



# Commentary: Engineered symbionts activate honey bee immunity and limit pathogens

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## A Commentary on

### Engineered symbionts activate honey bee immunity and limit pathogens

by Leonard, S. P., Powell, J. E., Perutka, J., Geng, P., Heckmann, L. C., Horak, R. D., et al. (2020). *Science* 367, 573–576. doi: 10.1126/science.aax9039

In a recently published paper, Leonard et al. (2020) described a genetically modified gut bacterium for the delivery of dsRNA to adult honey bees. Furthermore, by engineering the symbiont to interfere with the expression of some *Varroa* genes, the authors showed the potential of this method for the control of the most important threat to honey bees: the parasitic mite *Varroa destructor*. The paper, beyond presenting a powerful, novel tool for the study of functional genomics in bees, rekindled hopes that an effective method to control the *Varroa* mite could be developed (Paxton, 2020). However, a careful evaluation of the proposed method in light of ecological and evolutionary principles reveals that it may be less promising than hoped.

The need to consider honey bee diseases in the framework of ecological and evolutionary principles has been recognized (Brosi et al., 2017); however, some peculiar features of the biological cycle of *V. destructor*, have been overlooked so far. Importantly, little attention has been paid to the possible adaptation of the mite (Eliash and Mikheyev, 2020).

The *Varroa* mite, together with the pathogenic deformed wing virus, causes huge losses of honey bee colonies in the northern hemisphere (Carreck and Neumann, 2010), threatening the pollination service provided by *Apis mellifera* (Potts et al., 2010). The mite's life cycle includes a phoretic phase, on adult bees, and a reproductive phase, within the brood cells (Nazzi and Le Conte, 2016). Only mites entering a brood cell before sealing can reproduce while phoretic mites are exposed to high mortality, including that caused by control methods applied by beekeepers. In fact, most available chemical control methods for the mite, including both synthetic chemicals (e.g., the pyrethroid Tau-fluvalinate), essential oil components (e.g., Thymol), and widely used organic acids (e.g., Oxalic acid), act only upon phoretic mites (Rosenkranz et al., 2010). Actually, even the possible novel methods based upon engineered symbionts (Leonard et al., 2020), would act primarily upon phoretic mites; in fact, differently from adult bees, the preimaginal stages, where mite reproduction takes place, are colonized only by an erratic gut community (Kwong and Moran, 2016) and may therefore be not suited for a method based on an engineered gut bacterium.

Therefore, we can conclude that the majority of control methods, by impacting the parasites on adult bees, likely select for mite strains with a reduced phoretic phase, resulting in a high proportion of mites in brood, and an accelerated population growth.

Any possible hereditary trait influencing mite's cell invasion, such as, for example, a differential response to semiochemicals from brood cells (Nazzi et al., 2004), would determine the proportion of mites in brood and thus reproduction. Therefore, such traits play a critical role in the development of infestation and are likely under intense selective pressure. However, some interventions can influence the mortality of mites within brood cells, thus attenuating that pressure

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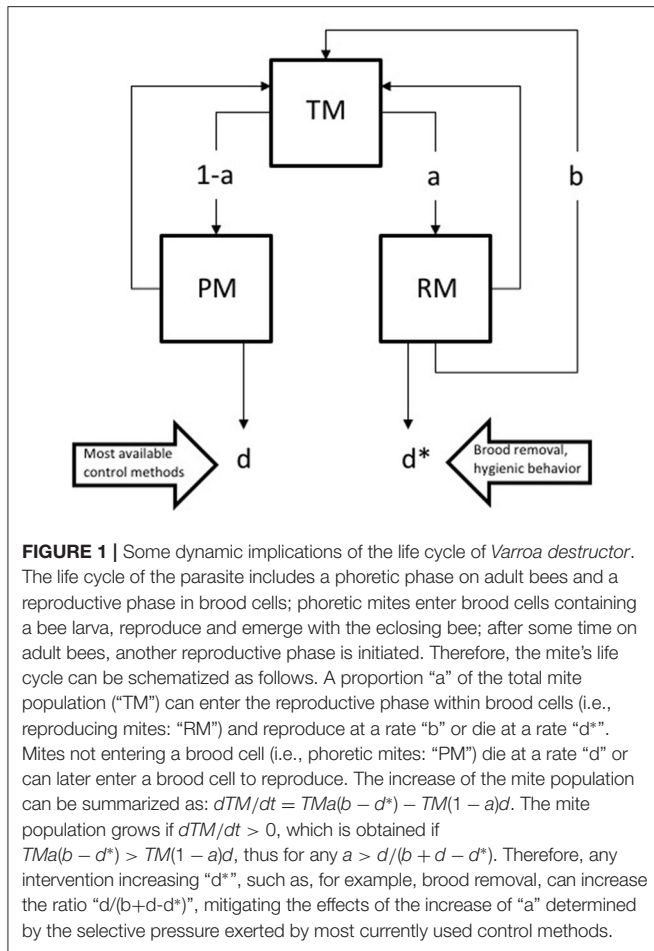
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(Figure 1). These methods include the selection of hygienic bees that recognize and remove infested brood, biotechnical control

