

Features of the honey bee *Apis mellifera* genome versus fruit fly *Drosophila melanogaster*

Abstract

The analysis of the nuclear and the mitochondrial genomes of the honey bee *Apis mellifera* in comparison with the well-annotated, finished fruit fly *Drosophila melanogaster* genome was presented in this article. The nuclear genome of the honey bee has about 245 millions b.p. which distributed in 16 chromosomes and contains about 10 thousands genes. The mitochondrial genome of the *A. mellifera* has about 16 thousands b.p. which located in mitochondrion's and contains 35 genes. The nuclear genome of the fruit fly has about 144 millions b.p. which distributed in 4 chromosomes and contains about 17 thousands genes. The mitochondrial genome of the *D. melanogaster* has about 19 thousands b.p., which located in mitochondrion's and contains 37 genes. Despite the full sequencing of the nuclear and the mitochondrial genomes of the *A. mellifera* the function of several genes and loci of *A. mellifera* are not disclosed fully. A comparative analysis of the genomes of *A. Mellifera* and *D. melanogaster* using bioinformatics techniques allowed to reveal the features of the structure and function of the honey bee *A. mellifera* genome. The genome of *A. Mellifera* have more similarity with the vertebrate genome than *D. melanogaster*. The genome of *A. Mellifera* contains less genes of the native immunity, of detoxification enzymes, of cuticle proteins and taste receptors compared with *D. melanogaster*. However, *A. mellifera* contains new genes associated with olfactory receptors, the processing of pollen and nectar, poison organs, wax glands, caste determination and labor division which absent at *D. melanogaster*. Probably, this is due to the ecology of bees and their social evolution.

Keywords: nuclear genome, mitochondrial genome, *apis mellifera*, honey bee, genes, chromosomes

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Ilyasov RA

Institute of Biochemistry and Genetics, Russian Academy of Sciences, Russia

Correspondence: Ilyasov RA, Institute of Biochemistry and Genetics, Ufa Research Center, Russian Academy of Sciences, Ufa, 450054, Russia, Email apismell@hotmail.com

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Abbreviations: RTK, receptor tyrosine kinase; HH, hedgehog; TGF-B, transforming growth factor-B; JAK, janus kinase; STAT, signal transducer and activator of transcription; EAAT, excitatory amino acid transporters; SCR, sex combs reduced; ANTP, antennapedia, ABD-A, abdominal-A; EN, engrailed; MSH, muscle segment homeobox

Introduction

There was only two sequenced genomes of the two Dipterans species *Drosophila melanogaster*¹ and *Anopheles gambiae*² before the recent sequencing of the honey bee *Apis mellifera* (Hymenoptera), *Tribolium castaneum* and *Bombyx mori* genomes. Hymenoptera diverged from Dipterans about 300 million years ago, and recent phylogenetic evidence implies that the *Apis* are the most distant group of holometabolous insects from *Drosophila*.³⁻⁵ The honeybee genome was compared with the well-annotated, finished *D. melanogaster* genome. The *D. melanogaster* genome is most studied of all the genomes. Despite *A. mellifera* is very economically important insect a few studies of its full genome have been published. Therefore, comparative analysis of two genomes the *A. mellifera* and *D. melanogaster* is very interesting. Differences between *A. mellifera* and *D. melanogaster* caused by not only the nucleotide polymorphism of the genes but also by their different epigenetical regulation. Superficially, *A. mellifera* development is similar to that of *D. melanogaster*, in that it is a holometabolous. However, *A. mellifera* are different in their development and biology from the *D. melanogaster* in a number of ways. There is a hypothesis that all the differences that are observed between *A. mellifera* and *D. melanogaster*, have occurred since their divergence. This hypothesis is confirmed by the differences observed between *A. mellifera* and *D. melanogaster* in the

early stages of development.⁶⁻⁸ Thus, *A. mellifera* use haplodiploidy to determine sex, a process different from that of sex determination in *D. melanogaster*. The adult honey bee's *A. mellifera* has several novel evolutionary innovations not present in *D. melanogaster*, including poison organs and wax glands. Most important are the caste determination and labor division associated with the social nature of the honey bee.⁵

