Transcriptomics: Open Access
ISSN: 2329-8936

Fedorova et al., Transcriptomics 2016, 4:2
DOI: 10.4172/2329-8936.1000137

Review Article Open Access

# Genes and Ontogenes in Drosophila: The Role of RNA Forms

**Fedorova NB*, Chadova EV and Chadov BF**

*Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences, Novosibirsk, Russian Federation*

## Abstract

The independent hereditary factors, such as Mendelian genes, are not sufficient for the existence and operation of genetic systems. The hereditary factors of different type were searched for. A new class of mutations, referred to as conditional mutations, was discovered in *Drosophila melanogaster*. Such a mutation dies in a restrictive genotype but survives and reproduces in a permissive genotype. Besides their conditional nature, mutations in a permissive genotype display a set of specific features that drastically distinguish them from conventional mutations, namely, they (1) are dominant; (2) are as a rule, lethal; (3) have drastically decreased fertility; (4) interact with chromosomal rearrangements; (5) switch the genome from a stable to an unstable state; (6) increase the basal metabolism; (7) induce modifications and morphoses; and (8) their manifestation is inherited in a parental manner. Four properties of these mutations-conditional manifestation together with (1), (4), and (8) suggest that the mutant genes (1) are segments of DNA; (2) their products are RNA duplexes (3) active in germ cells and (4) repeated in the genome. Emergence of morphoses in mutants suggests that the genes are involved in the control of ontogeny. Correspondingly, these genes were named ontogenes. Thus, the genetic system comprises the genes working according to a DNA-RNA-protein script and the ontogenes following a DNA-RNA script. The first entity is engaged in production of the "building material" for the organism, proteins, while the second entity controls this process during preparation of the individual developmental program. These different functions of genes depend on the type of transcript formed from DNA as well as the time and place of its origin on DNA.

**Keywords:** Drosophila; Conditional mutation; Ontogene; Short RNA

## Introduction

The goals of genetics are to explore and establish the link between a trait and a heredity factor. In turn, the central dogma of molecular biology posits the flow of genetic information from DNA through RNA to protein, which ultimately forms a trait. In this currently accepted scenario, the genetic system is formed by universal genes that function to produce proteins. Nonetheless, multiple lines of evidence indicate that this is not the sole scenario of how genetic systems may operate.

Let us begin with logics. Modern genetics is based on the classic postulates that (i) any living organism represents a composite of individual traits, (ii) each trait is controlled by independent heredity factors, i.e., genes, and (iii) changes in genes may result in changes in traits. Mendel's idea on the independence of heredity factors is central to the classical genetics. Yet, is it universally true that all heredity factors are independent?

It is clear that a living organism and a genome are systems. However, a functioning system cannot be composed only of the units all of which are independent of each other. Some units must be interdependent for a system to work. Modern genetics is very vague about existence of such interdependent units except for rather infrequent cases when certain proteins encoded by different genes interact and produce epistatic, pleiotropic, and other effects.

The goal of the work was to discover the units of genetic system (genes) that would depend on each other. We postulated that mutations in these genes, as a rule, should be dominant lethals; however, these mutations in exceptional cases had to survive. Any evolution of the living matter would be inconceivable without this possibility [1]. The target mutations in experiment should be in the form of a conditional dominant lethal, so that a mutation in one genotype kills its carrier versus another (permissive) genotype where this individual survives. The target mutations were searched for using *Drosophila melanogaster* [2,3].

It has emerged that the obtained mutations possess a set of specific features distinguishing them from the common mutations. Moreover, some of these specific features suggest that the mutant genes do not produce messenger RNA (mRNA) further translated into protein but rather give short RNA with a regulatory function. Eventually, the existence of two huge groups of genes (common genes and the so-called ontogenes) is determined by the production of two different types of RNA transcripts on the genomic DNA template, namely, mRNA and short RNA.

## Recovery of Conditional Mutations

Mutations were induced by ionizing radiation. The searched mutation was manifested in one genetic background and not in another. Figure 1 schematically shows how conditional dominant lethals were obtained in the X chromosome of *Drosophila melanogaster* [4,5]. Males were gamma-irradiated and crossed with the attached X females. Sons of the parents were individually crossed to yellow females. Sons that gave no female progeny from this cross were chosen as mutants. These sons contained the conditional mutation in the X chromosome. The mutation did not affect their viability. However, once present in the genome of a *yellow*/+ female, it became a dominant lethal: daughters died at the embryonic stage and the adult progeny contained only sons. The conditional mutation in this exemplary case is a dominant lethal. It is called conditional because it manifests as lethal in the mutant females heterozygous for yellow (one genetic background) but not in mutant males (another genetic background).

