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Microbiology

Engineering bacteria to save honey bees

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Honey bees are essential industrious insects, which pollinate crops and help ensure you have enough food to eat. But their health is threatened by viruses and parasites. New technology genetically engineers bacteria inhabiting the bee gut to boost bee immunity and help them fight off their enemies.

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Humans have kept honey bees for millennia, and scientists love to study them because of their unique societies (80,000 bees can live and work together in a single hive!) and communication (they exchange information by "dancing"). Honey bees also help produce much of the food that you eat. These industrious insects work hard: moving pollen from flower to flower and sparking the growth of nuts, fruits, and other delicious foods.

But many honey bee colonies die each winter, far more than we would like. These deaths mean beekeepers spend time and money rebuilding colonies, which increases pollination costs and food prices. We do not know all of the exact causes of these hive deaths, but in fact, small dangerous enemies have jumped from wild bee species to honey bees while humans have moved crops and bees around the globe. Among the worst are the *Varroa* mite (imagine a basketball-sized tick latched on to your back) and viruses like *Deformed Wing Virus* known as DWV.

In this research, we developed a new approach to study honey bees and support bee health. Like humans, honey bees have a community of numerous bacteria that live in their gut. Some of these bacteria are beneficial to bees, and naturally help keep bees healthy. Our approach uses genetic engineering to modify beneficial bacteria naturally living in bee guts and enhance them to produce a key biomolecule called double-stranded RNA. Double-stranded RNA resembles some viruses at the molecular level, enough to trick the bee immune system into mounting a response to destroy specific targets.

Our study used these genetically modified bacteria and fed them to bees we cared for in the laboratory. Raising bees in the laboratory allowed us to control some variation between hives and the environment to precisely test our bacteria and their effects in ideal conditions.

Genetic engineering in bacteria can result in unexpected consequences and even sometimes threaten their life. Therefore, for quality control, we first tested whether our engineered bacteria were able to return to the bee gut and live there. We fed our engineered bacteria to bees in the lab, and the bacteria grew within their guts. We also found that our engineered bacteria that produce the virus-like double-stranded RNA activated the bee immune response from inside the gut.

Next, we set about to test if this bacterial genetic engineering can help train the bee immune system to fight threats: viruses and mites. First, we fed bacteria engineered to mimic DWV virus to bees. These bacteria acted like a vaccine, priming the bee immune system to respond to the DWV virus. To our delight, when we further injected these bees with the virus, a real threat, the bees with the protective bacteria lived longer than bees without them. Second, we asked whether this approach could protect bees from parasitic mites too. The bacteria used in this trial contained genetic material mimicking the *Varroa* mite. We fed these bacteria to bees and then placed the mites onto individual bees. Mites on bees fed with the engineered bacteria died more quickly. In this case, the double-stranded RNA made in bacteria actually travels throughout the bee in the bee blood. When mites eat bee tissues, this poison pill activates the mites' own immune system and triggers mite suicide.

We have shown that engineered bacteria could act like an in-house vaccine and help protect honey bees from health threats. This novel approach could be used to help study how bee biology works, and widely applied in other insects or other animals too, to protect their health, to kill them, or to study them. What does the future hold for this technology? As with any medicine, it is important to see how it works in honey bees' natural environments: hives in fields. Because we are dealing with genetically engineered bacteria, we must also ensure these bacteria can be adapted within hives and do not spread genetic material to unexpected places.

Genetically engineered beneficial bacteria have great potential, and these same techniques may be used in systems outside of honey bees to solve many challenges. We haven't "saved the bees" yet, but the future is bright!