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Ontogenes and Their Role in Cellular Construction

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Abstract

The genes referred to as ontogenes are responsible for conditional mutations. Based on the results of the research of conditional mutations in *D. melanogaster*, we attempt to figure out the biological role of ontogenes. We conclude that ontogenes in the process of individual development control the construction of the living organisms of cells (cellular construction), which comprises the induction of cell division, determination of division plane, and the location of daughter cells after the division is completed. The process of morphogenesis consists of cellular construction and protein synthesis. Protein synthesis is controlled by protein-coding (Mendelian) genes. Mendelian genes are switched on by ontogenes. In terms of the two-component genome composed of Mendelian genes and ontogenes, we consider 1) the concept of biological character; 2) interspecific incompatibility; 3) ontogenesis; 4) phylogenesis; and 5) mutagenesis. Ontogenes, which control cellular construction, possess the specific features unusual for Mendelian genes, namely, 1) the activity in germ line tissue; 2) remote interaction; and 3) activity in a compacted state (heterochromatization). These specific features of ontogenes suggest that unlike the Mendelian genes with their chemical activity, ontogenes possess another type of activity (biophysical) involving induction of an electromagnetic field.

Keywords

Cell, Morphogenesis, Ontogene, Ontogenesis, Electromagnetic Field, Drosophila

1. Introduction

Genetics traces its origin back to the experiments by Gregor Mendel on the inheritance of alternative characters [1]. Alternative characters are *the characters determining the intraspecific differences*. A century and a half later, the idea

came up to the authors of this paper that a living organism would possess the traits of quite another category, namely, *the traits determining the intraspecific similarity* [2] [3]. Since the traits of this kind by definition have no variants within a species, whereas the variants of the former traits (determining the intraspecific differences) do exist, we assumed that the genes responsible for intraspecific similarity are somewhat different from the genes determining the intraspecific differences [4].

The genes responsible for intraspecific differences are the well-known Mendelian protein-coding genes, long ago regarded as the only and unique units of heredity. Correspondingly, we decided to experimentally test whether there were special genes responsible for the intraspecific similarity [5] [6]. This is how the mutations, named *conditional*, were discovered in drosophila [7] [8]; the corresponding genes were named *ontogenes* [9] [10].

A phenotypic appearance of conditional mutation is peculiar. A Mendelian mutation is *a variant of the phenotype* versus a conditional mutation, which is *a specific variant of phenotype inheritance*. The conditional mutations are inherited a manner other than the Mendelian pattern. The mutation manifests itself in the individuals of one genotype but does not appear in the individual of another genotype. The overwhelming majority of the obtained conditional mutations are dominant lethals. However, a dominant lethality takes place in the individuals of a certain genotype and is absent in the individual of another genotype. Occasionally, conditional mutations have an obvious manifestation: a mutant phenotype is observable in a certain genetic environment but is absent in another one. Thus, the genotypes where a particular conditional mutation is manifested are determined by the form of selection when producing this mutation.

Similar mutations have been described in the genetic literature. These are the conditional mutations that manifest themselves depending on environmental factors: temperature, food chemical ingredients, and so on [11]. Another type is the mutations with incomplete penetrance [12] [13]. The mutations we discovered differ from both categories: from the former, by changing their manifestation depending on the genetic rather than environmental conditions and from the latter, by that a manifestation or the absence of manifestation of conditional mutations is strictly associated with particular genotypes, which is untypical of the mutations with incomplete penetrance.

A conditional manifestation, forming the background for selection of conditional mutations, alone indicates the difference of the selected genes (ontogenes) from the Mendelian genes. While Mendelian genes are independent units of inheritance, ontogenes look as if dependent. Along with a conditional manifestation, the experiments with the obtained conditional mutations have shown many distinctions of ontogenes from Mendelian genes [7] [8] [9]. Currently, the content of the concept of *ontogene* coincides or is very close to the concept of *long noncoding RNA genes*, which has recently appeared in molecular genetics [14]. After the ontogenes were discovered, the genetic system ceased being a mere sum of hereditary units but rather has become the system comprising two simi-

lar but not identical elements—Mendelian genes and ontogenes [15]. The question arises on the biological purpose of ontogenes and the way the Mendelian genes and ontogenes coordinate their functions.

Some of the unusual manifestations of conditional mutations in drosophila suggest that ontogenes control the process of how living organisms are constructed of cells [16]. The developmental biologists have been always intrigued by this biological process [17]; however, any attempts to study the genetics of this process have failed [18]. As it will be clear from the following narrative, the underlying reason is that the protein-coding genes do not control this process, while genetics until recently has been unaware of any other genes. The goal of this paper is to describe the experimental data suggesting that ontogenes are in charge of the construction of living organisms with cells as the bricks and to grasp the place of this unique process in the scope of biological issues.

2. Ontogenes Control Cellular Construction (Experimental Proofs)

2.1. Morphoses

A characteristic manifestation of the conditional mutations in *Drosophila melanogaster* is development of morphoses in mutants and their offspring [19] [20] [21]. Morphoses are monstrous morphological changes in the appearance of an adult fly resembling the normal structures but lacking any functional role. The absence of a certain normal structure or its part(s) is a variant of morphosis. Frequently, morphosis looks as a failure of assembly using the usual correct elements. **Figure 1** and **Figure 2** show some examples (of approximately 1000 available cases of morphoses) recorded when working with the mutations of ontogenes. The images of about hundred of them classified according to the fly body parts have been published [20] [21].

2.2. Asymmetry of Morphoses

A hallmark of morphoses is their asymmetry. As a result of morphoses, normal bilaterally symmetric structures (wings, legs, eyes, and so on) appear on the one side of the body, left or right, rather than on the two sides (**Figure 1**). The cases of a total absence of a body structure are also unilateral (**Figure 2**). Note that the Mendelian mutations in drosophila appearing as morphological defects are rather frequent; however, the defects are much simpler as compared with morphoses and *are always the same at both sides* if it is a bilaterally symmetrical trait.

The difference in the symmetry between morphoses and Mendelian mutations was observed in an experiment. In one case, Mendelian mutations were introduced to the fly strains carrying ontomutations and in the other, Mendelian mutations emerged spontaneously. The difference in the symmetry of a morphosis and a Mendelian mutation is evident when they emerge in the same individual (**Figure 3**). The morphosis resides on one side of the fly body (left or right) versus the Mendelian mutation, which is found on both sides.

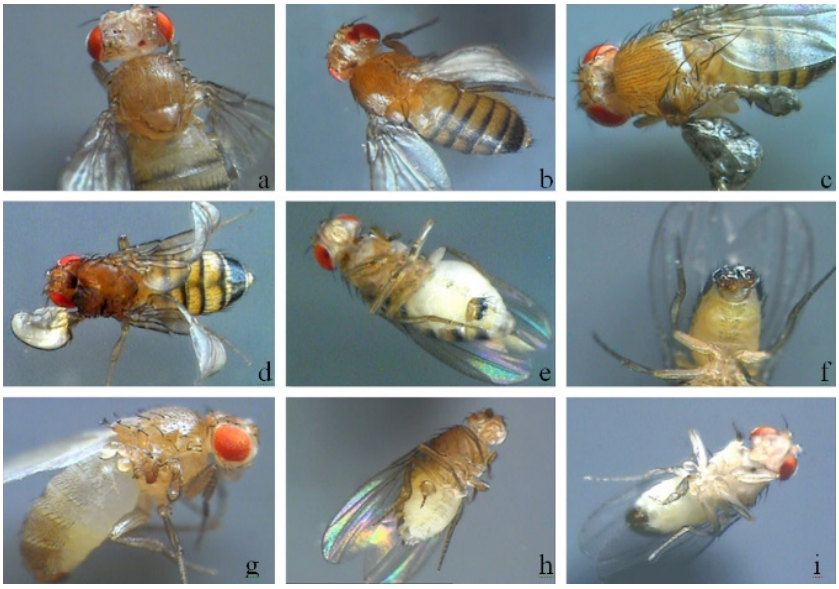

Figure 1. The morphoses of the "plus tissue" type (surplus morphological structures): (a) groups of eye ommatidia (red spots) on the occiput; (b) an additional eye on the right side; (c) an additional thorax with an altered wing on the right side and a normal wing on the right side in a form of a structureless bubble; (d) an additional wing on the right side (directed forward) and an altered thorax on the right side; (e) a tergite fragment with bristles on the abdomen; (f) doubling of the external male genitalia; (g) four wing-like appendages with bristles instead of a normal wing on the right side; (h) tarsus on the abdomen; and (i) an additional altered seventh leg [22].