Another cross was used to recover conditional dominant lethals in chromosome 2 [4,5] (Figure 2). The mutation behaved as a dominant lethal when homologous chromosome 2 was structurally normal (one genetic background) but not as a lethal when the homologous chromosome contained the *Ins(2LR)* Curly inversion (another genetic

***Corresponding author:** Nina B Fedorova, Detskii proezd 9, Apt. 5, Novosibirsk, 630090, Russian Federation, Tel: +7(383)330-35-98; E-mail: bonife@bionet.nsc.ru

**Received** October 05, 2016; **Accepted** November 26, 2016; **Published** November 29, 2016

**Citation:** Fedorova NB, Chadova EV, Chadov BF (2016) Genes and Ontogenes in Drosophila: The Role of RNA Forms. Transcriptomics 4: 137. doi:10.4172/2329-8936.1000137

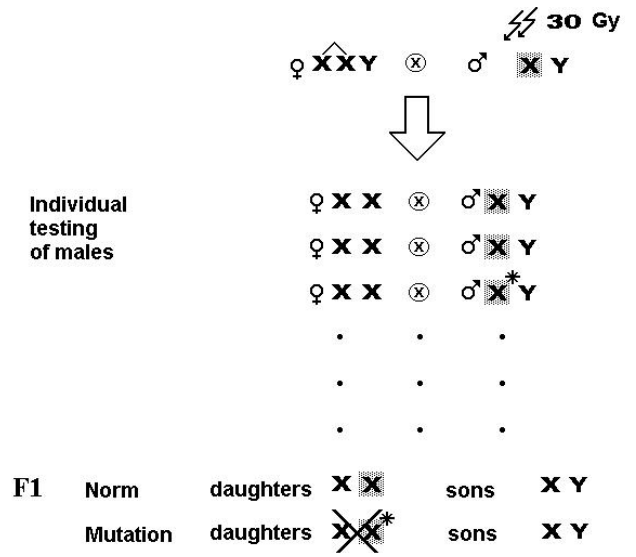


**Figure 1:** Detection of conditional dominant lethals in the X chromosome of *D. melanogaster*. Gamma-irradiated (30 Gy) Drosophila males were mated to females containing attached X chromosomes. Sons of this progeny were individually crossed to females from yellow mutant line. The X chromosome of the irradiated male is hatched. Asterisk indicates the same chromosome with mutation. In contrast to sons without lethal mutation, those that received the X with a dominant lethal were daughterless [5].

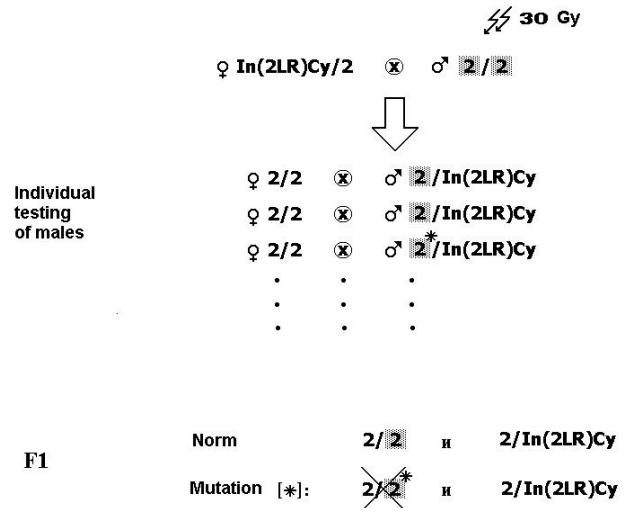


**Figure 2:** Detection of conditional dominant lethals in chromosome 2 of *D. melanogaster*. Gamma-irradiated (30 Gy) Drosophila males were crossed to females containing inversion *In(2LR)Cy* with dominant marker Curly in one of the chromosomes 2. The sons having this chromosome together with irradiated chromosome 2 (hatched) were individually crossed to yellow females, containing structurally normal chromosomes 2. The sons receiving chromosome 2 with a dominant lethal produced only Curly progeny [5].

background). A lethal effect of mutation obtained using this scheme is sex-independent, unlike the case of the conditional dominant lethals in the X chromosome [2,3].

Yet another way for obtaining conditional dominant lethals in the X chromosome took advantage of a modified version of recovery of recessive lethal mutation by Muller-5 method [6]. A collection of these mutants as *l/Muller-5* females was mated to males with a marked structurally normal X chromosome. Four cultures with a recessive lethal mutation in the X chromosome displaying unusual properties were distinguished. The lethal was a typical recessive lethal in the cross of an *l/Muller-5* female with a *Muller-5 male* (the routine way of maintaining recessive lethal mutations in the X chromosome). In this cross, the mutant female yielded one type of daughters (*l/Muller-5*) and one type of sons (*In(1)M-5*). However, the crosses of *l/Muller-5* females to structurally normal males gave sons of two phenotypes rather than one: *Muller-5* and wild type. The latter also received a recessive allele from the mutant female but it ceased to behave as a lethal because the paternal genotype with the inversion was changed [6].

