projects name is "eliminate Dengue". It is a non-profit collaboration.



Picture 7: Normal Dengue cycle without Wolbachia



Picture 8: Dengue cycle with Wolbachia

Insecticides

The problem with this currently used method to fight the mosquitoes is the big environmental damage as well as the fact that the mosquitoes become resistant against many of the insecticides. Because they often reproduce in urban areas, houses have to be sprayed with them which is very expensive as well as unhealthy for humans. In some cases the mosquitoes developed immunity against four out of six insecticides.

Picture 9: Insecticides used inside a school

2.7 Where and why is the GM technique used?

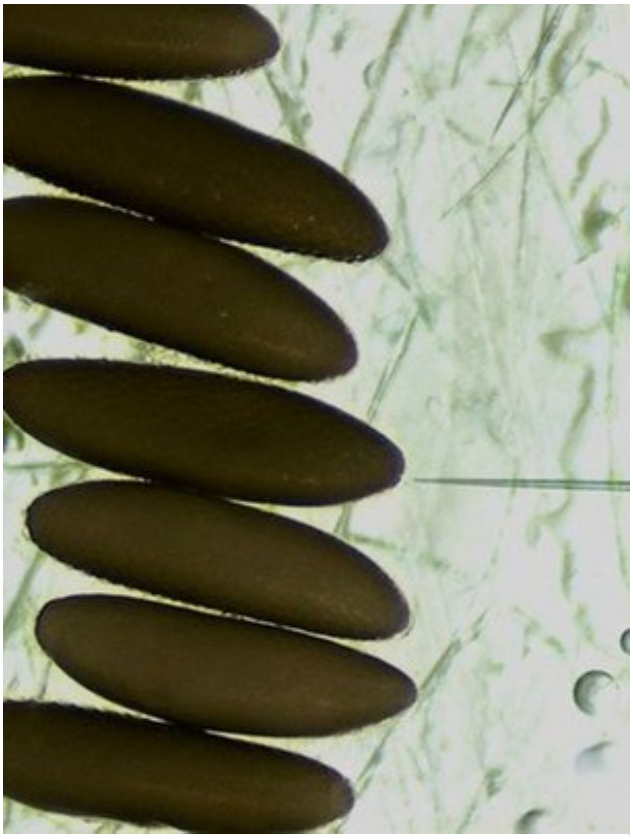
Up to now it has been used on the Cayman Islands, Malaysia and Brazil. There are a number of reasons why it has been tested there. As the Cayman Islands are British Overseas Territory, has no biosafety law and dengue fever occurs there, it was a suitable place for the first big experiment.

Malaysia and Brazil both hosted experiments, smaller than the Cayman Island's one.

It is employed and interesting for countries such as Brazil, because it is environmentally friendlier than commonly used insecticides. Another point is the financial perspective, as dengue fever cases are increasing. Brazil is spending over 1 billion US dollars to control mosquitoes with traditional chemical methods per year, so it might be a lucrative business, but there is currently no information about estimated costs for users.

3. Description of the engineering technique

"Oxitec uses advanced genetics to insert a lethal gene into its mosquitoes. The gene is passed on to the modified insect's offspring, so when Oxitec mosquitoes are released into the wild and mate with wild females their offspring inherit the lethality trait. The resulting offspring will die before reaching adulthood and the local mosquito population will decline."[2]