Figure 2. The morphoses of the "minus tissue" type (lacking morphological structures): (a) loss of a wing (stump) and bristles on the left thorax; (b) loss of a prothoracic leg on the left side; (c) loss of the head capsule and a major part of the right eye; (d) loss of the left wing and circular bristle pattern on the left thorax; (e) one pair of legs instead of three pairs in the normal fly and different shapes of the right and left legs in the remaining pair; (f) reduced tarsus of the left metathoracic leg; (g) loss of a half thorax on the left side, including the wing, and a right wing with a Notch-type indentation; (h) circularly cut right wing; and (i) loss of the left wing and a cone-like stretched left thorax [22].

Figure 3. Secondary mutations and morphoses: (a) speak mutation; (b) cabin mutation; (c) plexus mutation; (d) Bar mutation (an eye as a band) in the short legs strain and a morphosis of the left wing; (e) dumpy mutation (obliquely cut wings) and a morphosis (absent right wing); (f) black mutation on the left side and a morphosis of the right wing (its shortening and a bubble on it); (g) a morphosis (bifurcation of the thorax and a bubble-like left wing) in yellow strain; (h) white-apricot mutation and a morphosis (absent half thorax and the left wing); and (i) Bar mutation and a morphosis (a decreased second head instead of the left eye; the eye on the small head copy has the same phenotype as on the main head) [20].

2.3. Parental Inheritance of Morphoses

The Mendelian mutations are inherited according to the rules of Mendel. As for the morphoses, induced by disturbances of ontogenes, they are inherited according to a parental type. This means that the morphoses in the offspring of a mutant parent emerge in both the progenies that received the mutation from parents and the progenies that did not receive the mutation [22] [23]. Thus, it turns out that the main point in the inheritance is that a trait is present in a parent rather than a progeny receives the corresponding gene from the parent. **Figure 4** and **Figure 5** illustrate the parental inheritance of morphoses. In the first case (**Figure 4**), a male carried a mutation in an ontogene located in the X chromosome. Nonetheless, its progenies from the cross with *yellow* females that have not received the mutant chromosome (the progenies with a *yellow* phenotype) have morphoses. In the other case (**Figure 5**), females carried a mutation in an ontogene in the X chromosome. Nonetheless, their progenies that inherited the second X chromosome (lacking mutation) from mother (with a $B\ w^a$ phenotype), had morphoses.

2.4. Abnormalities of Meiotic Division in Ontogene Mutants

In total, 30 mutations of this type residing in the *Drosophila melanogaster* X chromosome have been assayed for their ability to cause meiotic nondisjunction

[24]. The level of X nondisjunction in the females heterozygous for the mutation in ontogene appears to be very high. The share of matroclinous daughters reaches 24.7% of the overall offspring and of patroclinous males, 24.9%. Neither inversion in the opposite X chromosome nor additional Y chromosome has any effect on the X nondisjunction. The balance of the XX and X0 egg cells is disturbed: exclusive daughters are prevalent in the offspring of the females with a normal opposite X chromosome and exclusive sons, in the offspring of the females with an inverted X chromosome. In addition, 12% of the matroclinous daughters of the females with a normal opposite X chromosome are homozygous

Figure 4. Morphoses in the offspring of conditional mutants. I. Parental effect of a paternal type. Conditional mutation was in the X chromosome of a normal male 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 [22].

Figure 5. Morphoses in the offspring of conditional mutants. II. Parental effect of a maternal type. Conditional mutation was in the X chromosome (+) of a +/*In*(1)*Muller*-5, *B* w^a female. The daughters *In*(1)*Muller*-5, *B* w^a/*In*(1)*Muller*-5, and *B* w^a and sons *In*(1)*Muller*-5, *B* w^a with a *B* w^a phenotype (bar-shaped apricot eyes) did not receive the X chromosome with conditional mutation from their mother but formed the following morphoses: (a) wings of different lengths with bubbles; (b) narrowed wing, impaired veining, and a bubble; (c) opaque wings of various shapes; (d) the right wing filled with lymph; impaired veining; (e) asymmetric wings; (f) tissue overgrowth instead of left eye ommatidia; (g) reduced right wing with irregular shape and a bubble; (h) absent right wing; colored tissue in the thoracic base; (i) reduced wing blade from the left side; (j) absence of macrochaetes and microchaetes in the right side of the thorax; (k) deformed femur of the right mesothoracic leg; and (l) sickle-shaped right wing [22].

for the marker of one of the maternal X chromosomes ("equational" nondisjunction). A "fading" parental effect of the mutation in ontogene on the X chromosome nondisjunction is also observed [24]. It is worth recalling that the mutations in Mendelian genes very rarely cause any abnormalities in meiosis and even when this happens, manifest themselves in a homozygote (*mei* mutants) rather than in heterozygote, as is the case with ontogenes.

2.5. Abnormalities of Mitotic Division in Ontogene Mutants

The abnormalities of cell division in meiosis in the mutants in ontogenes are

observable mitosis as well. The aneuploids for autosomes are unnoticeable in somatic cells because such cells fail to survive; however, the aneuploidy for sex chromosomes is recognizable. A loss of one X chromosome in a female XX set gives a somatic cell of a male X0 type [25] and formation of a mosaic spot of these cells. Mutants in ontogenes and their progenies frequently developed mosaic spots of the X0 type. They gave themselves away by manifestation of a recessive mutation in the X chromosome, which was unnoticeable in the XX cells because of heterozygosity (**Figure 6(c)**, **Figure 6(f)**, **Figure 6(g)**, and **Figure 6(i)**. In the case if the loss of the X chromosome took place early (first cleavages of the zygote), the mosaic spot occupied up to half of the fly ectoderm and acquired a male phenotype, *i.e.*, gynandromorph (**Figure 6(a)**, **Figure 6(b)**, **Figure 6(d)**, **Figure 6(e)**, and **Figure 6(h)**).

Thus, we have briefed above the five unique manifestations of ontogenes: 1) emergence of morphoses; 2) asymmetry in the development of morphoses; 3) parental inheritance of morphoses; 4) meiotic abnormalities in the mutants in ontogenes; and 5) mitotic abnormalities in the mutants in ontogenes. The first three manifestations are related to morphogenesis and the last two, to cell division. Not a single manifestation of the list is observable for Mendelian mutations although many of them are typical defects of morphogenesis.