In all three schemes, conditional mutations were recessive lethals in a usual permissive background. In the two first schemes, the mutations became dominant lethals when transferred to a provocative restrictive background. In the third scheme, the mutation lost its lethality when transferred this background. Permissive and restrictive backgrounds are arbitrary. What is important is that the response of mutations to change in the genetic background is reproducible in repeated crosses [2,3]. All three approaches to recovery of mutations are jointly referred to as the method of conditional lethals [4].

In one of the experiments, four mutant females tested for dominant lethality using yellow females produced homozygotes with a visible mutant phenotype. These were the females with two mutant X chromosomes. As for the males that had one mutant X chromosome, their phenotype was normal. We initially designated these conditional mutations *dimorphic* because the same mutations could give rise to two phenotypes, one in male (normal) and the other female (mutant) [7]. These four mutants may also be regarded as conditional mutations but with a visible phenotype. Sex here is the condition providing manifestation of the mutant phenotype.

The formation of unilateral defects in individual development termed morphoses [8-12] is a distinguishing feature of all recovered conditional mutations [7]. This phenomenon will be described in the section Conditional mutations and their unusual manifestation. The fourth approach for recovering conditional mutations utilized on the ability to develop morphoses. The idea was to select the individuals with developmental defects, i.e., morphoses, from the first generation progeny of irradiated parents. These flies were then tested for the presence of recessive lethals [13]. This methodological strategy allowed for recovery of another conditional mutation with visible phenotype and designated Small barrel (Smba) [13,14].

In total, we have performed eight experiments since the year of 2000 to recover conditional mutations in *D. melanogaster*. As a result, 60 conditional dominant lethals have been identified in the X chromosome; ten, in chromosome 2; and four, in chromosome 3. Six mutations had a visible phenotype.

## Conditional Mutations and their Unusual Manifestation

### Conditionality, lethality, and reduced fertility

Table 1 shows the numbers of flies in the progeny of the first 20 mutants for the X chromosome isolated in 2000 [2,3]. All of them were "daughterless". Mutations were conditional, i.e., *yellow*/+ daughters (restrictive genotype) died, whereas their fathers were viable carriers of mutation (permissive genotype). Mutants survived in the permissive genotype yet fathers were not entirely normal. The males were semisterile. The last column in Table 1 summarizes the fertility tests. The rate of laid eggs that developed to give larvae was very low.

### Morphoses, modifications, secondary mutations, and gynandromorphs

The progeny of mutant males frequently displayed morphoses [7,15]. Figures 3 and 4 illustrate the most striking examples of morphoses: two heads instead of one, an additional thorax with wing,

et al. Two specific features of morphoses are their unilateral pattern and absence of inheritance. The rate of the progenies carrying morphoses varied from several percent to tens of percent (Table 2). Sometimes all the progeny of mutant males had morphological defects.

The progeny of mutant males frequently displayed secondary mutations (Figure 5). Mutations were inherited and often were similar to the mutations well known in genetics. However, they have different genetical pattern despite similar phenotypes.

Phenotype-wise, the modifications [16] are copycats of the known

| Male mutant strain | Cross 2♀*y* × ♂+ | | Cross 6 ♀ *y* × ♂+ | | Male fertility* |
|---|---|---|---|---|---|
| | Total number of progenies | Rate of daughters | Total number of progenies | Rate of daughters | |
| 1 | 119 | 0.00 | 191 | 0.00 | 0.02 |
| 2 | 650 | 0.00 | 435 | 0.00 | 0.15 |
| 3 | 112 | 0.00 | 180 | 0.00 | 0.12 |
| 4 | 114 | 0.00 | 293 | 0.00 | 0.07 |
| 5 | 50 | 0.00 | 303 | 0.02 | 0.14 |
| 6 | 47 | 0.00 | 283 | 0.02 | 0.14 |
| 7 | 47 | 0.02 | 100 | 0.00 | – |
| 9 | 182 | 0.07 | 529 | 0.00 | 0.40 |
| 10 | 162 | 0.03 | 297 | 0.04 | 0.09 |
| 26 | 92 | 0.03 | 89 | 0.01 | – |
| 27 | 68 | 0.00 | 93 | 0.00 | 0.18 |
| 29 | 15 | 0.07 | 61 | 0.00 | 0.14 |
| 30 | 122 | 0.00 | 115 | 0.00 | 0.19 |
| 31 | 106 | 0.00 | 83 | 0.00 | 0.15 |
| 32 | 81 | 0.00 | 117 | 0.00 | 0.13 |
| 33 | 144 | 0.00 | 90 | 0.00 | 0.16 |
| 34 | 88 | 0.00 | 110 | 0.00 | 0.12 |
| 35 | 102 | 0.03 | 115 | 0.04 | 0.35 |
| 36 | 95 | 0.00 | 110 | 0.01 | 0.14 |
| 37 | 52 | 0.02 | 68 | 0.04 | 0.14 |
| 38 | 54 | 0.06 | 84 | 0.01 | 0.10 |

* Male fertility is determined as the ratio of the number of imagoes that emerged from the eggs laid by yellow females crossed with mutant males to the number of laid eggs