Picture 10: The gene is injected with a micro

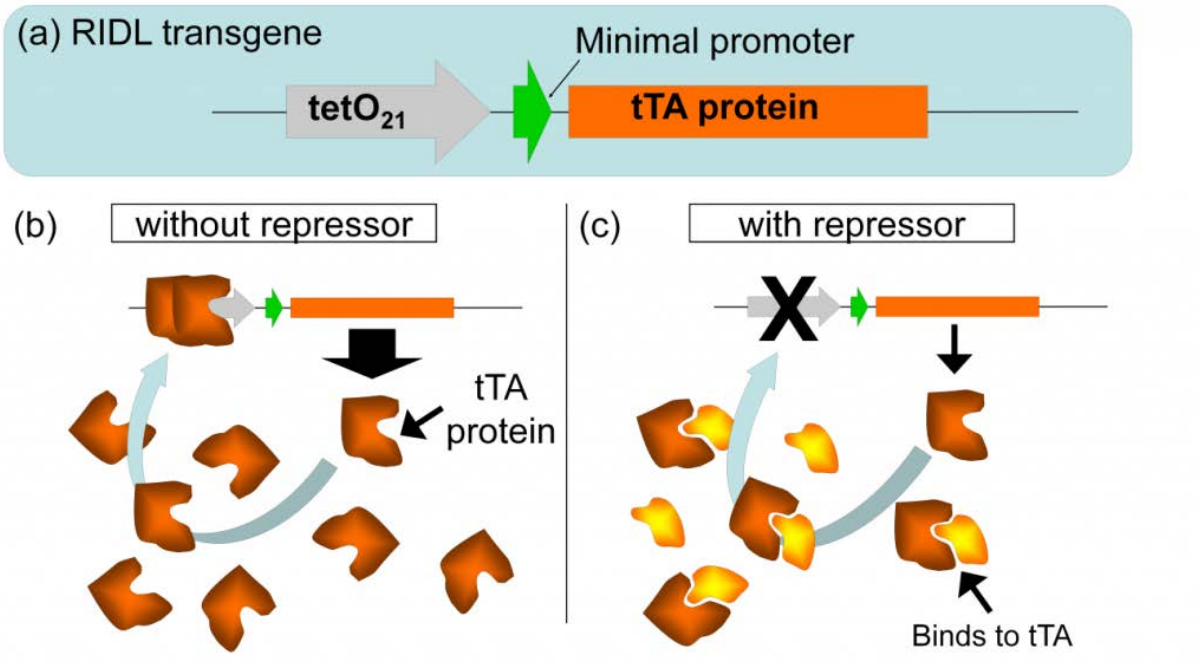
Oxitec inserts a gene into the mosquitoes, which causes them to produce a protein called tTA. This protein can control the activity of other genes, like a power switch that turns them on or off. Since this also applies for its own gene, a lot of tTA is produced. Also, another gene is injected that marks the mosquito with a color. You can only see the difference to wild mosquitoes under light with a certain wave length. This is used to measure the percentage of GM mosquitoes in the environment. This makes it easier to see if more mosquitoes have to be released.

tTA does not kill the mosquito by producing poisonous substances; therefore there is no influence on other animals that eat the affected mosquitoes. It prevents essential genes from working by interacting with proteins that the mosquito needs to control the genes thus the cell cannot turn on any.

The modified mosquitoes are raised in the laboratory. There, they do not die because tTA can be controlled by tetracycline, which binds with it and therefore stops the interaction with other proteins. Therefore they can be bred in large numbers while containing the lethal gene.

[2] http://www.oxitec.com/health/how-it-works/ (last visited: 19.01.15)

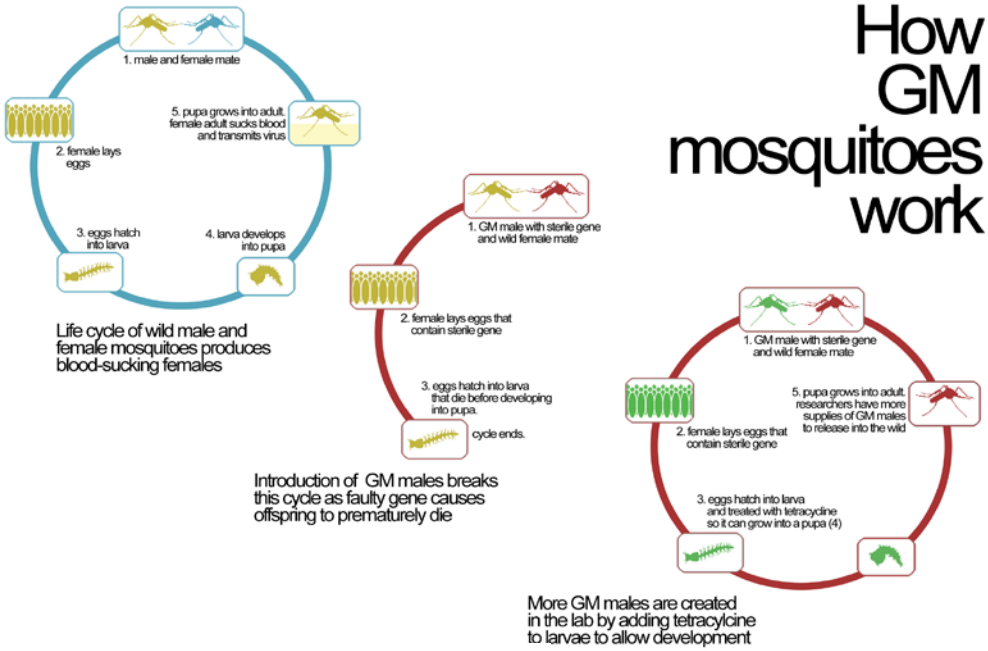
The mosquitoes in the laboratory get the necessary amount of tetracycline with their food so they do not die.