The contrast in the symmetry helps to understand the cause underlying the unique manifestations of ontogenes: *the asymmetry of defects is present in ontomutants* and *is absent in Mendelian mutations*. A bilateral asymmetry of

Figure 6. Mosaics in strains with conditional mutations: (a) the left half of the abdomen is gray the right half, yellow; (b) sex comb is present only on the right front leg; (c) eyes of different colors in the offspring of a w^a/+ female; (d) colorless left half of last tergites; (e) left half of the abdomen of a female type color and, right, of a male type; (f) different shapes of eyes in the offspring of a B/+ female; (g) as spot of red ommatidia on the background of white ommatidia; (h) yellow left wing and part of the thorax of a gray fly; and (i) right half of the thorax and scutellum are hairless and have no bristles [20].

morphoses *is actually the difference in the number of cells* forming the altered structure on the left and on the right. The absence of asymmetry is the absence of the difference in the number of cells. Thus, these are ontogenes that determine the ratio of the cells on the left and on the right, whereas Mendelian genes have nothing to do with it; that is, ontogenes control the process of cell multiplication, whereas Mendelian genes do not. As is known, Mendelian genes code for the synthesis of proteins. Correspondingly, *the morphological defects in the mutants in Mendelian genes are determined by proteins*, *whereas in the mutants in ontogenes*, *by cells* [16].

The linkage of ontogenes to cell division and of Mendelian genes to protein production explains all above considered differences between Mendelian genes and ontogenes. As is known, Mendelian genes are inactive in germ line tissue. Assuming that ontogenes are on the contrary active in germ line tissue, it becomes clear why the Mendelian mutations strictly follow the Mendelian rules in their inheritance, whereas morphoses are inherited according to a parental type. Next, it is known that the Mendelian genes are inactive during the process of cell division. Assuming that the ontogenes are active during the cell division, it becomes clear why Mendelian mutations do not interfere with meiosis and mitosis (except for homozygous *mei-mutants*), whereas mutations in ontogenes (even in a heterozygote) interfere with these processes. Thus, the overall set of peculiar manifestations of ontomutations complying with one another suggests that ontogenes control the process of cell division leading to formation of cell ensembles. This is the key difference between ontogenes and Mendelian genes, involved in protein synthesis.

The inference on the controlling role of ontogenes does not "discover America" in either the reason of cell being or the theoretical necessity in the genetic control of cell. The important point is that the presence of the control is accompanied by the description of a novel and quite real mechanism underlying this control. Until recently, only a protein-coding gene could pretend to act as a genetic controller since no other kinds of genes were known. The variants of such control in the form of regulatory proteins, "organizers", and even predecessor structures have been proposed [18]. However, they have not received any experimental confirmation. As a result, the question on the existence of the process of cellular construction with its own regulation remained twisting in the wind: not proved but still possible. The conclusion on the control with the help of new type genes (ontogenes) removes this uncertainty to a considerable degree by virtue of its concreteness.

The described data suggest that ontogenes are *the particular genes that control the generation of shape* and create *the body plan* of an organism. They are responsible for initiation of cell division, the number of divisions, and the mutual arrangement of cells in a cell agglomeration. These processes determine a particular structure of a living organism constructed of a certain number of specifically arranged cells and the overall organism. The method used to construct the shape *is the control of cell division*. As for Mendelian genes, their role reduces to

coordination of the protein synthesis in the groups of cells arranged by ontogenes [16].

3. Cellular Construction and Problems in Biology

The inference on a special genetic controls over cellular construction means that a separate area exists in developmental biology (ontogenesis) and biology in general, particularly, the "cellular construction". Genetics, earlier operating only with the protein-coding genes, confined itself to consideration of a protein-based side in biological processes omitting the other processes and their genetic control. In this section, we will consider separate biological problems from a new standpoint, namely, in terms of cellular construction. The amount of currently available information about ontogenes makes it possible to propose the solutions for several earlier formulated problems. In addition, the very fact of reached solutions is an additional argument favoring the presence of special category of genes, ontogenes, in the genome.

3.1. Biological Character

A genetic interpretation of the concept of "biological character" in the literature is contradictory. A "normal character" or the "norm" is regarded as an alternative to a mutant character. In the case of a monogenic character, the norm should logically be monogenic as well; however, it is not and cannot be. Norm is formed in the process of ontogenesis and, correspondingly, is the result of activity of many genes. As a tradeoff, it is considered that there are no "genuine" monogenic characters [26]. In this case, it is unclear how to deal with the notions of monogenic character, polygenic character, monogenic cross, and so on still used in the literature.

The concept of *ontogene* makes the concept of "biological character" less controversial and more distinct. A biological character is a part of a living organism; the part consists of proteins and cells; the proteins are controlled by Mendelian genes and the cells, by ontogenes. Each biological trait is polygenic since it is controlled by at least two genes: one coding for protein and the other for cell structure. There are and can be no monogenic character at all; however, there can be a multitude of *monogenic variants of a character*. A monogenic variant emerges as a result of a change in one of the genes responsible for the character. The existence of viable variants of a character resulting from a change in the corresponding single protein-coding gene makes it possible to perform crosses, which can be reasonably referred to as monohybrid ones. The presence of viable variants in nature allowed Mendel to discover the existence of *factors*, *i.e.*, discrete units of heredity.

The concept of biological character used in the current literature corresponds to formally logical definition of the character. According to this definition, the character is not a component of an organism, as is proposed above, but rather denotes the similarity or difference between objects [27]. In this case, *the variants of characters* (eye color or wing shape) may be regarded as characters

(which is commonly done), for example, *white* eye color or *obliquely cut* wings (briefly, *white* or *obliquely cut*), resulting from a monogenic defect of protein-coding genes. Reckoning the variants of characters as characters leads to contradictions. One of these contradictions is mentioned at the beginning of this section. The current definition of the so-called "quantitative traits" contains even more contradictions [26].

Commencing the clarification of the genetic structure of a particular mutant phenotype now (that is, after the discovery of ontogenes), it is necessary to clearly understand that 1) any of the biological characters is polygenic but 2) a particular phenotype may result from a mutational change of one or several genes responsible for the character; however, 3) these genes may be both Mendelian protein-coding genes and ontogenes. 4) The variants of traits caused by monogenic defects of Mendelian genes will be inherited in a different manner as compared with the variants of the traits caused by the monogenic defects of ontogenes. 5) The same is true for the polygenic defects in Mendelian genes and ontogenes. Finally, 6) the cases of a combined damage of Mendelian genes and ontogenes are also possible and are the most intricate for their classification.

3.2. Interspecific Isolation and the Syndrome of Interspecific Incompatibility

The individuals of the same species can cross and give fertile progeny, whereas the individuals belonging to different species are unable to do it. It has long been clear that the nature of interspecific isolation is of a genetic nature; however, it is unclear in what it consists. Representatives of the same species may dramatically differ in the phenotypes but without any consequences for hybridization. On the other hand, the representatives of different species indistinguishable in their appearance emerge to be absolutely sterile when crossed. The insight into conditional mutations clarifies the nature of species isolation: this is determined by the difference between species in their sets of ontogenes in the genomes [14].

The conditional mutations in drosophila were selected using the test for conditional dominant lethality [5] [6] [7] [8]. The studies of mutants have also demonstrated that they display 1) a high level of sterility in different crosses; 2) parental pattern of inheritance; 3) formation of monstrosities and mosaics in their offsprings; and 4) dramatic abnormalities of meiosis. The set of listed abnormalities is rather specific. These abnormalities are absent in the Mendelian mutations but ideally fit the set of abnormalities characteristic of distant hybridization. It is logical to regard the syndrome of interspecific incompatibility to result from heterozygosity in ontogenes; moreover, this syndrome appears even in the case of heterozygosity in one ontogene. The heterozygosity even involving a large number of Mendelian protein-coding genes does not lead to any incompatibility [14] [15].

