Honey bee colony aggression linked to gene regulatory networks

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Dissimilarity of brain GRN architecture between soldiers and foragers is greater in high-aggression honeybee colonies. Credit: *Nature Ecology & Evolution* (2023). DOI: 10.1038/s41559-023-02090-0

Collective behaviors are present across many different animal groups: schools of fish swimming in a swirling pattern together, large flocks of
birds migrating through the night, groups of bees coordinating their behavior to defend their hive.

These behaviors are commonly seen in social insects where as many as thousands of individuals work together, often with distinct roles. In honey bees, the role a bee plays in the colony changes as they age. Younger bees perform duties inside the hive, such as nursing and wax building, while older bees transition to roles outside of the hive, either foraging for food (foragers) or defending the colony (soldiers).

What determines whether older bees become foragers or soldiers is unknown, but a new study published in *Nature Ecology and Evolution* explores the genetic mechanisms underlying the collective behavior of colony defense, and how these mechanisms relate to the colony's overall aggression.

"Honey bees do not have a size-based division of labor, like you might see in termites or ants," said Ian Traniello, former graduate student at University of Illinois Urbana-Champaign, now an associate research scholar at Princeton University and first author on the study.

"If you ask anyone off the street to guess which ant is a soldier versus a forager, they probably will guess it right 100% of the time, because the soldiers are huge. Honey bees instead have an age-based division of labor, where older bees tend to be foragers or soldiers, both of which are dangerous and potentially lethal roles."

A *genome-wide association study* conducted previously on a sub-species of honey bee in Puerto Rico that had evolved to be less aggressive in recent years, revealed strong associations between variation in the sequence of some *genes* and the level of overall colony aggression. Researchers called these "colony aggression genes."
In the current study, researchers compared the expression and regulation of genes in the brains of soldiers and foragers, and across colonies that varied in aggressiveness. Researchers measured colony aggressiveness by counting the number of stings on suede patches placed outside the hives after a disturbance.

They identified soldiers as the bees that attacked the patches and foragers as the bees that returned to the hive with pollen. The researchers then used single-cell transcriptomics and gene regulatory network analysis to compare the brains of forager and soldier bees, from low and high aggression colonies.

The researchers found that, although there were thousands of genes in the brain that differed in their expression between soldiers and foragers, none of them were part of the colony aggression gene list. However, when they created models of brain gene regulatory networks, which control when and where specific genes are expressed, the researchers found that the structure of these networks differed between soldiers and foragers—and the differences were bigger when the soldiers and foragers came from a more aggressive colony.

"What we think is happening is that the regulation of genes associated with collective behavior affects the mechanisms that underlie division of labor," Traniello explained. "So, colonies can become more or less aggressive by influencing the aggression level of the individuals within that colony. Basically, a forager may be more or less likely to transition to a soldier-like state if the environment calls for it."

The findings highlight the importance of gene regulation to our understanding of the relationship between genes and behavior.

"While a few studies have found potential heritable differences between soldiers and foragers, this study demonstrates that older honey bees may
have the potential to take on either role," said Gene Robinson (GNDP), IGB Director and author on the paper. "In colonies that are more aggressive, likely due to increased danger in the environment, older bees may just be more predisposed to become soldiers to help defend the colony."

Plans for future directions include developing functional tests to explore the role of the gene networks identified in the study, and to identify spatially where they are being expressed in the brain. Traniello says that he looks forward to exploring these new questions.

"We have extraordinary technologies to probe genes and behavior at an unprecedented scale, both with single-cell and, now, spatial transcriptomics," Traniello said.

"These give us new means for understanding old questions, like the relationship from individual to collective, or the relationship between genotype to phenotype. It's exciting to be able to take these tools and apply them in naturalistic contexts, and I hope this work inspires others to do the same."
