

Honeybee genome

The Western honeybee, *Apis mellifera*, is a key model for social behavior and is essential to agriculture and global ecology because of its pollination activity. There are striking differences in the size of gene families in the honeybee genome relative to other sequenced genomes for several important protein and domain families. These differences, which involve both larger and smaller gene numbers, as well as other novel features of the honeybee genome, have been suggestively related to the social lifestyle of the honeybee.

Compared with other sequenced insect genomes, the *A. mellifera* genome has high DNA contents of A+T (adenosine plus thymidine); lacks major transposon families (a transposon is a genetic element that comprises large discrete segments of DNA capable of moving from one chromosome site to a new location); has evolved more slowly; and is more similar to vertebrates with regard to circadian rhythm, RNA interference, and DNA methylation genes, among others. Furthermore, *A. mellifera* has fewer genes for innate immunity, detoxification enzymes, cuticle-forming proteins; and gustatory receptors; more genes for odorant receptors; and novel genes for nectar and pollen utilization—consistent with its ecology and social organization. Compared with *Drosophila*, genes in early developmental pathways differ in *Apis*, whereas similarities exist for functions that differ markedly, such as sex determination, brain function, and behavior. Population genetics suggests an African origin for the species *A. mellifera* and provides insights into whether Africanized bees (also known as “killer bees”) spread throughout the New World via hybridization or displacement.

Social behavior. Honeybees are known as paragons of sociality, living in societies that rival human societies in complexity and cohesion. Honeybees are eusocial, which means their colony’s population is differentiated into queens that produce offspring and nonreproductive altruistic workers that communally gather and process food, care for young, build nests, and defend their hive.

Social evolution endowed honeybees with impressive traits. Queens and workers come from the same genome, but queens—usually one per colony—have 10 times the life span of workers (typically queens live for several years), lay up to 2000 eggs per day, and store sperm for years without losing viability. Workers, numbering tens of thousands per colony, display sophisticated cognitive abilities, despite a brain containing only 1 million neurons, which is five orders of magnitude less than the human brain. Worker bees can learn to associate a flower’s color, shape, scent, or location with a food reward, thereby increasing the efficiency with which they gather nectar and pollen. Worker bees can even learn abstract concepts such as “same” and “different,” which presumably also increases their ability to home in on the most profitable flower patches. Honeybees that find a good source of food return to the hive and



Honeybee on a DNA fragment analysis map. (Photo by Peggy Greb/USDA)

communicate their discovery with a “dance language,” the only known nonprimate symbolic language, in which information regarding the location of a food source is transmitted from a “finder” bee to others within the hive.

Benefits to humans. Honeybees benefit humankind in exceptionally broad ways. In agriculture, honeybees are the most important pollinators of food and fiber crops, with a value of about \$15 billion dollars annually in the United States alone. Of course, they also produce honey. In biology and biomedicine, honeybees are popular model research organisms in diverse areas including allergic disease, development, gerontology, neuroscience, social behavior, and venom toxicology. However, honeybees are also threatened by human activity, perishing due to insecticides that indiscriminately may kill both pests and beneficial insects, and exotic parasitic mites vectored around the world by human commerce. The sequencing of the genome of the Western honeybee, *A. mellifera* (see **illustration**), was carried out in order to advance basic biology and applied apiculture.

Genome sequencing project. With primary financial support from the National Institutes of Health–National Human Genome Research Institute and a contribution from the U.S. Department of Agriculture, the honeybee genome sequencing project began in December 2002. The results of this sequencing effort, led by the Baylor College of Medicine’s Human Genome Sequencing Center, but with contributions from over 100 research laboratories from 16 countries, were published in over 50 papers in many prominent scientific journals.

The genome of the honeybee contains a total of approximately 250 million bases of DNA. Approximately 10,000 genes have been identified to date, primarily on the basis of computer programs for gene prediction. This is lower than the 13,000 genes identified from the genome of the fruit fly (*Drosophila melanogaster*), which is one of the most intensively studied genomes in all of biology. It is expected that the number of genes identified in the honeybee genome will increase in the future.

The honeybee genome contains a greater proportion of the adenine (A) and thymine (T) nucleotides than does the *Drosophila* genome. Moreover, genes are not distributed evenly throughout the bee genome, but show a tendency to appear in (A+T)-rich regions. This is the exact opposite of the situation in the human genome, in which the preponderance of genes are located in regions of the genome that contain greater proportions of the guanine (G) and cytosine (C) nucleotides. Understanding the basis of these fundamental differences promises to illuminate our understanding of genome organization and illustrate the benefits of comparative genomics.