The linkage of the function of cell division control to ontogenes makes the cause underlying the interspecific isolation ever clearer. The ontogenes form the particular background for the unique program of ontogenesis of the individuals

belonging to the same species. The uniqueness here means the absence of the variants and homozygosity in the constituent ontogenes in all representatives of the species. The joining of two different programs (heterozygosity according to the program of ontogenesis) blocks the development or makes a normal meiosis unfeasible. This issue will be further discussed in the sections below.

3.3. Ontogenesis

The consecutive triggering of genes in individual development intrigues geneticists for a long time yet the challenge remains unresolved. It is now clear why: the key genes controlling ontogenesis remained beyond the consideration of researchers. These omitted genes are ontogenes. Until recently, they tried to reconstruct the mechanism of ontogenesis involving only protein-coding genes.

The studies by Jacob and Monod on the regulatory genes in microorganisms [28] suggested that the program of individual development in multicellular organisms consisted of the Mendelian genes switched on by regulator genes, also belonging to protein-coding genes. Thus, the program of ontogenesis is composed of protein-coding genes alone. This hypothesis have not been experimentally confirmed, and, indeed, could not. There are also some theoretical objections. They should be kept in mind because they highlight the specificity of ontogenesis. First, the regulator cannot be a protein since it will need another protein regulator and so on ad infinitum [29]. Second, both a protein and the Mendelian gene coding for the protein admit the existence of viable variants, which is inadmissible for the program of individual development of a species level, which is conserved to the highest degree.

The above listed requirements are an insurmountable barrier for the protein-coding genes as the main regulators but do not present any hindrance to ontogenes. First, ontogenes do not need any regulators. Second, ontogenes are protected from mutations since the variants of ontogenes formed via a DNA mutation are eliminated in the zygote (see Section 3.4). Find below some additional problems in individual development resolvable with the help of ontogenes.

3.4. Growth of Cell Population and Its Functional Differentiation

The mutations in ontogenes, used in our work, can be combined with known mutations in Mendelian genes to observe how the morphological changes resulting from morphoses go together with the phenotypic manifestations of a known Mendelian mutation [14]. The phenotypes of resulting compounds suggest that the ontogenes responsible for formation of a particular structure (and its change in the case of a morphosis) control the switch-on of a certain set of Mendelian genes, namely, the particular Mendelian genes that create this structure in the norm [14] (and their phenotypic manifestation). It turns out that ontogenes initiate cell division and this division is the trigger for switching on of a set of Mendelian genes [14] [30]. The event of triggering (regulation) of protein-coding genes is combined with the event of cell morphogenesis (an increase

in the number of cells). It is important that the protein-coding genes are activated without involvement of any protein.

3.5. Formation of Three-Dimensional Structures in Three-Dimensional Space

The incorporation of the event of cell division into the program of ontogenesis as a key element of this program suggests the hypothesis on how the structural body plan (*Bauplan*) of an organism is implemented. We assume that this consists in the enumeration of the cell divisions starting from the zygote and determination of the spatial orientation of the plane of each subsequent division (**Figure 7**). Once we have division poles A and B and division plane ECFD, the formation of two daughter cells will enhance the expansion of cell aggregate in an anterior-posterior direction. If we have division poles C and D and division plane AFBE, the formation of two daughter cells will enhance the expansion of cell aggregate in an upper-lower direction. If we have division poles E and F and division plane ACBD, the formation of two daughter cells will enhance the expansion of cell aggregate in a lateral (left and right) directions.

The same mechanism is able to provide the growth of cell mass in one of the two directions of the following set: forward or backward, upward or downward, and leftward or rightward. Thus, it is now possible to explain the construction of normal structures, both symmetric and asymmetric, as well as the emergence of a morphosis on one body side. The parental type of development of a morphosis unambiguously suggests that the emergence of a monstrosity is associated with the events taking place with ontogenes in the germline during premeiosis (editing of the program of individual development), while the asymmetry of the morphosis indicates that these events determine the spatial parameters of cellular construction, which will start upon the formation of the zygote. The question arises on how the ontogenes manage to tag the developmental axes of living structures to space. The section "Biophysical nature of the activity of ontogenes" will dwell on this issue.

Initially, the genes responsible for the formation of conditional mutations were formally named ontogenes because of the ability of these mutations to induce in drosophila the abnormalities of individual development in the form of morphoses [19] [20] [21]. By now, the involvement of ontogenes in the process of cellular construction is shown and it is evident that this name reflects the role of the genes belonging to this category in ontogenesis.

3.6. Phylogenesis

According to current genetics, changes in the genomes of living organisms over historical time intervals form the background of biological evolution; however, a particular mechanism and the logic of this process are the matter of discussion. The discovery of ontogenes is a new contribution to this long-running discussion: the properties of ontogenes allows for solutions of long-disputed issues and for basically new hypothesis [31].

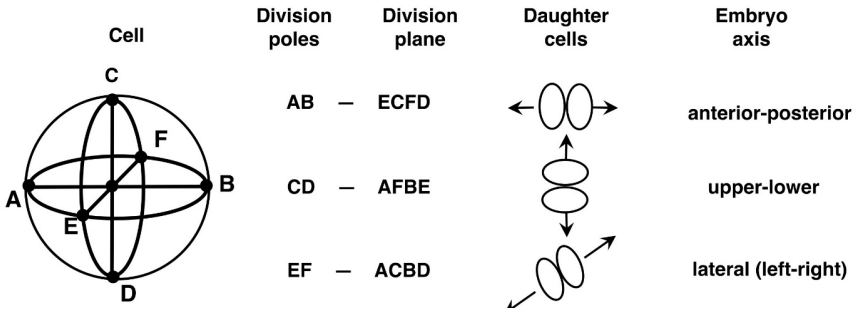

Figure 7. The division planes of a stem cell and the growth of embryo's inner cell mass in three-dimensional space (see text for details).

Undoubtedly, the object of evolutionary changes is the overall genetic material but ontogenes, controlling cells, are the chief, at least among the eukaryotes. They are directly involved in the construction of an organism of cells and switch on the protein-coding Mendelian genes in the cells. The key role of ontogenes in speciation is suggested by the similarity between the manifestation of the mutations in ontogenes and the syndrome of interspecific incompatibility.

Ontogenes demonstrate how with their help a nascent species *is isolated* from its initial parental species. The isolation results from dominant lethality, which appears in a heterozygote for ontogene. The experiments with mutations of ontogenes suggest the mechanism underlying the development of isolation and its transformation into the complete incrossability of different species. The dominant lethality of ontogenes is *conditional*. The conditionality makes it possible to increase the amount of genetic differences between the nascent and parental species to the point of sterility in the crosses with an overwhelming majority of the variants of the parental species.

An unexpected form in which dominant lethality appears is of a paramount interest. Lethality takes place in the zygote, when the parental genomes are still not active. Here, the so-called natural selection, declared by Charles Darwin, steps up; however, this is not the Darwinian selection of living organisms according to their fitness. This is a novel form of selection, namely, *the selection of genomes at the stage of zygote* (*zygotic selection*) [32].

We cannot but emphasize the peculiarity of the mechanism underlying zygotic lethality. This mechanism guarantees the selection of genomes in a maximally economical way, as early as the stage of zygote. This selection avoids the death of the formed organisms and, which is especially important, proves the existence of a specific form of evolution of the genetic system not directly connected with viability. See Chadov *et al.* [31] [32] for a comprehensive description of the role of ontogenes in phylogenesis.