The nuclear genome of the honey bees *A. mellifera* has 246 927 000 b.p. which subdivided into 16 chromosomes and containing 10 157 genes (Gene Bank access AADG00000000).^{6,7} The mitochondrial genome of the honey bees has 16 343 b.p. which represented by a circular molecule of DNA and containing 35 genes (Gene Bank access NC_001566).⁸ All chromosomes of the honey bees has different sizes: LG 1 (NC_007070) 30 000 b.p. contains 1669 genes (25 non coding genes); LG 2 (NC_007071) 15500 b.p. - 814 genes (27 non coding genes); LG 3 (NC_007072) 13200 b.p. - 735 genes (20 non coding genes); LG 4 (NC_007073) 12700 b.p. - 709 genes (46 non coding genes); LG 5 (NC_007074) 14400 b.p. - 874 genes (13 non coding genes); LG 6 (NC_007075) 18500 b.p. - 844 genes (15 non coding genes); LG 7 (NC_007076) 13200 b.p. - 596 genes (9 non coding genes); LG 8 (NC_007077) 13500 b.p. - 873 genes (33 non coding genes); LG 9 (NC_007078) 11100 b.p. - 584 genes (17 non coding genes); LG 10 (NC_007079) 13000 b.p. - 768 genes (11 non coding genes); LG 11 (NC_007080) 14700 b.p. - 968 genes (16 non coding genes); LG 12 (NC_007081) 11900 b.p. - 504 genes (14 non coding genes); LG 13 (NC_007082) 10300 b.p. - 418 genes (13 non coding genes); LG 14 (NC_007083) 10300 b.p. - 612 genes (8 non coding genes); LG 15 (NC_007084) 10200 b.p. - 730 genes (30 non coding genes); LG 16 (NC_007085) 7200 b.p. - 420 genes (26 non coding

genes)(Gene Bank - <http://www.ncbi.nlm.nih.gov>, EnsemblMetazoa - <http://metazoa.ensembl.org>). For comparison, the nuclear genome of the fruit flies *D. melanogaster* has 143 726 000 which sub divided into four chromosomes(2 large, 1 small autosomes and the X/Y sex chromosomes) and containing 17 651 genes(3 384 non coding genes)(Gene Bank access GCA_000001215.4).¹ The mitochondrial genome of the fruit flies has 19 524 b.p. which represented by a circular molecule of DNA and containing 37 genes(Gene Bank access NC_024511.2).⁵ All chromosomes of the fruit flies has different sizes: 2L(NT_033779.5) 23510 b.p. contains 3485 genes(770 non coding genes); 3L(NT_037436.4) 28110 b.p. contains 3453 genes(666 non coding genes); 4(NC_004353.4) 1350 b.p. contains 112 genes(26 non coding genes); X(NC_004354.4) 23 540 b.p. contains 2661 genes(408 non coding genes); Y(NC_024512.1) 3 670 b.p. contains 113 genes(28 non coding genes)(Gene Bank- <http://www.ncbi.nlm.nih.gov>, Ensembl Metazoa - <http://metazoa.ensembl.org>).

The nuclear and mitochondrial genome of *A. mellifera* differ from *D. Melanogaster* by high containing of AT-rich regions. Since the *A. mellifera*'s nuclear genome contains 67% and the mitochondrial genome - 85% AT whereas *D. melanogaster*'s nuclear genome contains 58% and the mitochondrial genome - 79% AT nucleotides.⁹ The nuclear and mitochondrial genome of *A. mellifera* characterized by greater spatial heterogeneity of AT-rich areas, higher content of CpG islands and absence of the most common families of transposons than at *D. melanogaster*. The genes of *A. mellifera* predominantly located in AT-rich areas and characterized by high content of GC nucleotides. The A and T nucleotides of AT-rich areas in protein coding genes of *A. mellifera* are located in second and third positions predominantly.^{6,7} The structure and localization of most common genes in *A. mellifera* differ from *D. melanogaster*. In the *A. mellifera* mitochondrial genome 11 genes of tRNA has shift position as compared with *D. melanogaster*. The genetic code of *A. mellifera* similar to *D. Melanogaster* but two anticodons of tRNA differ(tRNALYS -TTT, tRNASER - TCT in *A. mellifera* and tRNALYS - CTT, tRNASER - GCT in *D. melanogaster*).⁸

Some nuclear genes of the *A. mellifera* are orthologs to the *D. melanogaster* genes, which has differences in sizes. Thus in *A. mellifera* the genes of Yellow/Major Royal Jelly Protein is larger, the genes of cuticular proteins is smaller, the genes of odorant receptors is larger, the genes of gustatory receptors is smaller, the genes of immunity is smaller, the detoxification genes is smaller than in *D. Melanogaste*.^{6,10} In the *A. mellifera* genes the trans versions occurred more frequently than transition whereas in *D.melanogaster* it is conversely. In the *A. mellifera* genes trans versions occurred on third position of codons. Some genes of *A. mellifera* arisen as a result of evolutionary changes of the genes of common with *D.melanogaster* ancestors. Thus, the gene of *A. mellifera* encoding the major protein of royal jelly is derived from the ancient gene yellow, which presented in *D. melanogaster*. Many genes of *A. mellifera* and *D.melanogaster* is similar, but some genes of *D. Melanogaster* is absent in *A. mellifera*. For example, in *A.mellifera*, the genes of WNT cell signalling pathways as Hedgehog(HH), Transforming Growth Factor-B(TGF-B), Receptor Tyrosine Kinase(RTK), NOTCH, Janus Kinase(JAK), Signal Transducer and Activator of Transcription(STAT) are similar with *D. melanogaster*. However, the genes of cell signalling systems(Terminal Embryo Fate, TRUNK, TORSO), of component of the dorso-ventral signalling system(GURKEN), of the G-protein-coupled receptor(mGluR-like) family(BOSS) are missing from the *A. mellifera* genome.⁶

