



## Biotechnology and Life Sciences in Baden-Württemberg

03.12.2009

---

### Matthias Giese: DNA vaccine to combat worldwide honeybee deaths

**Some years ago, scientists introduced an Asian honeybee species to Europe for research purposes, and with the bees Varroa mites came as hidden cargo. These parasitic mites attach to the body of the bees and weaken them by sucking hemolymph, infecting them with viruses that are believed to be the cause of the mass death of European honeybee colonies. In a very short period of time, the parasites have managed to eradicate around half of all European honeybee colonies. Matthias Giese of the Heidelberg-based Institute for Molecular Vaccines is extremely concerned about this massacre, as honeybees play an indispensable role in the pollination of wild and agricultural plants. A DNA vaccine he developed might just lead to a breakthrough in the quest to get rid of the Varroa parasites. Giese tells us about his project in the following interview.**

**Dr. Giese, the death of honeybee colonies is not only an ecological threat, but is also of economic importance in terms of the pollination of agricultural crops. Can you give us some concrete figures?**

Concrete figures are available in the USA where it is estimated that the economic damage caused to agriculture by the collapse of honeybee colonies amounts to an annual figure of around 15 billion US dollars. I do not have any information about the economic damage caused in Germany. But the death of honeybees might have drastic consequences for world nutrition.



Internationally renowned vaccine expert: Dr. Matthias Giese. (© private)

**Are there no natural or chemical ways of attacking the mite problem? Has the breeding of Varroa-resistant honeybees had any success, and if so, what has been achieved?**

Ways to successfully reduce the disastrous effect of mites do exist but they only work for a limited period of time. The major problem is the development of resistances and it is believed that the currently used methods no longer have any effect. Over the last ten years attempts have been made to breed Varroa-resistant, Western European honeybees, but this has not yet been successful. African honeybees are resistant to Varroa, but they are also very aggressive and are not suitable for the production of honey.

**How are you trying to combat the mites?**

We are seeking to develop a vaccine against the Varroa mites. But it must be said that our bee vaccine is different from classical vaccination. We have developed a DNA plasmid, a kind of shuttle system, which we add to the sugar solution fed to the bees. The bees absorb this plasmid when they feed on this nutrient solution. The DNA absorbed by the bees then causes a protein or RNA to be produced that in turn kills the mites but not the bees. The substance enters the Varroa mites when they attach to the bees and suck the bees' hemolymph.

In our newly founded institute, we are pursuing three different approaches to develop a vaccine. The first approach is based on the finding that the mites switch off genes of the bees' immune system when they suck the hemolymph. We hope to be able to switch on these immunologically

relevant genes again by introducing a suitable DNA plasmid into the bees, stimulating the bees' immune system and making them resistant to Varroa infestation. Our second approach is based on the principle of RNA interference. The DNA plasmids that are introduced lead to the production of short RNA sequences in the bees which are taken up by the mites when they suck the bees' hemolymph. These RNA sequences attach to Varroa RNA, thereby preventing the creation of proteins that are vital for the mites. We plan to introduce sequences that damage the mites' suckers or digestive organs. The third approach focuses on creating a DNA plasmid that leads to the production of a toxin which kills the mites but not the bees.

**Have you already carried out experiments to test these approaches?**

Yes, we have already completed preliminary tests. We have developed a DNA plasmid using green fluorescent protein (GFP) as "placeholder". Using a range of different methods, we have been able to show that the plasmid enters the bee during feeding. The plasmid is subsequently translated into a protein and enters the mites while they are sucking the blood. This is an important initial step in combating the Varroa mites.

**Your preliminary experiments have shown that the principle of introducing a DNA plasmid into the bees through the sugar solution and the subsequent uptake of a deadly protein by the mites works. But which DNA sequences are you aiming to use as a vaccine?**

The next step is to find the relevant sequences. We are about to start a comprehensive literature search and carry out additional experiments. The biology of Varroa is still largely unknown and very few people have done any investigations in this area. Therefore, we are initially going to focus on house dust mites, which are well characterised.

**Varroa infestation not only kills adult bees but also the brood. Is your vaccine also suitable for bee larvae?**

In fact, Varroa is very selective and mainly damages the bee larvae. But we have come up with some clever ideas. In order to specifically target the bee larvae, we are planning to develop a vaccine spray and spray the honeycombs. When the larvae feed on the sugar solution containing the DNA plasmid they also take up our drug.

**Is there a risk that the DNA plasmid enters the honey or the environment?**

We do not want the DNA vaccine to enter the environment. We know from our experiments that the DNA plasmid is not found in bee excretions. We plan to use the vaccine after the honey has been harvested. In spring 2010, we will carry out experiments to find out whether the vaccine is able to enter the bees' honey stomach at all. So far we have not found any signs that this is the case.

**Have DNA plasmids already been successfully used for vaccination?**

Such vaccines are already successfully used in veterinary medicine to vaccinate large animals and fish. They also play an important role in human medicine, especially in experimental research.

**Is your approach unique?**

Our literature searches have shown that no publications exist on this topic. So, I would say our approach is unique. An Israeli research group is doing similar experiments, but they focus on RNA interference. Our method has the advantage that DNA is far more stable than RNA - RNA falls apart if you as much as look at it. In addition, the development of our approach promises to be far cheaper.

**When will the vaccine be fully developed?**

We believe that it will take two more years, including obtaining marketing authorisation and the approval from public authorities.

**What do you think is the economic potential of the vaccine?**

Varroa is a global problem. As far as I know, there is only one country that remains unaffected by Varroa - New Zealand. But there is evidence that the mites have already reached an island off

the New Zealand coast. Therefore, there will be worldwide interest in our product. If the bee vaccine is successful, we might even be able to produce a blockbuster remedy.

**How will you finance your research projects in the coming years?**

We have already started to look for investors and strategic partners. We hope to be able to work in partnership with a pharmaceutical company to ensure the worldwide commercialisation of the vaccine. In addition, BIOPRO and its CEO, Dr. Ralf Kindervater, are providing us with a great deal of help in this process and are making sure that we contact the right partners. Things are looking quite good at the moment.

**And now to my last question. Are you also in contact with beekeepers? What do they think of your idea?**

Beekeepers have told us that Varroa is a huge problem for them. They are unable to completely eliminate Varroa from their colonies with the authorised means that exist at the moment. They hope that there will soon be a new drug available that works.

**Dr. Giese, thank you very much for talking to us.**

Andrea van Bergen - 03.12.2009  
© BIOPRO Baden-Württemberg GmbH

A contribution from:



**Contact information:**

Dr. Matthias Giese  
Im Schaffner 24  
69123 Heidelberg, Germany  
Tel. +49 (0)6221-73.73.33  
Fax: +49 (0)6221-73.94.08  
E-mail: m.giese-hd(at)t-online.de

<http://www.bio-pro.de/magazin/index.html?lang=en>