3.7. Mutagenesis

For mutations to emerge, the gene material should be in an active state [33]. Taking into account the protein-coding genes, which are active during the period of somatic development, all or the overwhelming majority of the formed

mutations die together with their hosts without being transmitted to progenies. A natural question comes up on the place and time when mutations, forming the basis of evolution of the living, are formed.

The experiments with the mutations of ontogenes directly suggest the source of mutations: this is the active DNA in the germline. The parental inheritance of the manifestation of conditional mutations indicates this activity [7] [8] [14] [22] [24] [34]. The parental type of inheritance (in its broad sense) becomes feasible if a gene is active before meiosis and generates the gene product that loses the connection with the gene that produced it [34]. Thanks to ontogenes, the gene material in the germline gets the status of "active". The earlier discovered phenomena, such as transposition of mobile elements [35] [36] [37], hybrid dysgenesis [36], epigenetic inheritance [38] [39], and genome editing [40], are in full compliance with this status. All these phenomena are associated with genetic material in the germline.

In general, the above data demonstrate an important role of the ontogenes in fundamental biological processes: ontogenesis, phylogenesis, and mutagenesis. This role is determined by the ability of ontogene to control cellular construction via influencing the process of cell division. Before the ontogenes were discovered, many of the most important questions related to fundamental biological problems remained beyond the focus of active research. The "explanations" utilizing ontogenes have also another important meaning since they implicitly confirm that genetic material has another genetic function along with the control of protein synthesis, namely, the control of cellular construction.

4. Some Specific Features in the Manifestation of Ontogenes

The ability of ontogenes to control cellular construction distinctly distinguishes them from the Mendelian genes, involved in the construction of proteins. It is reasonable to expect that ontogenes and Mendelian genes will also differ in their work style. Experimental data confirm this assumption: the ontogenes 1) interact with their own kind in a remote manner; 2) are active in a compact state; and 3) manifest the so-called paradox of homologous pairing. The classical genetics, operating with Mendelian genes has not encountered such specific features.

4.1. Remote Interaction

Two variants of remote interaction have been discovered. The first one was observed when studying the nondisjunction of chromosomes in the meiosis of ontomutants [24]. The phenomenon of meiotic nondisjunction of drosophila chromosomes is long known [41] [42] and well studied [43] [44]. The frequency of nondisjunction increases in the genomes with chromosome rearrangements and additional chromosomes [41] [45] but the point Mendelian mutations in heterozygous state do not increase the nondisjunction frequency [46]. It has quite unexpectedly emerged that mutations in ontogenes induce a superhigh frequency of the X chromosome nondisjunction in the meiosis of female flies [2]. The

high rate of chromosome nondisjunction is the phenomenon most likely characteristic of any ontomutation [24].

It is commonly believed that the nondisjunction of homologous chromosomes results from an independent orientation of homologs relative to the poles caused by the absence of pairing [45] [47]. If so, a high nondisjunction frequency in ontomutants means that 1) ontomutations decrease the ability to pair and 2) ontogenes are responsible for pairing. In other words, a normal interaction between the ontogenes residing in homologous chromosomes draws the homologs together in meiosis (guaranteeing a normal pairing), whereas the interaction damaged by the presence of a mutation fails to provide their approaching (pairing). In this process, it is important that this refers to the *remote* interaction of ontogenes, that is, *in the absence of their physical contact*.

In the presence of inversions and translocations in heterozygote, unconventional meiotic figures—loops and crosses—are observed [48] [49]. They suggest that gene (ontogene) interaction brings homologs together in an individual manner. The genetic data on crossing over in the chromosome rearrangements, dating back to the period of classical genetics (attraction-repulsion hypothesis) confirm the conclusion that the meiotic pairing of homologs is an integrated effect of the interaction of homologous genes [50] [51].

Similar to Mendelian genes, ontogenes are nucleotide sequences within DNA. They can be identical (homologous ontogenes) and different (nonhomologous ontogenes). Unusual meiotic figures in the presence of rearrangements suggest that the pairing of homologous chromosomes in meiosis is the result of interaction of homologous ontogenes. Since the homologs before the meiotic pairing reside at a distance from one another, the fact of successful pairing is the proof of *a real physical interaction between the homologous ontogenes separated by a distance*.

The second variant of the remote interaction between homologous ontogenes was discovered when studying the effect of maternal genome on a lethal manifestation of an ontomutation in the father [52]. In the cross between *yellow* females with the males carrying an ontomutation in the X chromosome, part of the laid eggs do not develop and the other part develops into males. Both facts taken together suggest that *the laid eggs are fertilized* but the development of female progenies is blocked. If a *yellow* female is replaced with a female of another genotype, the daughters of the mutant male are formed.

The undeveloped eggs of *yellow* females retain white color [22] [23] as if they were not fertilized. Although the fertilization took place, neither synkaryon nor blastomeres are formed. Otherwise, the dead embryos would color the egg brown as is the case with developing aneuploid embryos. The arrest of development in this case is explainable with only the blocking of mutual approach of the female and male pronuclei. We believe that the homologous ontogenes in the parental genomes being in one cell (zygote) interact with one another. A normal interaction makes the pronuclei to move towards one another and fuse. As for the interaction disturbed by a mutation, it fails to induce the approaching

movement and no fusion occurs, thereby leading to an early death of the zygote [14] [53]. See section 3.4 for the biological significance of this process.

4.2. Activity within Heterochromatin

The chromosome material in a dividing meiocyte is in a compacted state. Consequently, *the ontogenes that initiate the pairing of homologs are active although being themselves in a compacted state*. The interaction of ontogenes in the zygote after fertilization, mentioned above, also suggest the activity of ontogenes when being compacted. As is known, the chromosomes in gametes are also highly compacted. This demonstrates that the chromosome material displays activity not only being uncoiled (Mendelian protein-coding genes during protein synthesis) but in a coiled state as well (ontogenes).

The discovered maternal effect of ontomutations on chromosome nondisjunction [24] provides the important information about the compaction of ontogene's DNA. This effect suggests that the possibility of influencing meiosis and the degree of this effect are formed during the maturation of a gamete in the parental germline. The compaction of ontogene, predetermined as early as the premeiosis of the parent, is implemented in the meiosis of a progeny. Thus, the compaction of ontogene's DNA is a regulated property and can be seen as a component of DNA editing, going on in the premeiotic cell on a regular basis.

The inference on the activity of ontogenes in a compacted state brings us to the issue of the functional activity of heterochromatin in eukaryotic genome. The fact of activity of compacted regions explains a high abundance of heterochromatic regions in the genome. The total share of heterochromatin in the drosophila karyotype is 33% [54]. The activity of compacted ontogenes explains numerous facts of how heterochromatin influences the chromosome distribution in meiosis [43] [54]-[60], of gene position effect [61], and of the possible role of ontogenes as a universal regulator of gene activity [62]. If the activity of compacted regions is exclusively ascribed to ontogenes, the inconsistency of the statement on inactivity of compacted (heterochromatic) regions is resolved [63]. Indeed, the inactivity of Mendelian protein-coding genes in a compacted state does not exclude the activity of compacted ontogenes.