**Table 1:** Progeny of the mutant males (+) in crosses with *yellow* females.

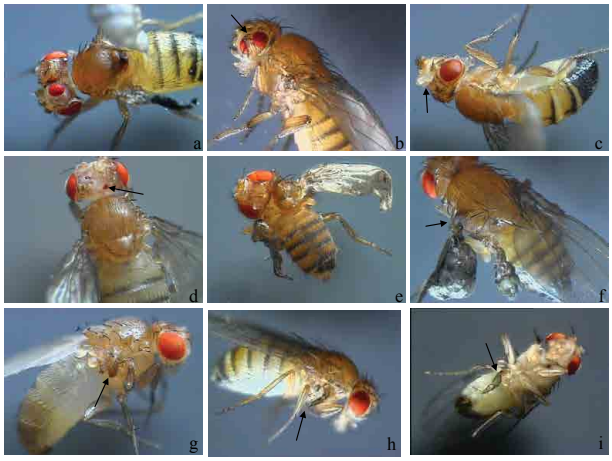

**Figure 3:** Morphoses in the strains with conditional dominant lethals: (a) two heads on single neck; (b) reduced head copy instead of eye; (c) increase in the head tissues; (d) groups of eye facets in the head tissues; (e) two thoraxes with wings; (f) thorax with wings instead of the left wing; (g) three rudimentary wings and two halteres; (h) additional seventh leg on the right side; and (i) the seventh leg on the abdomen.

**Figure 4:** Morphoses in the strains with conditional dominant lethals (continued): (a) the absence of wings and a twisted metathoracic leg; (b) reduced wings and twisted metathoracic leg; (c) abdomen rotation by 180°; (d) reduced thorax with single normal wing; (e) doubling of tibia on the front leg; (f) fragment of tergite on the abdomen; (g) replacement of tergites on sternites; and (h and i) doubling of male and female external genitals, respectively.

| Stock of mutation | Total number of progenies | Rate of progeny with morphoses (%) |
|---|---|---|
| 2 | 485 | 11.3 |
| 3 | 244 | 10.7 |
| 5 | 362 | 26.0 |
| 6 | 596 | 2.4 |
| 7 | 317 | 17.9 |
| 8 | 405 | 14.0 |
| 9 | 428 | 14.7 |
| 10 | 271 | 6.6 |
| 11 | 390 | 16.7 |
| 27 | 108 | 6.5 |
| 29 | 471 | 3.2 |
| 30 | 243 | 11.1 |
| 31 | 417 | 8.6 |
| 32 | 415 | 12.8 |
| 33 | 97 | 15.5 |
| 34 | 737 | 10.9 |
| 35 | 478 | 11.9 |
| 36 | 327 | 25.7 |
| 38 | 126 | 3.2 |
| 41 | 408 | 16.4 |
| Control | 3687 | 0 |

**Table 2**: Formation of morphoses in "*mutation/y*$^2$ *ec cv ct v f* " females.

mutations. They would suddenly appear in the progeny and suddenly disappear after several generations [7,15]. Figure 6 shows some of them.

Mosaics and gynandromorphs also emerge in the progeny of mutants [7]. Gynandromorphs are genetic mosaics that consist of both male and female cells. As is evident from Figure 7, the first two objects display altered eye color and shape and others, a combination of male and female traits in one individual. Particularly, the object in the last two photos looks like a male from its left side and like a female from its right side.

## Increase in energy metabolism

We could not help but notice that the mutant males had extremely high locomotor activity. The locomotor activity of mutants was assessed using a special device [17,18], which demonstrated their higher diurnal

locomotor activity as compared with the control (Figure 8). We also assessed their basal metabolism according to the $CO_2$ content in the exhaled air. Left histogram (Figure 9) shows that the locomotor activity in the control fly strains (red and blue bars) was lower as compared with the tested four mutant strains. The same applies to the $CO_2$ content in exhaled air suggesting that a higher level of the basal metabolism is characteristic of the mutants [17,18].

## Transition of the genome from a stable to an unstable state

Conditional mutations make the genome switch from a stable to an unstable state. This was inferred based on a set of the phenomena observed when studying conditional mutations: (1) loss of a lethal effect of the conditional mutations in the X chromosome; (2) loss of a phenotypic manifestation of the dominant markers in chromosome 2; (3) loss of the X chromosome in meiosis of conditional mutants; (4) more active transposition of mdg-2 mobile element in dimorphic mutants [18-21], and the phenomena listed above (Conditionality, lethality, and reduced fertility). Instability becomes evident as early as the heterozygotes for conditional mutations (permissive genotype). In

**Figure 5:** Secondary mutations in the strains with conditional dominant lethals: (a) black and Lobe; (b) Lobe and cinnabar; (c) Lobe and Bar; (d) apricot and echinus; (e) gap in the second vein like in radius incompletus; (f) net; (g) speck; (h) Dichaete; and (i) Dichaete and speck.

