Honeybees harbor antibiotic-resistance genes

October 30 2012

Bacteria in the guts of honeybees are highly resistant to the antibiotic tetracycline, probably as a result of decades of preventive antibiotic use in domesticated hives. Researchers from Yale University identified eight different tetracycline resistance genes among U.S. honeybees that were exposed to the antibiotic, but the genes were largely absent in bees from countries where such antibiotic use is banned. The study appears on October 30 in *mBio*, the online open-access journal of the American Society for Microbiology.

"It [resistance] seems to be everywhere in the U.S.," says Nancy Moran of Yale University, a senior author on the study. "There's a pattern here, where the U.S. has these genes and the others don't."

Honeybees the world over are susceptible to the bacterial disease called "foulbrood", which can wipe out a hive faster than beekeepers can react to the infection. In the U.S., beekeepers have kept the disease at bay with regular preventive applications of the antibiotic oxytetracycline, a compound that closely resembles tetracycline, which is commonly used in humans. Oxytetracycline has been in use among beekeepers since the 1950s, and many genes that confer resistance to oxytetracycline also confer resistance to tetracycline.

Using sensitive molecular techniques, Moran and her colleagues screened honeybees from several locations in the United States and from Switzerland, the Czech Republic, and New Zealand as well as several wild bumblebees from the Czech Republic, for the presence and abundance of tetracycline resistance genes. They found that U.S.

honeybees have greater numbers and a more diverse set of tetracycline resistance genes than honeybees from the other countries.

Moran says it is reasonable to expect to see widespread resistance among bees, considering the decades-long use of oxytetracycline in honeybee hives. "It seems likely this reflects a history of using oxytetracycline since the 1950s. It's not terribly surprising. It parallels findings in other domestic animals, like chickens and pigs," says Moran.

Moran notes that beekeepers have long used oxytetracycline to control the bacterium that causes foulbrood, but the pathogen eventually acquired resistance to tetracycline itself. Of the foulbrood pathogens *Melissococcus pluton* and *Paenibacillus larvae*, Moran says, "They carry tetL, which is one of the eight resistance genes we found. It's possible that the gene was transferred either from the gut bacteria to the pathogen or from the pathogen to the gut bacteria."

Switzerland, the Czech Republic, and New Zealand do not allow beekeepers to use oxytetracycline in hives, so it is perhaps predictable that honeybees and wild bumblebees from these countries harbored only two or three different resistance genes and only in very low copy numbers, suggesting that the bacteria did not require the genes very frequently.

The authors of the study point out that by encouraging resistance and altering the bacteria that live in honeybee guts, decades of antibiotic applications may have actually been detrimental to honeybee wellbeing. Studies have suggested that the bacterial residents of the honeybee gut play beneficial roles in neutralizing toxins in the bees' diet, nutrition, and in defending the bee against pathogens. By disrupting the honeybee microbiota and reducing its diversity, long-term antibiotic use could weaken honeybee resistance to other diseases. Hence, the treatment that was meant to prevent disease and strengthen the hive may actually

weaken its ability to fight off other pathogens.

Moran says while the study is interesting from the perspective of honeybee health and could have implications for how honeybee diseases are managed, the presence of resistance genes in the honeybee gut doesn't pose a direct risk to humans. These gut bacteria, says Moran, "don't actually live in the honey, they live in the bee. We've never actually detected them in the honey. When people are eating honey, they're not eating these bacteria."

Provided by American Society for Microbiology