4.3. Paradox of Homologous Pairing

The conclusion that the approaching of homologs in meiosis is caused by the attraction of homologous ontogenes suggests considering in more detail the pairing of homologs with one of them carrying an inversion (**Figure 8**). By the moment when homologous ontogenes (A-A, B-B, and C-C) start to approach, their sequences are inverted; nonetheless, the approach occurs, as is demonstrated by loop formation. Actually, the homologous sequences turned by 180˚ relative to each other *are nonhomologous*. The arrangement of nucleotides in these sequences is in no way different from that in the sequences referred to as nonhomologous. *The paradox consists in that two actually nonhomologous sequences approach each other as is takes place with homologous sequences* [64].

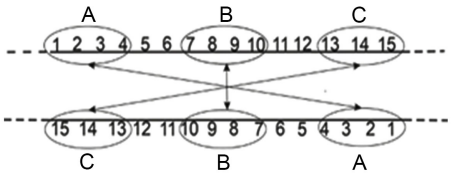

Figure 8. Juxtaposition of homologous ontogenes in a heterozygote for a chromosome inversion. Two homologous chromosomes before pairing. The field of vision contains a segment of the chromosomes containing nucleotides from 1 to 15. The segment is inverted in the lower homolog. Each homolog contains three ontogenes: A (1 - 4), B (7 - 10), and C (13 - 15). Arrows show the directions of attraction of homologous ontogenes for a bivalent to be formed [64].

This paradox has no solution for the pairing of Mendelian genes since the fact that the interaction of actually nonhomologous nucleotides is admitted cancels the general principle of genetic coding based on the order of nucleotides. However, the solution exists for the case of approaching determined by ontogenes: *the ontogenes are the source of a factor that acts regardless of the spatial position of the sequence*. Because of this factor, two ontogenes with the same sequence act in meiosis as homologous independently of their mutual arrangement in the space of cell before the beginning of meiotic pairing [64].

The proposed solution asserts that the ontogenes possess *an activity that propagates in space in all three directions*. We postulate that the ontogene is able generate a physical field, which is 1) specific and depends on the composition of the nucleotide sequence of the ontogene; 2) guarantees the remote interaction of ontogenes; 3) is a prerequisite for approaching of homologs; and 4) allows for the interaction of sequences independently of their orientation in the field.

5. Biophysical Nature of the Activity of Ontogenes

The results of our work with mutations of ontogenes, starting from the method used for their generation and selection, demonstrates that the ontogenes are the regions of DNA molecule with the properties typical of DNA nucleotide sequence, namely, the capability of carrying, transferring, multiplying, mutating, and so on. However, the ontogenes fundamentally differ from the Mendelian genes by that they control cellular construction and activate Mendelian genes without employing protein synthesis. The function of ontogenes is unique because of 1) their capability of remote interaction; 2) pairing paradox; and 3) the activity displayed by ontogene's DNA in a compacted state. These three specific features are logically interconnected and all three suggest that the ontogenes function in a basically different manner despite their chemical kinship with Mendelian genes.

According to the current understanding, the living organism is a chemical reactor containing chemical compounds in a state of chemical interactions. The properties of ontogenes listed above misfit the chemical style of work. The chemical interaction of genes requires their contact; however, the ontogenes, on

the contrary, interact at a distance. The chemical contact is a nucleotide-wise alignment of sequences; however, homologous ontogenes do not need this. The chemical interaction of genes demands the DNA sequences to be linear, whereas ontogenes, on the contrary, display their activity with their homologous sequences tightly compacted.

The remote interaction independent of the mutual arrangement of nucleotide sequences in space directly suggests that this interaction is provided in a physical rather than a chemical manner, namely, via the induction of a physical field, say an electromagnetic one. A compacted state, characteristic of active ontogenes according to our data, perfectly agrees with the hypothesized electromagnetic nature of the interaction. Moreover, the construction of a three-dimensional structure, which a multicellular organism is, demands a spatial orientation in the process of addition of new cells, which is impossible without a spatially oriented external field and the genetic elements able to link them to the three-dimensional spatial position. The hypothesis that ontogenes generate a physical field theoretically looks necessary and experimentally looks substantiated. Thus, the challenge related to the novel genes—ontogenes—being initially genetic, moves out to the area of biophysics.

The hypothesis of DNA magnetic properties was first formulated in the experimental works by Blyumenfel'd as early as 1959 [65]. When studying the electrical conductivity of DNA, researchers discovered that the stacks of DNA bases are good conductors. They display the properties of semiconductors and are able to transfer both holes and electrons [66]. The formation of chemical bonds of a certain type referred to as resonance bonds (benzene molecule is an example) creates a specific situation when some electrons become delocalized and thus able to freely travel across the entire molecule. The delocalized pi-electrons or delocalized protons of hydrogen bonds in DNA are able to migrate so that a stack of nucleotide bases acquires the properties of an isolated conductor [67], while the DNA strand on nucleosomes becomes an inductance coil generating magnetic field. Myakishev-Rempel *et al.* [68] [69] [70] believe that several nucleosomes with a DNA region become an oscillatory circuit that forms an oscillating magnetic field. The DNA regions that form the oscillating magnetic field are able to induce the oscillation of the DNA regions similar or close in their molecular structure.

6. Conclusions

The research into the control of cellular construction by ontogenes is at the very beginning of its experimental development; however, the theoretical consequences of the very fact that this control is revealed are already evident. The concept of a genetic trait is changing. From "planar" it becomes "three-dimensional". Another "cellular" dimension is added to the "protein" dimension of the trait. Even when a genetic mutation that alters the corresponding protein is considered, the genes responsible for formation of the cells containing this protein are present on the

background. Thus, we have to take into account as an indisputable fact that the manifestation of a protein-coding gene is determined not only by the gene itself, but also by the cell ensemble produced by ontogenes. Correspondingly, the perception of a trait in terms of three dimensions allows its transformations in ontogenesis and phylogenesis to be traced.

In current biology, *the living is regarded as the derivative of DNA*. The popular genetic concept implies that the living is the protein and the protein is the product of protein-coding genes. The discovery of the role of ontogenes in cellular construction requires that the concept is changed. The control of cell does not mean its de novo construction as in the case of protein: *although ontogenes control the construction of the structures formed of cells*, *they neither generate cells nor determine their ability to divide*. Unlike a protein molecule, cell is the product of division of a pre-existing cell rather than a derivative of DNA. Similar to DNA molecule, cell is an elementary structure of the living. The popular formula "DNA → the living" is incomplete; the complete variant is "cell + DNA → the living".

We propose to keep in mind that the two objects, *protein* and *cell*, are under genetic control rather than one object, *protein*, alone. The cell-based organization determines the specific features of a living organism and, along with the informational DNA, creates the organisms with different degrees of complexity. The cell envelope allows for autonomous energetics of both the cell and the overall organism. One of the amazing manifestations of ontomutations is the change in the level of basal metabolism. The locomotor activity of individuals changes as well [71]. The insight into cellular construction with the help of mutations in ontogenes for the first time offers the opportunity to study the energy aspect of vital activities [72].

The current biology regards a living organism as a chemical reactor, and genetics also considers the genetic function as exclusively chemical processes. The performed study of the genetic control of cellular construction demonstrates *the existence of a physical control* (with the help of a field). Cells are elementary bricks of which three-dimensional organisms are constructed. Ontogenes are the carriers of the program used in this construction. They are intended for the construction in a three-dimensional space and can manage this task only if they have spatial awareness, that is, are able to induce a physical field and respond to the physical field. The conclusion on the existence of a biological field induced by certain DNA regions—ontogenes—is inevitable. The current genetics demonstrates how great and diverse the world of DNA chemical interactions is but just imagine how the significance of DNA will increase with the information about its functioning with the help of a physical field.