Some genes of the *D. melanogaster* has novel features in the

A. mellifera. Thus, the gene of the Glucose-methanol-choline oxidoreductases family(NINAG) in *A. mellifera* presents as two putative NINAG-like genes, the gene of the receptor protein tyrosine kinase family(INR) in *A. mellifera* is duplicated; the gene of the phosphor lipase C family(NORPA) in *A. mellifera* is duplicated, the gene of the photoreceptor-cell-specific nuclear receptor family(PNR) in *A. mellifera* presents as three genes versus two genes in *D.Melanogaster*,the gene of the TRPA subfamily of transient receptor potential channels family(TRPA) are missing in *D. melanogaster*, but has two extra TRPA channels(GB14005 and GB16385) in *A. mellifera*; the gene of the ligand-gated ion channels family(NACR) in *A. mellifera* presents as 11 subunits instead of 10 in *D. Melanogaster*; the gene of the ligand-gated ion channels family(NMDAR) in *A. mellifera* presents as 3 genes instead of 2 in *D. Melanogaster*; the gene of the excitatory amino acid transporters family(EAAT) in *A. mellifera* presents as 5 genes instead of 2 in *D. Melanogaster*.⁶ In *A. mellifera* 96 homeobox domains were found in 74 genes, similar to *D. melanogaster*. More than 90% identity represented by homeobox genes(Sex Combs Reduced(SCR), Antennapedia(ANTP), Abdominal-A(ABD-A); Engrailed(EN), Muscle Segment Homeobox(MSH)). For the remaining *A. mellifera* genes, a *D.melanogaster* homologue is not known. This indicates that structurally homologous genes are involved in the control of *A. mellifera* and *D. Melanogaster* development.^{6,11}

The nuclear genes of *A. mellifera* which responsible for circadian rhythms(CRY-M, CLK, CYC, PDP1, VRI, PER), RNA interference(RNAi) and DNA methylation(381 genes in eggs and sperm of *A. mellifera* with CpG methylation) have more similarity with genes of vertebrate than with genes of *D. Melanogaste*.¹²⁻¹⁵ The circadian rhythms genes Timeless(TIM1) and Crypto chrome(DCRY) of *D. melanogaster* are absent in *A. mellifera* genome. The similarity with vertebrate may be explained by the parallel evolution of the some genes during adaptation to the environment conditions. The genome of *A. mellifera* contains less genes of the native immunity, of detoxification enzymes, of cuticle proteins and taste receptors compared with *D. melanogaster*. However, *A. mellifera* contains new genes associated with olfactory receptors, the processing of pollen and nectar which absent at *D. melanogaster*. Probably, this is due to the ecology of bees and their social organization.^{5,16}

The rate of the evolutionary transformations of the nuclear and mitochondrial genome of *A. mellifera* less than in *D. melanogaster*. However, the genome of *A. mellifera* diverged more from common ancestor than *D. Melanogaster*.^{17,18} Probably, this is due to the small effective population size of *A. mellifera* and to low rate of the reverse mutation compared with *D. Melanogaster*.¹⁹ Micro RNA(miRNA) of the nuclear genome of *A. mellifera* plays an important role in the regulation of social organization and caste differentiation via post-transcriptional regulation of gene expression. About 300 honey bee miRNAs deposited in miRBase (<http://www.mirbase.org>).²⁰ For example, differentially expressed miRNAs between 4day-old queen and worker larvae of honey bees: up-regulated in queen larvae(ame-bantam, ame-let-7, ame-mir-10, ame-mir-100, ame-mir-6001-3p); equally expressed in queen larvae(ame-mir-11, ame-mir-1175, ame-mir-190, ame-mir-6065, ame-mir-989); down-regulated in queen larvae(ame-mir-13b, ame-mir-252a, ame-mir-2765-5p, ame-mir-996, ame-mir-9a).²¹ In the nuclear genome of *A. mellifera* found miRNA, which characterized by caste specific expression: the miRNA C5599F most expressed in the queens, C689F - in the pupae, C5560 - in the pupae of workers.⁷ Thus, the genome of *A. mellifera* have more similarity with the vertebrate genome than *D. melanogaster*. The genome of *A. mellifera* contains less genes of the native immunity,

of detoxification enzymes, of cuticle proteins and taste receptors compared with *D. melanogaster*. However, *A. mellifera* contains new genes associated with olfactory receptors, the processing of pollen and nectar, poison organs, wax glands, caste determination and labor division which absent at *D. melanogaster*. Probably, this is due to the ecology of bees and their social evolution. A comparative analysis of the genomes of *A. mellifera* and *D. melanogaster* using bioinformatics techniques allowed revealing the features of the structure and function of the honey bee *A. mellifera* genome. It is very important for understanding the human genome also.

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Conflict of interest

Author declares that there is no conflict of interest.

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