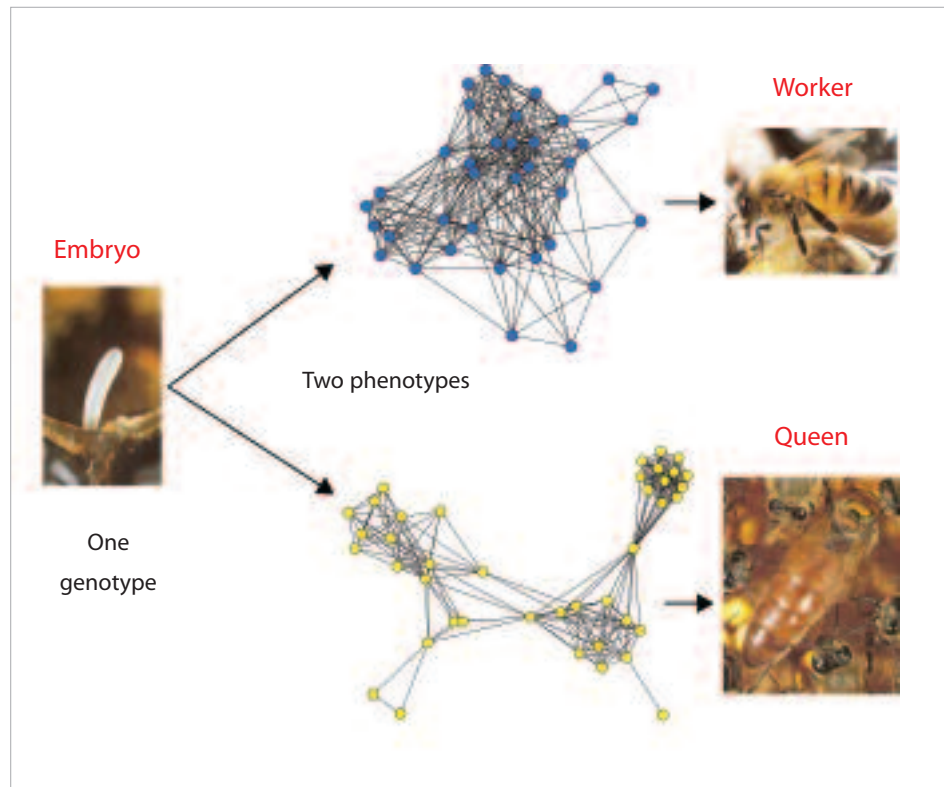


***Apis mellifera* FUNCTIONAL GENOME – SEARCH FOR NEW GENES AND INTEGRATED NETWORK IN THE CONTEXT OF DEVELOPMENT, REPRODUCTION AND CASTE DIFFERENTIATION**

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With an active contribution (5021 ORESTES, deposited in the GenBank) and participation in the annotation of the recently sequenced genome of the honey bee our group now has consolidated knowledge and expertise in all aspects required for large-scale analyses of gene expression in honey bees. Following our long term questions of interest on mechanisms underlying caste and sex determination and those involved in reproduction and division of labor, already formulated in the pré-genomic era of honey bee research, we are now proposing a large-scale analysis of gene expression in different phases of the honey bee life cycle. We will focus on the following questions: the identification of genes involved in caste development, in programmed cell death of the larval ovary, in integument differentiation, in the activation of the adult ovary of queens and workers, in the functional cycle of the hypopharyngeal glands, and in early embryonic sex determination. In addition, we will screen our libraries for putative micro-RNAs to unveil the participation of this novel group of post-transcriptional regulators in the above contexts. The project adopts a dual strategy, a) the identification of candidate genes in the honey bee genome based on prior knowledge of gene function in other organisms, especially Gene Ontology attributes registered in



*Networks depicting gene interaction based on the occurrence of overrepresented motifs in the Upstream Control Regions of Differentially Expressed Genes between *A. mellifera* castes*

flybase, and b) the search for novel genes by microarrays, subtractive hybridization strategies, and the generation of an embryonic cDNA library. The differential expression of all these genes will be tested and candidates of specific interest will be investigated by quantitative RT-PCR and silencing by RNAi. The joint information on gene expression in these contexts will be subjected to network analysis in order to detect functional linkage and organization in gene expression networks.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

Investigating molecular underpinnings of honey bee caste development, differential reproduction and division of labor were perceived as core elements of our proposal. Our group had participated and coordinated the annotation of genes related to caste development and reproduction in the genome sequence project of *Apis mellifera*. The companion paper produced by our group comprised a bioinformatics analyses of genes specifically expressed in caste development. A subsequent expansion on this analysis on differential gene expression in queen versus worker development was based on new experimental data from micro array analyses and used a network approach to connect genes via their revealed putative upstream control region elements. These results paved the way for novel approaches to the study of developmental processes and their regulation in honey bees, for example the study of genes underlying the hormonally controlled expression of caste-specific morphological characters, such as the corbicula on the hind leg of workers and the massive autophagic cell death in the ovaries of worker larvae leading to the highly divergent ovary phenotypes observed in adult honey bee queens and workers. Further analyses along these lines are now being performed which will contribute to our understanding of queen/worker development by expression analyses of candidate genes or large scale differential gene expression screens. Such expression analyses, however, are only the first step towards understanding gene function, and in this direction our group has contributed to the field of honey bee functional genomics through the establishment of a successful RNAi approach, silencing gene function of the yolk protein vitellogenin. We focused on this gene, which is abundantly expressed in the female sex, both in queens and workers. There are novel functions postulated to vitellogenin, as a major regulator of longevity, which clearly is a major difference between queens and workers. In addition, vitellogenin was postulated to interact with juvenile hormone in a negative feedback circuitry to regulate the transition of a worker bee from within-hive tasks to foraging. Such aspects of functional genomics on major life history determinants were and are successfully being explored by our group in collaboration with Dr. Gro Amdam (Arizona State University) and Dr. Dolors Piulachs (Institut de Biologia Molecular de Barcelona, CID, CSIC).

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