The discovery of the role of ontogenes in the control of cellular construction makes conceptually complete the general idea about the gene control in the living organism. The objects of genetic control are not only the renewable proteins, but also the cells housing them as well as the material that perform this control.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Gaisinovich, A.E. (1988) The Birth and Development of Genetics. Nauka, Moscow. (In Russian)

[2] Chadov, B.F. (2001) Mutations Capable of Inducing Speciation. In: Stegnij, V.N., Ed., *Evolution Biology*, Tomsk State University Press, Tomsk, 138-162. (In Russian)

[3] Chadov, B.F. (2005) Features of Intraspecific Similarity and Peculiarities of Mendel's Approach to Study of Heredity. *Philosophy of Science*, **3**, 94-114. (In Russian)

[4] Chadov, B.F., Chadova, E.V., Kopyl, S.A., Artemova, E.V., Khotskina, E.A. and Fedorova, N.B. (2004) From Genetics of Intraspecific Differences to Genetics of Intraspecific Similarity. *Russian Journal of Genetics*, **40**, 945-958. https://doi.org/10.1023/B:RUGE.0000041372.16880.02

[5] Chadov, B.F., Chadova, E.V., Kopyl, S.A. and Fedorova, N.B. (2000) A New Class of Mutations in *Drosophila melanogaster*. *Doklady Biological Sciences*, **373**, 423-426.

[6] Chadov, B.F. (2000) Mutations in the Regulatory Genes in *Drosophila melanogaster*. *Proceedings of the International Conference on Biodiversity and Dynamics of Ecosystems in North Eurasia*, *IC@G*, Novosibirsk, 21-26 August 2000, 16-18.

[7] Chadov, B.F., Fedorova, N.B., Chadova, E.V. and Khotskina, E.A. (2011) Conditional Mutations in Drosophila. *Journal of Life Sciences*, **5**, 224-240.

[8] Chadov, B.F., Fedorova, N.B. and Chadova, E.V. (2015) Conditional Mutations in *Drosophila melanogaster*: On the Occasion of the 150th Anniversary of G. Mendel's Report in Brünn. *Mutation Research/Reviews in Mutation Research*, **765**, 40-55. https://doi.org/10.1016/j.mrrev.2015.06.001

[9] Chadov, B.F. (2007) Ontogenes in *Drosophila melanogaster*: Genetic Features and Role in Onto- and Phylogeny. In: Korogodina, V.L., Chini, A. and Durante, M. (Eds.), *Modern Problems of Genetics*, *Radiobiology*, *Radioecology and Evolution*, Joint Institute for Nuclear Research, Dubna, 80-91.

[10] Fedorova, N.B., Chadova, E.V. and Chadov, B.F. (2016) Genes and Ontogenes in Drosophila: The Role of RNA Forms. *Transcriptomics*, **4**, Article ID; 1000137.

[11] Ashburner, M. (1989) Drosophila. A Laboratory Handbook. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 427-432.

[12] Timofeeff-Ressovsky, N.V. (1927) Studies on the Phenotype Manifestation of Hereditary Factors. I. On the Phenotypic Manifestation of the Genovariation *Radius incompletes* in *Drosophila funebris*. *Genetics*, **12**, 128-198. https://doi.org/10.1093/genetics/12.2.128

[13] Timofeeff-Ressovsky, N.V. (1996) Relation between Gene and Phenotypic Character. In: Gazenko, O.G. and Ivanov, V.I., Eds., *N.V. Timofeeff-Ressovsky*, *Selected Works*, Meditsina, Moscow, 59-84. (In Russian)

[14] Chadov, B.F. and Fedorova, N.B. (2020) Conditional Mutations and New Genes in Drosophila. In: Fasullo, M. and Catala, A., Eds., *Mutagenesis and Mitochondrial-Associated Pathologies*, IntechOpen, London.

[15] Chadov, B.F. and Fedorova, N.B. (2020) Inbreeding Depression and Heterosis as the Phenomena of Two-Component Genome. In: *Advances in Genetics Research*, Vol. 19, Nova Science Publishers, Inc., Hauppauge, 161-190.

[16] Chadov, B.F. and Fedorova, N.B. (2019) The Mutations Disturbing the Bilateral Symmetry in Drosophila. *SCIOL Genetic Science*, **2**, 139-152.

[17] Neifakh, A.A. and Timofeeva, M.Ya. (1977) Molecular Biology of Developmental Processes. Nauka, Moscow. (In Russian)

[18] Waddington, C.H. (1962) New Patterns in Genetics and Development. Columbia University Press, New York. https://doi.org/10.7312/wadd92142

[19] Chadov, B.F., Chadova, E.V., Kopyl, S.A., Khotskina, E.A. and Fedorova, N.B. (2004) Genes Controlling Development: Morphoses, Phenocopies, Dimorphs and Other Visible Expressions of Mutant genes. *Russian Journal of Genetics*, **40**, 271-281. https://doi.org/10.1023/B:RUGE.0000021627.82588.41

[20] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2012) Epigenetic Phenomenology in Conditional Mutants of *Drosophila melanogaster*: Morphoses and Modifications. In: Zakijan, S.M., Vlasov, S.M. and Dement'eva, E.V., Eds., *Epigenetics*, SD RAN, Novosibirsk, 499-533. (In Russian)

[21] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2015) Images of Morphoses and Modifications in *Drosophila melanogaster* Conditional Mutants. https://doi.org/10.13140/RG.2.1.2721.9042

[22] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2017) The Genetics of Conditional Mutations and Individual Developmental Program in *D. melanogaster*. *SCIOL Genetic Science*, **1**, 3-21.

[23] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2018) Conditional Mutations in Drosophila: Concept of Genes That Control Individual Development. *Advances in Bioscience and Biotechnology*, **9**, 243-272. https://doi.org/10.4236/abb.2018.96017

[24] Chadov, B.F. and Fedorova, N.B. (2022) Ontogenes and Chromosome Nondisjunction in the *D. melanogaster* Meiosis. *Advances in Bioscience and Biotechnology*, **13**, 317-335. https://doi.org/10.4236/abb.2022.138020

[25] Ashburner, M. (1989) Mosaics. In: *Drosophila. A Laboratory Handbook*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 931-968.

[26] Vasil'eva, L.A. (1999) Quantitative Traits: Genetic Properties and Methods of Analysis. ITsiG SO RAN, Novosibirsk. (In Russian)

[27] Kondakov, N.I. (1975) Logicheskii slovar'—Spravochnik (Logical Dictionary—Handbook). Nauka, Moscow, 477. (In Russian)

[28] Jacob, F. and Monod, J. (1961) Genetic Regulatory Mechanisms in the Synthesis of Proteins. *Journal of Molecular Biology*, **3**, 318-356. https://doi.org/10.1016/S0022-2836(61)80072-7

[29] Belousov, L.V. (2006) A Morphomecanical Aspect of Epigenesis. *Genetica* (*Russ.*), **42**, 1165-1169. https://doi.org/10.1134/S1022795406090031

[30] Chadov, B.F. and Fedorova, N.B. (2003) The Elementary Event of Development. *Doklady Biological Sciences*, **389**, 183-187.

https://doi.org/10.1023/A:1023403800039

[31] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2019) Ontogenes and the Problem of Speciation. *Journal of Evolutionary Science*, **1**, 33-47. https://doi.org/10.14302/issn.2689-4602.jes-18-2431

[32] Chadov, B.F. and Fedorova, N.B. (2018) Zygotic Selection in *Drosophila melanogaster* and a New Edition of Darwin's Concept of Speciation. In: Podobina, V.M., Ed., *Evolution of Life on the Earth*, *Proceedings of the V International Symposium*, Publishing House of TSU, Tomsk, 49-51.