**Figure 6:** Modifications in the strains with conditional dominant lethals: (a) three individuals with defects of eyes like in Lobe; (b) curlywings and changes in eye shape; (c) changes in eye shape; (d) narrow wings; (e) wings take aside; (f) immature wings; (g) curled and short wings; (h) narrow and bubbled wings; (i) gaps in the fourth veins like in cubitus interruptus mutation.

**Figure 7:** Mosaics and gynandromorphs in the strains with conditional dominant lethals: (a) eyes of different color in progeny of $w^a$/+ female; (b) different eye shape in the progeny of B/+ female; (c) right half of the head and thorax are of a male type (stripe-like eye, sex comb on the prothoracic leg, and yellow colored legs); the remaining body of a female type; (d) colorless left half of last tergites; (e) the left half of the abdomen of a female type and color and the right half, of a male type; (f) left part of the body is of a male type (yellow body and shorter wing) and the right part of a female type; (g) male with doubled female genitals; (h) the left part of the fly is of a male type; (i) the right part of the same fly have a female type.

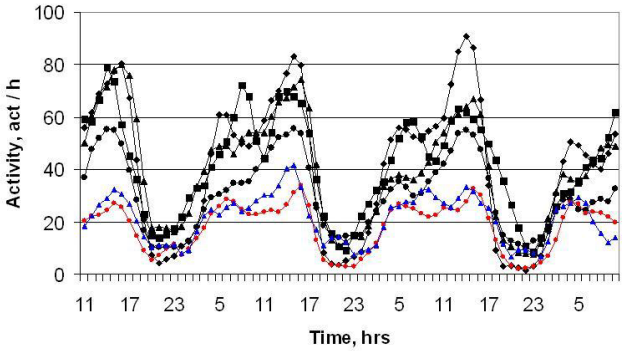


**Figure 8:** Locomotor activity of the of *D. melanogaster* adults of six strains for 3 days. Four mutant lines, nos. 7 (black diamond), 46 (black square), 101 (black circle), and 103 (black triangle), and two control strains, nos. 61 (light circle), 62 (light triangle). The Y axis shows the number of times a fly crosses the tube midline and the X axis, time of day, h [16].

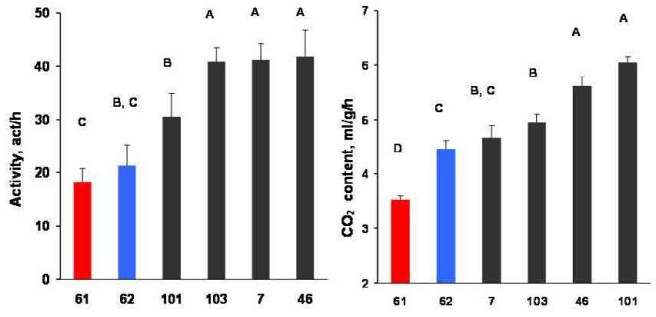


**Figure 9:** Average diurnal locomotor activity (left panel) and $CO_2$ expiration (right panel) in the control (nos. 61 and 62) and mutant (nos. 7, 46, 101, and 103) strains. The letters above columns denote statistically significant differences in the average values of locomotor activity (F5, 123=7.34, $p$<0.001) and $CO_2$ expiration values (F5, 148=31.89, $p$<0.001). LSD test was used for multiple comparisons of averages [16].

| Male mutant strain | Female *y/y; +/+* | | Female *y/y; +/Cy* | | | | Female *y/y; + /Pm* | | | | Female *y/y; +/D* | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Daughter + | Son *y* | Daughter + | | Son *y* | | Daughter + | | Son *y* | | Daughter+ | | Son *y* | |
| | | | *Cy+* | *Cy* | *Cy+* | *Cy* | *Pm+* | *Pm* | *Pm+* | *Pm* | $D^+$ | *D* | $D^+$ | *D* |
| 1 | – | 230 | – | – | 178 | 163 | – | – | 107 | 57 | – | – | 115 | 8 |
| 2 | – | 230 | 14 | 13 | 127 | 134 | 4 | 3 | 70 | 72 | – | – | 42 | 7 |
| 4 | – | 270 | 9 | 4 | 185 | 159 | 1 | 7 | 86 | 81 | – | – | 162 | 7 |
| 5 | – | 197 | 23 | 21 | 80 | 95 | 6 | 4 | 47 | 48 | – | – | 37 | 3 |
| 27 | 2 | 167 | 1 | 0 | 102 | 113 | 2 | 1 | 53 | 65 | – | – | 9 | 2 |
| 29 | 4 | 163 | 32 | 27 | 71 | 56 | 26 | 24 | 55 | 20 | 6 | 6 | 88 | 10 |
| 30 | – | 184 | 15 | 13 | 81 | 76 | 9 | 12 | 60 | 47 | – | – | 38 | 6 |
| 31 | – | 242 | 32 | 20 | 127 | 102 | 5 | 4 | 28 | 29 | – | – | 70 | 6 |
| 32 | – | 197 | 22 | 10 | 90 | 77 | 9 | 17 | 36 | 32 | – | – | 48 | 2 |
| 33 | – | 209 | 20 | 18 | 95 | 101 | 11 | 8 | 87 | 47 | 24 | 2 | 85 | 12 |
| 34 | – | 140 | 11 | 14 | 88 | 101 | 25 | 20 | 68 | 54 | – | 10 | 103 | 3 |

**Table 3:** Suppression of "prohibition on daughters" effect of conditional mutations by chromosomal rearrangements in chromosomes 2 and 3.