Picture 11: Function of Tetracycline

When they are adults, for safety reasons only the male mosquitoes get sent out to nature, because the females bite people and this could probably have dangerous effects on humans.

The affected male mosquitoes now mate with the females and the offspring carry the lethal gene which produces the tTA. This causes them to die before they are adults and therefore also before they can repopulate or bite humans. Right now there are three different products by Oxitec. They are called OX513A/OX3604C (*A. aegypti*) and OX3688 (*Stegomyia albopicta).*



Picture 12: Technique of GM mosquitoes

4. Discussion

4.1 What progress has been made by applying genetically engineered mosquitoes?

The genetically modified mosquitoes not only reduced the number of people infected by dengue fever significantly, they are also a much more environmentally friendly solution than other commonly used control methods, since they are not toxic.

4.2 What are the future research steps?

Oxitec wants to apply their technique to other diseases like malaria. Furthermore, they plan to extend their program to other countries like the USA and Panama.

4.3 Discussion of ethical aspects

Advantages

As already mentioned, it does not harm the environment as do other toxic chemicals that are commonly used to kill mosquitoes. Often these chemicals not only kill mosquitoes but also other insects and animals, while the modified mosquitoes simply die without harming other animals.

Furthermore, this method is more efficient than others because it kills the next generation before it can lay eggs or bite instead of just the adults.

Disadvantages

As Oxitec is a private company, it is bound to making profit. In contrast to the group of scientists that are studying the possibility of using Wolbachia bacteria to eliminate dengue, Oxitec is trying to get rid of A. aegypti. Therefore, unforeseen consequences might not only affect the mosquitoes, the virus or humans directly, but possibly also other parts of the ecosystem. If there were an 80% or even bigger decline in the A. aegypti population, this would almost certainly affect their natural surroundings. This has never been considered in studies led by Oxitec.

In order to keep the numbers of mosquitoes low, GM mosquito males have to be released over and over again whereas the approach with Wolbachia bacteria, if working properly, would spread automatically and therefore would be much more cost effective. Also the fact that Oxitec never mentioned anything accountable about the products price is rather suspicious, and lets us come to the conclusion that it will be rather expensive.

This might be a big problem for 3rd World countries, especially since the product has to be bought over and over again to be effective over longer periods of time.

Another ethical question is, whether the goal is to wipe out mosquito populations or lower them, or if the goal is to eliminate the dengue virus only. In this case the project “eliminate dengue” would definitely be the better approach.

4.4 Dangers and unforeseen consequences

The biggest problem is that we do not have much experience with this kind of modified mosquitoes. Therefore there are a lot of questions that still need to be answered.

It could happen that a modified female is accidently released. We do not know the consequences of a mosquito with a lethal gene biting us and how our body may react although Oxitec claims humans would not be affected.

Also there is the chance that at some time there will be a mutation that is resistant against that lethal gene and this species could be even more dangerous than the normal mosquitoes.

Another danger is that when Oxitec's products are sold all over the world it would have too much power and would be able to control a huge part of our eco system.

4.5 Our opinion

We are convinced that Oxitec´s approach to fight dengue (as well as yellow fever and Chikungunya) has huge potential and is possibly even a good solution.

It definitely is important to find a solution, as it does affect huge parts of the world´s population, and might even affect us in the near future.

Oxitec´s solution seems perfect at first and we have not found many opponents speaking out against it, but when taking a closer look there are some difficulties that are likely to arise. There are several aspects that Oxitec has not considered in their studies, one of them seems quite obvious and also caused us to distrust them.

As a fact, many of the regions infested with A. aegypti are also habitat to Stegomyia albopicta which is, as mentioned above, also host to dengue, Chikungunya and yellow fever. As both species are in the same ecological niche, the disappearance of one of the species would therefore most likely favor the occurrence of the other. Oxitec never mentioned anything about such problems and also tends to only report their success, whereas other scientists from, for example Gene Watch UK, do not share all of their views in this matter. All in all we support Oxitec´s innovation, though with precaution, due to some similarities with Monsanto.

It was great to research a topic as significant and newsworthy as this one with new information coming up while working on it. We learned a lot about genetic engineering and the different approaches to solving the problem.

