

## Transcriptional Response of Honey Bee to Differential Nutritional Status and Nosema Infection

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**Abstract :** Bees are confronting several environmental challenges, including the intermingled effects of malnutrition and disease. Intuitively, pollen is the healthiest nutritional choice; however, commercial substitutes, such as BeePro and MegaBee, are widely used. Herein we examined how feeding natural and artificial diets shapes transcription in the abdomen of the honey bee, and how transcription shifts in combination with Nosema parasitism. Gene ontology enrichment revealed that, compared with poor diet (carbohydrates (C)), bees fed pollen (P > C), BeePro (B > C), and MegaBee (M > C) showed a broad upregulation of metabolic processes, especially lipids; however, pollen feeding promoted more functions and superior proteolysis. The superiority of the pollen diet was also evident through the remarkable overexpression of vitellogenin in bees fed pollen instead of MegaBee or BeePro. Upregulation of bioprocesses under carbohydrates feeding compared to pollen (C > P) provided a clear poor nutritional status, uncovering stark expression changes that were slight or absent relatively to BeePro (C > B) or MegaBee (C > M). Poor diet feeding (C > P) induced starvation response genes and hippo signaling pathway, while it repressed growth through different mechanisms. Carbohydrate feeding (C > P) also elicited 'adult behavior', and developmental processes suggesting transition to foraging. Finally, it altered the 'circadian rhythm', reflecting the role of this mechanism in the adaptation to nutritional stress in mammals. Nosema-infected bees fed pollen compared to carbohydrates (PN > CN) upheld certain bioprocesses of uninfected bees (P > C). Poor nutritional status was more apparent against pollen (CN > PN) than BeePro (CN > BN) or MegaBee (CN > MN). Nosema accentuated the effects of malnutrition since more starvation-response genes and stress response mechanisms were upregulated in CN > PN compared to C > P. The bioprocess 'Macromolecular complex assembly' was also enriched in CN > PN, and involved genes associated with human HIV and/or influenza, thus providing potential candidates for bee-Nosema interactions. Finally, the enzyme Duox emerged as essential for guts defense in bees, similarly to Drosophila. These results provide evidence of the superior nutritional status of bees fed pollen instead of artificial substitutes in terms of overall health, even in the presence of a pathogen.

**Keywords :** honeybee, immunity, Nosema, nutrition, RNA-seq

**Conference Title :** ICE 2018 : International Conference on Entomology

**Conference Location :** Paris, France

**Conference Dates :** October 29-30, 2018