**Figure 10:** Morphoses in the offspring of conditional mutants. Parental effect of a paternal type. Phenotypically normal males containing conditional mutations in the X chromosome were crossed to yellow females. The yellow sons did not receive the mutant chromosome from their father but still developed morphoses. In two cases, a male was crossed to the *C(1)DX, y w f* females. The *y w f* daughters (f and i) did not get the mutant X chromosome from their father but had morphoses. The morphoses included (a) the absence of the left metathoracic leg; (b) shortened right wing; (c) altered tergite pattern from the left side; (d) altered shape of the right wing; (e) absent tarsus in the right metathoracic leg and changed shape of this leg; (f) altered wing shape and structure; (g) reduction of the left thorax and left wing; (h) left wing replaced with two appendages; (i) reduction of the left wing; (j) myeloma of the right arista in the lower male; (k) shortened and deformed tibia of the metathoracic legs in males; and (l) impaired wing veining.

other words, instability was a dominant manifestation of conditional mutations. Summing up, the observed most unusual properties of the conditional mutations isolated using special tests suggest the existence of previously unknown class of genes.

## Ontogenes: Specific Structural and Functional Features

The mutations were induced by radiation and were inherited as conventional chromosomal defects, suggesting that the mutant genes are mere DNA fragments. The presence of morphoses demonstrates that these genes are involved in the control of ontogenesis, which suggested us to name them ontogenes [4,22-24]. The mutations in ontogenes display many amazing features, which are highly informative of the nature of the involved ontogenes.

### Ontogenes are active in germline tissue (parental effects of conditional mutations)

In the case of a classic gene, the trait is inherited only if the progeny gets the corresponding gene from its parent, whereas in the case of an ontogene, the inheritance of a trait follows the parental (paternal and maternal) patterns [18,25]. Although a mutation is the particular factor that causes manifestation of a trait, the very trait emerged in the progeny in the absence of the mutation as well (Table 3).

In the fertility example (Table 1), the daughters of a mutant male that inherited its mutant X chromosome were unviable. However, a high level of semi-sterility suggested that a considerable share of the sons of this mutant male also died even though they did not inherit this mutant chromosome.

The same applies to morphoses. Monstrous flies were consistently present in the progeny of mutant males regardless of whether they carried the mutant chromosome or not. Figure 10 shows the morphosis-bearing sons of a mutant male (wild type) crossed to yellow females. It is evident that all of them were yellow, indicating that they lacked the mutant chromosome. Nonetheless, the morphoses were present. The observed parental effects definitely show that the mutation have something to do with the germline cells [5]. A certain mutant product is formed in the germline progenitor cell. This product spreads throughout the cell, and meiosis ensues. Only a half of the gametes receive the mutation, yet all of them inherit this mutant product. Thus, the best explanation for the observed effects is that ontogenes are active in the germline.

### Ontogenes produce regulatory RNA (interaction between conditional mutations and chromosomal rearrangements)

One particularly important property of conditional mutations that distinguishes them from the classical mutations is that the manifestation of conditional mutations depends on the presence of chromosomal rearrangements in the genome (Table 3).

Mutant males were crossed to yellow females of four different genotypes [6,18]. The first group carried no rearrangements, while the second and third groups had Curly and Plum inversions in chromosome 2 and the fourth group carried a *Dichaete* inversion in chromosome 3 [26]. As was expected, the progeny of the first group of females lacked any daughters. This was not the case in the other