It often takes some time for the results of a genome sequencing project to lead to major scientific discoveries. However, already some tantalizing findings have emerged from the honeybee genome that might reflect the bee's intense social life. Five are listed below.

Pace of evolution. It appears that the honeybee genome evolved more slowly than the genomes of two other insects that have had their genomes sequenced, the fruit fly (*D. melanogaster*) and the malaria mosquito (*Anopheles gambiae*). One consequence of that slower evolutionary pace is that the bee genome contains versions of some important genes found in mammals that have been lost from these other two insect genomes. Is the honeybee more slowly evolving than most organisms, or have the fly and mosquito (both members of the order Diptera) evolved faster? Moreover, if the honeybee is evolving more slowly, is that because of the bee's social lifestyle? These questions can only be answered by future analyses of genome sequences for more species.

Killer bee invasion biology. Population genetic analyses based on the honeybee genome have generated exciting new insights into the longstanding controversy of whether Africanized bees ("killer bees," *Apis scutellata*) spread throughout the New World via hybridization or displacement. The answer is *both!*

Africanized honeybees were introduced to Brazil from Africa in 1956 in order to breed a strain more suited for the tropical climate. The plan was to breed out the aggressiveness of *A. scutellata* before releasing the bees, but they were accidentally released before this could happen. Africanized bees spread throughout the New World, reaching the United States in 1990. This spread of Africanized honeybees has been one of the most spectacular examples of a biological invasion.

Analyses of the honeybee genome reveal that this biological invasion has involved extensive hybridization with European subspecies, but the genomes of some subspecies appear to be more resistant to domination than others. Genes from *A. scutellata* have largely replaced many genes from one previously dominant subspecies of honeybee, *A. mellifera ligustica* (the "Italian bee"), while *A. m. mellifera* (the "German black bee") genes have been essentially unchanged. It will be fascinating to learn why these two subspecies show different "susceptibilities" to Africanization, and what this might mean for the genetics of aggressive behavior.

Genome deficiencies and risk. Relative to the fruit fly and mosquito, honeybees show a remarkable reduction in the size of gene families associated with the detoxification of harmful chemicals encountered in the environment. Honeybees also show a similar reduction in the size of gene families that encode components of the immune system. Why this is so is a mystery, especially since life in a densely populated beehive would seem to put bees at special risk for environmental toxins, pathogens, and parasites. Perhaps this is why honeybees are extremely vulnerable to many types of insecticides and have suffered major population losses in some agricultural regions of the world, including the recent reports of devastating losses due to Colony Collapse Disorder. On the other hand, it appears that bee social evolution has also led to novel behavioral mechanisms of protection, such as the ability of some "nurse bees" to detect and remove diseased larvae from the hive, and the collection by foragers of plant-produced resins with antimicrobial activity that are used to coat the walls of the beehive.

Sensible sensory genes. Honeybees have a smaller number of genes encoding taste receptors, but a larger number of genes encoding smell receptors. The limited gustatory receptor repertoire perhaps reflects their lessened need to avoid toxic chemicals in their food—unlike herbivorous insects, bees and plants enjoy a strongly mutualistic relationship. Plants need bees for pollination and produce nectar as a reward to entice them to visit. There are very few poisonous nectars in the world. By contrast, honeybees rely heavily on olfaction to find flowers outside and to exchange and interpret chemical messages in the hive. Chemical communication is especially well developed in the bee society, with over a dozen pheromones identified and many others remaining to be discovered.

Effect of methylation. The honeybee is the first insect known to possess all the genes necessary to encode a complete, vertebrate-like system for "epigenetic" control of gene activity by methylation (in general, DNA methylation has been found to have a repressive effect on gene activity). Epigenetics (the study of those processes by which genetic information ultimately results in distinctive physical and behavioral characteristics) is increasingly recognized as a potent force in the regulation of genome activity in humans and other organisms, implicated in

disease and normal processes such as nutrition, brain development, and social behavior. It is not yet clear why the honeybee possesses this form of genome regulation whereas some other insects do not, or what exactly it does in the honeybee, but these issues are fertile topics for future investigation. Further, the ability to use an insect to study methylation is expected to result in improved understanding of the process in general.

Outlook. As these results illustrate, the sequencing of the honeybee genome is expected to usher in a bright era of bee research for the benefit of agriculture, biological investigations, and human health.

For background information *see* BEE; BEEKEEPING; GENETIC CODE; GENETIC MAPPING; GENOMICS; INVASION ECOLOGY; POLLINATION ; POPULATION GENET-

ICS; SOCIAL INSECTS in the McGraw-Hill Encyclopedia of Science & Technology. Gene Robinson

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