Notes from the Lab: The Latest Bee Science Distilled

by Scott McArt

Everyone's getting vaccinated … Do honey bees run vaccination programs, too?

As I write this, 40% of people in the U.S. have received at least their first dose of the COVID vaccine and 26% are fully vaccinated. That corresponds to 133 million people receiving one dose and 86 million people being fully vaccinated. Wow, talk about an impressive mass-vaccination program!

So, are humans special in our ability to run mass-vaccination programs? Or do other social animals, such as honey bees, also run vaccination programs? If so, how do they do it? These are the topics for our forty-second Notes from the Lab, where we summarize **"Social immunity in honey bees: Royal jelly as a vehicle in transferring bacterial pathogen fragments between nestmates,"** written by Gyan Harwood and colleagues and published in the ***Journal of Experimental Biology*** **[224(7):jeb231076].**

Harwood and colleagues (Photo 1) started with the knowledge that honey bees live in highly social groups, and because of this, they practice something called social immunity. Social immunity is a set of behaviors and strategies that protect members of colonies from disease.

Several social immunity strategies are known for honey bees. For example, queens can transfer pathogen fragments into their eggs, which enables those eggs to have prior exposure to parts of the pathogens (e.g., part of a harmful bacterium) during development. Does this sound familiar compared to the COVID vaccine? Indeed, the COVID vaccine works in humans by exposing us to part of the SARS-CoV-2 virus, which allows our immune system to prime itself for the "real deal," if it ever comes along.

Pathogen fragments are known to be transferred from honey bee queens to their eggs via vitellogenin, an egg-yolk precursor protein. Because vitellogenin is also used by nurse bees to create royal jelly (Photo 2), the authors suspected jelly might be a vehicle for transferring pathogen fragments throughout the colony, not just between queens and eggs. Indeed, in previous work (Harwood et al. 2019), the authors showed that nurse bees who ingested bacteria were able to transfer it to their jelly-producing glands, and that vitellogenin regulated the transfer to glands.

For their new work, Harwood and colleagues first wanted to know whether nurses that ingested bacterial pathogens could incorporate them into their royal jelly. To do this, they fed heat-killed *Paenibacillus larvae* (the bacteria causing American foulbrood) to small queenless colonies, allowed the nurse bees to deposit royal jelly for three days, then collected the jelly. They assessed whether *P. larvae* fragments ended up in the jelly by applying a fluorescent tag to the bacteria

Photo 1. *Lead author Gyan Harwood with field assistants (L-R Salla Lohi, Siiri Fuchs, both of whom were graduate students at the University of Helsinki when this research was conducted)*

Photo 2. *Nurse bee with royal jelly*

and monitoring if the jelly contained the tag.

In addition, the authors wanted to know whether ingesting *P. larvae* increased antimicrobial proteins in the jelly produced by nurse bees. To do this, they took jelly from *P. larvae*-fed vs. control (sugar-fed) nurse bees and conducted a proteomics analysis. Briefly, they digested the proteins in jelly with enzymes, sequenced the resulting peptides, and matched the peptides to known proteins.

So, what did they find? Did fragments of *P. larvae* end up in royal jelly produced by nurse bees? Yes. On average, nurse bees that were fed sucrose containing fluorescent-tagged *P. larvae* produced jelly with 67 florescent particles per microliter, compared to control colonies that produced jelly without florescent particles. This result indicates that fragments of *P. larvae* are being secreted in royal jelly by nurse bees when those bees consume *P. larvae*. Very interesting!

What about antimicrobial proteins? Were those also included in the jelly containing *P. larvae* fragments? Yes. There were several antimicrobial proteins in both the control jelly and jelly containing *P. larvae* fragments. Overall, 496 proteins were identified, with 3 proteins only found in jelly produced by *P. larvae*-fed bees (Glutathione peroxidase, Peptidyl-prolylcis-trans isomerase, and an uncharacterized protein, LOC725202).