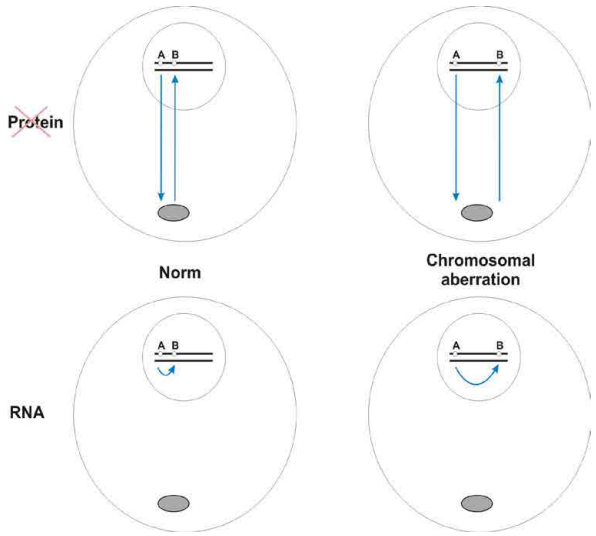


**Figure 11**: Protein or short RNA? Selection of the interface product explaining the interaction between chromosomal aberrations and conditional mutations. Large circle represents the cell; small circle, nucleus; A and B, genes (or ontogenes) in a pair of homologous chromosomes; and gray ellipse, a ribosome in the cytoplasm. Blue arrows show the routes to be taken by the corresponding interface product to implement the interaction between genes A and B. In the norm (left top), the distance between A and B is rather short and a chromosomal rearrangement (right top) alters this distance. If the interface product is represented by a protein (crossed out), this change in the distance will not be perceived, since it is negligible as compared with the distance to a ribosome and back. However, the change in the distance will be noticed if a short RNA is the interface product in question, since the trajectory of its movement resides within the nucleus, being comparable to the distance between A and B.

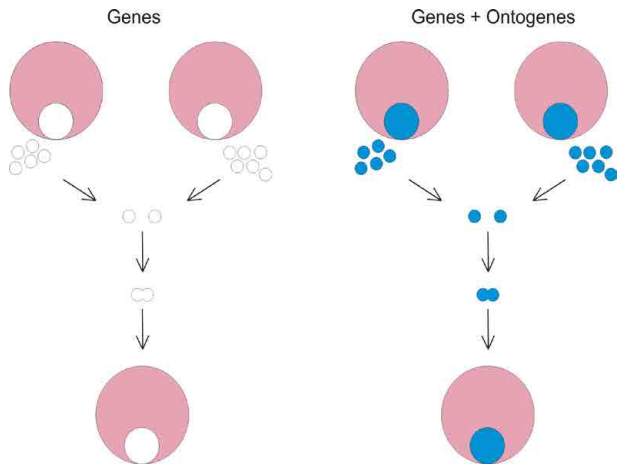


**Figure 12**: Activity of the genetic system in the light of classical and novel data. Large circle denotes the organism; small circle in the large one, germ line tissue; and individual small circles, gametes. Two variants of gamete formation in parents are shown. The classic variant (left) implies that the genetic system is active in the somatic tissues (red denotes that genes are active) and inactive in germ line tissue (empty circle). The proposed variant (right) implies that the genetic system is active in both the soma (red, genes are active) and in germ line tissue (blue, ontogenes are active).

three progenies; thus, the 'daughterless' rule was no longer working. The presence of inversion even in another pair of chromosomes caused the appearance of daughters in the progeny. It is well known that conventional mutations do not change their behavior regardless of chromosomal rearrangements present in laboratory collections. The question is why the two classes of mutations respond so differently to the introduction of chromosomal rearrangements.

The classical scenario of a DNA-RNA-protein pattern formally permits the interactions between two types of products, namely, RNA and protein (Figure 11). A chromosomal rearrangement changes the distance between two genes. Thus, we have to find out which type of interactions is sensitive to the distance between the genes. The interactions involving a protein do not fit, since it takes longer for an mRNA to shuttle from the nucleus into the cytoplasm and back into the nucleus as a protein. Correspondingly, we assume that a short RNA is a sole candidate and conclude that the interactions of ontogenes are confined to the DNA-RNA interactions within the nucleus [5,18]. This also explains why classical mutations do not respond to the presence of chromosomal aberrations: they follow a DNA-RNA-protein pattern wherein protein is the interface.

### Regulatory RNA functions as a duplex (dominant manifestation of conditional mutations)

Finally, conditional mutations are consistently 'visible' (manifest themselves) when heterozygous in both restrictive and permissive genotypes. This implies that the postulated RNA controlling element is a duplex [5,18]. Changes in just one of the RNA strands make the duplex to fall apart, which appears as a dominant mutation.

## Conclusions

To sum up, three independent lines of evidence suggest that an enigmatic class of non-Mendelian genes (ontogenes) is present in the genome: first, efficient screening tools and the resulting collections of mutants; second, highly unusual properties of the obtained mutations; and third, unusual temporal and tissue specificities of when these mutations work. We hypothesize that the genetic system has one and the same genetic template that controls the synthesis of two types of transcripts. One is mRNA, which is converted into the protein, and the other is a sort of regulatory small RNA.

Final Figure 12 summarizes the current understanding of a genetic system. The first variant is a long-standing classical scheme, wherein genes form the building blocks of the system. Two large circles denote two individuals, with somatic tissues shown in red and displaying strong transcriptional activity. Small circles correspond to the germline, which remains essentially silent. Its function is to carry out meiosis and produce gametes (small dots). When gametes fuse, a zygote is formed. Gene activity is restored upon restoration of diploidy.