5. Documentation and pictures of research institutions

Sadly we were not able to visit a research institution since the only place where this technique is applied is in the Oxitec laboratory in the U.K. We were still able to find some pictures of it in the internet:

Pictures 13&14: A. Aegypti larvae under a microscope

Picture 15: Researcher collects eggs of transgenic A. Aegypti mosquitoes

5.1 Interview

For the interview we got in touch with Oxitec's spokeswoman Chris Creese to get some first-hand information. The interview conducted per e-mail. We requested the interview 12.01.2015 and Mrs. Creese got back to us 16.01.2015

-How long did it take to realize the Dengue-fever project?

The Oxitec mosquito was created in 2002 to control the Aedes aegypti species that spreads dengue fever and Chikungunya. Oxitec is an international team of experts pioneering a safe and environmentally friendly way to control insect pests that spread disease and damage crops. And we're a spinout of Oxford University, where the research began!

-Is there still room for improvements in this project or are you still working on it?

The Oxitec mosquito was developed in 2002, and it's the same strain that is used today in projects in different countries. Because it's a new product though, Oxitec is working with the regulators in each country so they can evaluate it for their use. So far the Oxitec mosquito has been trialled in Cayman, Brazil and Panama and there is a proposed trial in Florida USA currently under review by the regulators there led by FDA. In every field trial the pest Aedes aegypti mosquito population was cut by more than 90%. To put this in context, the Florida Keys Mosquito Control District (FKMCD) – world leaders in mosquito control – using the best currently available control methods can only reduce the aegypti pest population by up to 50% at best. This is why they invited Oxitec to do a project there in the hopes they can add a new effective tool to their toolkit which is also environmentally friendly, to help keep people safe from the spread of diseases like dengue and Chikungunya. In the Florida Keys, aegypti has become resistant to four of the six pesticides they've been using to control it so there's an urgent need for new tools

-Is there a chance that this method will be adopted to fight other diseases such as Malaria?

Yes that is the hope. Oxitec is developing this technology for Aedes albopictus which also spreads dengue and Chikungunya (though aegypti is the primary vector that causes epidemics so is the first priority – this is why the Oxitec mosquito OX513A is aegypti). Prof Tony James at UC Irvine has also shown that Oxitec technology can work in the Anopheles mosquito that transmits malaria.

-Are there any other big projects planned for the future?

Yes, we're waiting to hear if the Florida trial will go ahead and we're hoping that will happen this year if FDA approves. Oxitec is working to tackle insect pests that spread diseases and damage crops – tackling disease and feeding the world are two of society's biggest challenges. To help farmers protect their crops, there's a need for new environmentally friendly pest control methods that work really well because there is a rise in insecticide resistance. Spraying insecticides can also affect other species too. Oxitec technology is species-specific so other beneficial insects like bees aren't targeted. For instance, we have an Oxitec diamondback moth to control this major pest of brassica crops (canola, broccoli, cabbage etc.). There's also Oxitec medfly to control the Mediterranean fruit fly which destroys about 300 different types of fruit and vegetable.

It's worth noting that the US has already used a GM insect with Oxitec technology. The USDA started releasing genetically engineered pink bollworm in 2006 in Arizona. This contains Oxitec's colour marker and is part of their Sterile Insect Technique program.

As background, SIT has been used successfully around the world for more than 50 years, and uses radiation to sterilise insects so when they mate with wild pest insects they don't produce offspring (sort of like birth control); but this method doesn't work for all insects, such as mosquitoes which are too fragile, and the radiation reduces the fitness of the insects. This is why Dr Luke Alphey came up with a much more carefully targeted method to produce this same 'birth control' kind of effect using genetic engineering. How it works is that instead of radiation, Oxitec

insects have two genes, a colour marker to track and trace them (and to distinguish between the helpful Oxitec insects and wild pest ones); and a pest control gene that ensures the offspring don't survive, to reduce the pest population each generation.

-As far as we are informed there have been a number of pilot tests with the GM mosquitoes. Is there a country that plans on a big exposure in the closer future?

Yes, Cayman is planning more releases of Oxitec mosquitoes. Also the national biosafety group in Brazil (CTNBio; The National Technical Commission for Biosecurity) has approved the Oxitec mosquito for commercialisation.

-GM mosquitoes are planned to have a smaller impact on the environment than currently used insecticides. Would they be more expensive compared to those alternatives for the, mostly developing, countries fighting Dengue fever?

The Oxitec technology has a light ecological footprint in addition to being affective at controlling insect pests that spread disease and damage crops. This is because it is species specific – Aedes aegypti only produces viable offspring with its own species, so other beneficial insects like bees aren't targeted, and the genes don't spread. The released insects and their offspring die and don't persist in the environment. For instance in Cayman after releases were stopped there were no adult mosquitoes left within 14 days.