There were few differences in protein abundance between the jelly from control vs. *P. larvae*-fed bees, but defensin-1, one of four focal immune proteins, was 68% more abundant in jelly from *P. larvae*-fed bees (Figure 1D).

So what do these results mean? Are nurse bees running a mass-vaccination program within honey bee colonies? That does indeed appear to be true! While insects do not have a true adaptive immune system like humans, they do have the ability to use elicitors to stimulate their innate immune systems. Pathogen fragments have been shown previously to stimulate immune function in honey bees. The results from Harwood and colleagues show that royal jelly can be an efficient conduit for transferring pathogen fragments and therefore potentially stimulating immune function.

At the same time, the authors found that defensin-1, an antimicrobial peptide, was elevated in jelly produced by *P. larvae*-fed bees. Thus, nurse bees aren't only passing along pathogen fragments so nestmates can mount their own immune responses, they're also providing an antimicrobial tool for their nestmates. That's analogous to us providing COVID patients with therapeutic drugs like Remdesivir, an anti-viral that blocks replication of coronaviruses. Pretty neat, right?

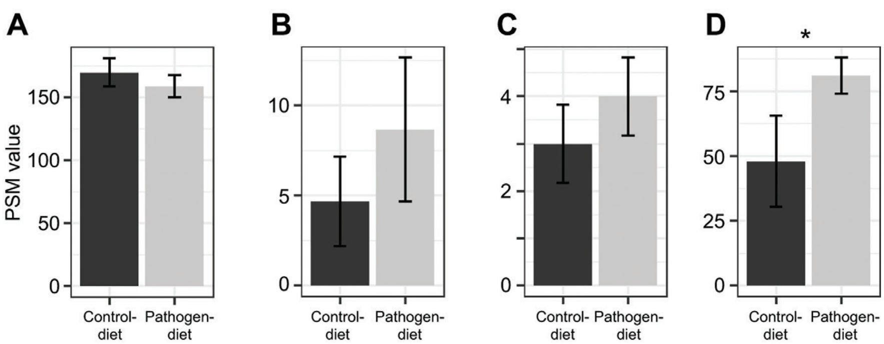

Figure 1. *The abundance of select immune proteins in control-diet and pathogen-diet royal jelly samples. (A) glucose oxidase; (B) bee venom serine protease (Bi-VSP); (C) lysozyme; and (D) defensin-1. Bar heights represent the mean peptide spectrum match values over 3 samples, with error bars denoting ±1 s.d. Of the 4 proteins compared, only the antimicrobial peptide defensin-1 was significantly upregulated in pathogen-diet samples. PSM = peptide serum match.*

Overall, the study from Harwood and colleagues provides a tantalizing peek into how honey bees keep each other healthy. The fact that royal jelly is constantly fed to the queen means she has lots of information (and antimicrobial weapons!) to keep herself and the eggs she lays from getting sick. Similarly, any nestmates that transfer jelly will be privy to these tools and information. In a world where disease can be a major threat, perhaps it's not surprising to see that honey bees can run vaccination programs similar to us.

Maybe one of us should mentor Dr. Anthony Fauci in beekeeping so he learns a thing or two about efficient social immunity mass-vaccination programs?

Until next time, bee well and do good work.

Scott McArt

Reference:

Harwood, G., G. Amdam and D. Freitak. 2019. The role of Vitellogenin in the transfer of immune elicitors from gut to hypopharyngeal glands in honey bees (*Apis mellifera*). *Journal of Insect Physiology* 112:90-100. **https://doi:10.1016/j.jinsphys.2018.12.006**

Harwood, G., H. Salmela, D. Freitak and G. Amdam. 2021. Social immunity in honey bees: Royal jelly as a vehicle in transferring bacterial pathogen fragments between nestmates. *Journal of Experimental Biology*. 224(7):jeb231076. **https://doi.org/10.1242/jeb.231076**

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