The alternative view (shown to the right) stems from the data briefed above. The genome is active in both the soma and germline (blue). This is exactly where the ontogenes operate and where the new organism emerges long before the fusion of gametes, namely, when the germline is established in the parents. Thus, the genetic system comprises two parts: the genes working according to a DNA-RNA-protein script and the ontogenes following a DNA-RNA script. The first entity is engaged in production of the "building material" for the organism, proteins, while the second entity controls this process during preparation of the individual developmental program [5]. These different functions of genes depend on the type of transcript formed from DNA as well as the time and place of its origin on DNA.

### Acknowledgement

The authors thank A.A. Fedorov for his assistance in preparing the artwork.

### References

1. Chadov BF (2001) Mutations capable of inducing speciation: Evolution Biology. Tomsk State University Press, Tomsk, Russia.
2. Chadov BF, Chadova EV, Kopyl SA, Fedorova NB (2000) A New class of mutations in Drosophila melanogaster. Dokl Biol Sci 373: 423-426.

3. Chadov BF (2000) Mutations in the regulatory genes in Drosophila melanogaster. Proc Intern Conf biodiversity and dynamics of ecosystems in North Eurasia. Novosibirsk, Russia.
4. Chadov BF, Chadova EV, Kopyl SA, Artemova EV, Khotskina EA, et al. (2004) From genetics of intraspecific differences to genetics of intraspecific similarity. Rus J Genetics 40: 945-958.
5. Chadov BF, Fedorova NB, Chadova EV, Khotskina EA (2011) Conditional mutations in Drosophila. J Life Sci 5: 224-240.
6. Chadov BF, Chadova EV, Khotskina EA, Artemova EV, Fedorova NB (2004) The main effect of chromosomal rearrangement is changing the action of regulatory genes. Russ J Genetics 40: 723-731.
7. Chadov BF, Chadova EV, Kopyl SA, Khotskina EA, Fedorova NB (2004) Genes controlling development: Morphoses, phenocopies, dimorphs and other visible expressions of mutant genes. Rus J Genetics 40: 271-281.
8. Frizen G (1935) Roentgen morphoses in Drosophila. Biol Zh 4: 687-704.
9. Rapoport IA (1939) Specific morphoses induced in drosophila melanogaster by chemical compounds. Byull Eksp Biol Med 7: 415-417.
10. Goldschmidt R (1957) Theoretical genetics. University of California Press, Berkley and Los Angeles.
11. Goldschmidt R, Piternick L (1957) The genetic background of chemically induced phenocopies in Drosophila. J Exp Zool 135: 127-202.
12. Goldschmidt R, Piternick L (1957) The genetic background of chemically induced phenocopies in Drosophila II. J Exp Zool 136: 201-228.
13. Fedorova NB, Chadova EV, Khotskina EA, Chadov BF (2010) Conditional mutations: Obtainment by the method of morphoses. Topics in experimental evolution of organisms (International conference), Logos, Kiev (in Russian).
14. Fedorova NB, Chadova EV, Chadov BF (2011) Parental effects of conditional mutations in Drosophila. Topics in Experimental Evolution of Organisms (international conference), Logos, Kiev (in Russian).
15. Chadov BF, Chadova EV, Fedorova NB (2012) Epigenetic phenomenology in conditional mutants of Drosophila melanogaster: Morphoses and modifications. Epigenetics. Novosibirsk (in Russian).
16. Ashburner M (1989) Drosophila. A Laboratory Handbook. (2nd edn.) Cold Spring Harbor Laboratory Press, USA.
17. Chadov BF, Fedorova NB, Chadova EV, Khotskina EA, Moshkin MP, et al. (2010) Change in the energy status of Drosophila resulting from genetic mutation. Rus J Genetics 46: 1062-1066.
18. Chadov BF, Fedorova N B, and Chadova EV (2015) Conditional mutations in Drosophila melanogaster: On the occasion of the 150th anniversary of G. Mendel's report in Brünn. Mutat Res Rev Mutat Res. 765: 40-55.
19. Chadov BF, Chadova EV, Khotskina EA, Fedorova NB (2005) Mutation in the ontogene-genome instability-appearance of new forms: Evolution biology. Tomsk State University Press, Russia (In Russian).
20. Chadov BF, Chadova EV, Khotskina EA, Federova NB (2009) Conditional lethal mutations shift the genome from stability to instability. Rus J Genetics 45: 276-286.
21. Fedorova NB, Chadova EV (2008) Mutation in ontogene causes transposition of retrotransposon 412. Factors of experimental evolution of organisms. 4: 210-215 (in Russian).
22. Chadov BF (2005) Ontogenes in drosophila melanogaster: genetic features and role in onto-and phylogenesis.
23. Chadov BF (2006) A new stage in the development of genetics and term epigenetics. Genetika 42: 1261-1275.
24. Chadov BF (2007) Ontogenes in Drosophila melanogaster: Genetic features and role in onto-and phylogeny. JINR.
25. Chadov BF, Fedorova NB, Chadova EV (2013) Parental effects of conditional mutations and their explanations. Russ J Genet 49: 141-150.
26. Lindsley DL, Grell EH (1968) Genetic variations of Drosophila melanogaster. Carnegie Institution of Washington, Washington.