

## Lessons from honeybee transcriptional profiles

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Our major goal is to understand the gene expression profiles and regulation in the highly eusocial honey bee, *Apis mellifera*. Here in brief, we summarize eight years of research. First, we generated 5,021 high-quality Open Reading frame Expressed Sequence Tags (AmORESTES) covering the entire worker life cycle. About 16% of the clusters shared homology to the Insecta clade, while 23% of the clusters represent *Apis* unique genes. Based on the *in silico* assignments, we chose 12 AmORESTES representing diverse gene families (*lipophorin*, *adh*, *esterase*, *sparc*, *hexokinase*, *idgf*, *hexamerin*, *abd-1*, *app-bp 1*, *famet p450*, *actin*) to learn worker gene expression patterns. These genes, categorized according to functional ontologies, are strikingly conserved throughout insect orders and several of them presented a temporal expression pattern, suggesting a hormonal regulation during development and metamorphosis. Second, in accordance with the honeybee genome consortium, we detected both highly conserved (meiosis-associated factors) and loss of reproduction genes (*gurke*, *torso* and *truck*). We also annotated differentially expressed genes during caste development and found specific upstream motifs, providing trends in cis-regulatory network regulating female differentiation. Further, using annotated honeybee microRNAs from miRBase, we scanned 1,000 nucleotides after the last exon (potential 3'UTR) of 10,157 predicted genes to detect miRNA targets for regulation. Most of the miRNAs were found to regulate several target genes, thus indicating cooperative translational control, for eg., miR-282 (518 targets) was the highly represented, regulating transport and sex differentiation genes. Third, toward post-genomic functional approaches, we developed a non-invasive method for honeybee gene knockdown, using *vitellogenin* RNAi (dsVg-RNA) delivered orally to the larvae that significantly decrease the mRNA target expression. The non-invasive method was feasible and culminates in a versatile cost-efficient approach. Overall, we are providing new insights for the comprehension of basic biological processes and gene regulation in this insect.

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