As for cost, the colour marker means that Oxitec can adjust in almost real time the number of mosquitoes being released to ensure control is both effective and cost effective. How it works is that mosquito eggs are collected from traps and mosquitoes are examined under a microscope using a special light to see the colour marker. If 50% or less of the mosquitoes have the colour marker (helpful Oxitec mosquitoes), and the rest don't (pest mosquitoes), that means we need to release more; if all the mosquitoes have the colour marker, then we might be able to release less. So releases can be adjusted. The Oxitec mosquito is also compatible with other integrated pest control programmes. And the approach is flexible. For instance, after the initial releases to suppress the pest species, releases could then be continued at a much lower level (much cheaper), or even stopped entirely (no cost at all) and then the area can be monitored. If mosquitoes start to creep back in there can be targeted releases. Another option is to do a proactive release before the wet high season to maintain control, or to target just the areas where they're most likely to re-enter (ports, airports, etc.). So the cost is flexible and will depend on the kind of programme a group wants to run.

5.1.1 Conclusion of the Interview

In this interview we got some useful first-hand information from a person who is directly involved in this project. We learned that Oxitec researched a long time to get to their GM mosquitoes, namely since 2002, and that their technique is very effective. Their plan from now on is to apply this plan to different areas in order to tackle diseases like dengue worldwide. They are also trying to apply their method to new species such as Anopheles to stop malaria and we are looking forward to hear more from them on this topic. In the future Oxitec is planning to release GM mosquitoes on a big scale in Brazil and the Cayman Islands, they are still waiting for approval from the FDA to carry out releases in Florida. From the financial point of view it still seems quite unclear what their programs will cost, and may vary as there are many possibilities to combine them with other commonly used pest control programs.

5.1.2 Interview with the Swiss Tropical Institute

We also requested the tropical institute for an interview to get some more information about sengue fever and to get a neutral opinion on Oxitec's work. Unfortunately they did not answer our interview request. This was very disappointing for us, as it would have been interesting to get their opinion on the matter.

6. Summary

In the summary we want to answer our questions which we expressed in chapter 1.3.

- **What is Dengue fever and how does it affect the body?**

  Dengue fever is a serious disease caused by the Dengue virus which is transferred from mosquitoes to the human body by a bite. Its symptoms are very variable, if you have the normal dengue fever the symptoms are among other things headache, fever, muscle and joint pains. The symptoms of the more serious disease patterns, the viral haemorrhagic Dengue fever (DHF) or the Dengue shock syndrome (DSS), are uncontrollable bleedings and blood plasma leakage.

- **How is Dengue fever spread?**

  Dengue fever is spread by the A. Aegypti which when they bite a human inject the virus into our blood circle where it attacks the human immune system.

- **How are the mosquitoes genetically changed?**

  A gene is injected which causes the cell to produce a protein. Because of that protein the offspring die before they are adults and therefore before they lay eggs or bite people.

- **How do the genetically engineered mosquitoes fight the wild type?**

  The modified males mate with the wild females which causes their offspring to die before they are adults.

- **What are the advantages and disadvantages of this process?**

  On the one hand, it is more effective, than the other commonly used methods. On the other hand, it could affect the ecosystem more than expected. Also you have to constantly release new males in order to keep the numbers of wild mosquitoes low.

- **Are there any possible consequences?**

  Since we do not have much experience with this method of fighting diseases, we do not know what could happen to the ecosystem or our body in specific circumstances which are created by these GM mosquitoes.

- **What are possible alternatives to Oxitec's GM mosquitoes?**

  The usual alternative for fighting dengue fever are insecticides which consist mainly of chemicals which harm the human body and nature. Another method to fight the disease is Wolbachia. These are bacteria that occur in 60% of insects and reduce their ability to spread diseases like Dengue fever.

7. References

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7.2 Pictures

- Cover picture: http://www.welt.de/wissenschaft/article129406158/Brasilien-setzt-Muecken-mit-Selbstmord-Gen-aus.html (last visited: 15.01.15)
- Picture 1: http://de.wikipedia.org/wiki/Denguefieber (last visited: 18.01.15)
- Picture 2: http://en.wikipedia.org/wiki/Dengue_fever (last visited 22.01.15)
- Picture 3: http://www.reisemed.at/krankheiten/dengue-fieber (last visited: 27.01.15)
- Picture 4: http://upload.wikimedia.org/wikipedia/commons/0/02/Albopictus_distribution_2007.png (last visited: 23.01.15)
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