## REFERENCES

- Brosi, B. J., Delaplane, K. S., Boots, M., and de Roode, J. C. (2017). Ecological and evolutionary approaches to managing honeybee disease. *Nat. Ecol. Evol.* 1, 1250–1262. doi: 10.1038/s41559-017-0246-z
- Carreck, N., and Neumann, P. (2010). Honey bee colony losses. *J. Apic. Res.* 49, 1. doi: 10.3896/IBRA.1.49.1.01
- Eliash, N., and Mikheyev, A. (2020). Varroa mite evolution: a neglected aspect of worldwide bee collapses? *Curr. Opin. Insect Sci.* 39, 21–26. doi: 10.1016/j.cois.2019.11.004
- Greatti, M., Milani, N., and Nazzi, F. (1992). Reinfestation of an acaricide-treated apiary by *Varroa jacobsoni* Oud.. *Exp. Appl. Acarol.* 16, 279–286. doi: 10.1007/BF01218569
- Kwong, W. K., and Moran, N. A. (2016). Gut microbial communities of social bees. *Nat. Rev. Microbiol.* 14, 374–384. doi: 10.1038/nrmicro.2016.43
- Leonard, S. P., Powell, J. E., Perutka, J., Geng, P., Heckmann, L. C., Horak, R. D., et al. (2020). Engineered symbionts activate honey bee immunity and limit pathogens. *Science* 367, 573–576. doi: 10.1126/science.aax9039
- Milani, N., Pechhacker, H., and Della Vedova, G. (1999). Reduced fertility in a European population of *Varroa jacobsoni* Oudemans. *Apidologie* 30, 435–436. doi: 10.1051/apido:19990211
- Nazzi, F., and Le Conte, Y. (2016). Ecology of *Varroa destructor*, the major ectoparasite of the western honey bee, *Apis mellifera*. *Annu. Rev. Entomol.* 61, 417–432. doi: 10.1146/annurev-ento-010715-023731

methods based upon brood removal and possible chemicals capable of crossing the cell sealing (Rosenkranz et al., 2010). As shown in figure legend, these latter control methods could balance the increase in the mite's invasion rate caused by the repeated use of currently available control methods; this, in turn, may have an important impact on the growth of the mite population. In fact, a selection program based on brood removal actually lead to the selection of an hypo-virulent mite strain (Milani et al., 1999).

Clearly, mite transfer between hives could hinder the development of such hypo-virulent mite populations and care should be taken to minimize this risk, for example by preventing robbing which represents a common cause of mite importation from collapsing hives into colonies with limited mite infestation (Greatti et al., 1992).

Indeed reinfestation, through which mites leading bee colonies to collapse can escape this dead end and get transferred to a new healthier colony, represents a critical point to be carefully considered under the evolutionary perspective outlined here.

Only sustainable beekeeping based upon an efficient control of Varroa mite, grounded on the evolutionary interpretation of this host-parasite interaction, will guarantee pollination continuity in a changing world.

## AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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- Nazzi, F., Milani, N., and Della Vedova, G. (2004). A semiochemical from larval food influences the entrance of *Varroa destructor* into brood cells. *Apidologie* 35, 403–410. doi: 10.1051/apido:2004023
- Paxton, R. J. (2020). A microbiome silver bullet for honey bees. *Science* 367, 504–506. doi: 10.1126/science.aba6135
- Potts, S. G., Biesmeijer, J. C., Kremen, C., and Neumann, P. (2010). Global pollinator declines: trends, impacts and drivers. *Trends Ecol. Evol.* 25, 345–353. doi: 10.1016/j.tree.2010.01.007
- Rosenkranz, P., Aumeier, P., and Ziegelmann, B. (2010). Biology and control of *Varroa destructor*. *J. Invertebr. Pathol.* 103 Suppl 1, S96–119. doi: 10.1016/j.jip.2009.07.016

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