[33] Auerbach, Ch. (1976) Mutation Research: Problems, Results, and Perspectives. Springer, New York.

[34] Chadov, B.F., Fedorova, N.B. and Chadova, E.V. (2013) Parental Effects of Conditional Mutations and Their Explanations. *Russian Journal of Genetics*, **49**, 141-150. https://doi.org/10.1134/S1022795413020038

[35] Finnegan, D.J. (1989) Eucaryotic Transposable Elements and Genome Evolution. *Trends in Genetics*, **5**, 103-107. https://doi.org/10.1016/0168-9525(89)90039-5

[36] Ratner, V.A. and Vasil'eva, L.A. (2000) Induction of Transpositions of Mobile Genetic Elements by Stress Impacts. *Sorosovskii Obrazovatel' nyi Zhurnal*, **6**, 14-20. (In Russian)

[37] Ashburner, M. (1989) Hybrid Dysgenesis and Related Phenomena. In: *Drosophila. A Laboratory Handbook*. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 969-1015.

[38] Russo, V.E.A., Martienssen, R.A., Riggs, A.D. and Briggs, A.D., Eds. (1996) Epigenetic Mechanisms of Gene Regulation. Cold Spring Harbor Laboratory Press, New York.

[39] Zakijan, S.M., Vlasov, S.M. and Dement'eva E.V., Eds. (2012) Epigenetics. SD RAN, Novosibirsk. (In Russian)

[40] Baranov, V.S., Kuznetsova, T.V., Pendina, F.F., *et al*. (2012) Epigenetic Mechanisms in Human Normal and Pathological Development. In: Zakijan, S.M., Vlasov, S.M. and Dement'eva, E.V., Eds., *Epigenetics*, SD RAN, Novosibirsk, 225-266. (In Russian)

[41] Bridges, C.B. (1916) Non-Disjunction as Proof of the Chromosome Theory of Heredity. *Genetics*, **1**, 1-52. https://doi.org/10.1093/genetics/1.1.1

[42] Bridges, C.B. (1921) Proof of Non-Disjunction for the Fourth Chromosome of *Drosophila melanogaster*. *Science*, **53**, 308. https://doi.org/10.1126/science.53.1370.308.a

[43] Chadov, B.F. (1991) From the Phenomenon of Nondisjunction to the Problem of Chromosome Co-Orientation (To the Commemoration of Bridges Paper Published 75 Years Ago). *Genetika*, **27**, 1877-1903. (In Russian)

[44] Ganetzky, B. and Hawley, R.S. (2016) The Centenary of *GENETICS*: Bridges to the Future. *Genetics*, **202**, 15-23. https://doi.org/10.1534/genetics.115.180182

[45] Sturtevant, A.H. and Beadle, G.W. (1936) The Relations of Inversions in the X Chromosome of *Drosophila melanogaster* to Crossing over and Disjunction. *Genetics*, **21**, 554-604. https://doi.org/10.1093/genetics/21.5.554

[46] Chadov, B.F. (1971) Nonhomologous Chromosome Pairing in Oogenesis of *Drosophila melanogaster*. Abstract of Dissertation for the Degree of PhD in Institute of Developmental Biology, Moscow. (In Russian)

[47] Merriam, J.R. and Frost, J.N. (1964) Exchange and Nondisjunction of the X Chromosomes in Female *Drosophila melanogaster*. *Genetics*, **49**, 109-122.

https://doi.org/10.1093/genetics/49.1.109

[48] Ashburner, M. (1989) Inversions. In: *Drosophila. A Laboratory Handbook*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 509-528.

[49] Ashburner, M. (1989) Translocations. In: *Drosophila. A Laboratory Handbook*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 549-574.

[50] Dobzhansky, Th. (1931) The Decrease of Crossing over Observed in Translocations, and Its Probable Explanation. *The American Naturalist*, **65**, 214. https://doi.org/10.1086/280364

[51] Dobzhansky, Th. (1932) Studies on Chromosome Conjugation. I. Translocations Involving the Second and the Y-Chromosomes of *Drosophila melanogaster*. *Zeitschrift für induktive Abstammungs- und Vererbungslehre*, **60**, 235-286. https://doi.org/10.1007/BF01850271

[52] Chadov, B.F., Chadova, E.V. and Fedorova, N.B. (2017) A Novel Type of Gene Interaction in *D. melanogaster*. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, **795**, 27-30. https://doi.org/10.1016/j.mrfmmm.2017.01.002

[53] Fedorova, N.B. and Chadov, B.F. (2020) Gene Interactions in Drosophila without Contacts and Chemical Intermediaries. *International Conference on Cell and Experimental Biology*, Virtual Conference, 9-11 December 2020, 6. https://cellexpbiol.unitedscientificgroup.org/proceedings/CEB-2020_Abstracts.pdf

[54] Zhimulev, I.F. (2002) General and Molecular Genetics. Novosibirsk State University Press, Novosibirsk. (In Russian)

[55] Chadov, B.F. and Podoplelova, M.L. (1981) Nonhomologous Pairing and Spontaneous Meiotic Interchanges in *Drosophila melanogaster* Females. *Mutation Research*, **81**, 311-327. https://doi.org/10.1016/0027-5107(81)90119-6

[56] Chadov, B.F. (1987) Near-Centromere Heterochromatin and Co-Orientation of Chromosomes in Dividing Cells of Drosophila. *Genetica* (*Russia*), **23**, 1082-1087.

[57] Chadov, B.F. (1996) Mechanism of Chromosome Nondisjunction in Drosophila Meiosis. In: Abbondandolo, A., Vig, B.K. and Roi, R., Eds., *Chromosome Segregation and Aneuploidy-III*, Ispra, E.C. Joint Research Center, Italy, 328-343.

[58] Hawley, R.S., *et al.* (1992) There Are Two Mechanisms of Achiasmate Segregation in *Drosophila* Females, One of Which Requires Heterochromatic Homology. *Developmental Genetics*, **13**, 440-467. https://doi.org/10.1002/dvg.1020130608

[59] Karpen, G.H., Le, M.H. and Le, H. (1996) Centric Heterochromatin and the Efficiency of Achiasmate Disjunction in Drosophila Female Meiosis. *Science*, **273**, 118-122. https://doi.org/10.1126/science.273.5271.118

[60] Hughes, S.E., *et al.* (2009) Heterochromatic Threads Connect Oscillating Chromosomes during Prometaphase I in *Drosophila* Oocytes. *PLOS Genetics*, **5**, e10000348. https://doi.org/10.1371/journal.pgen.1000348

[61] Zhimulev, I.F. (1998) Polytene Chromosomes, Heterochromatin and Position Effect Variegation. In: *Advances in Genetics*, Vol. 37, Elsevier Inc., Amsterdam, 1-555. https://doi.org/10.1016/S0065-2660(08)60341-7

[62] Panshin, I.B. (1992) The Second System of Hereditary Variation as a Consequence of Quantitative Regularities of Heterochromatic Gene Position Effect. In: Khvostova, V.V., Ed., *The Gene Position Effect in the Studies*, ICG SO RAN, Novosibirsk, 23-98. (In Russian)

[63] Prokofieva-Belgovskaja, A.A. (1986) Heterochromatic Regions of Chromosomes. Nauka, Moscow. (In Russian)

[64] Chadov, B.F. and Fedorova, N.B. (2021) Ontogenes and the Paradox of Homologous Pairing. *Advances in Bioscience and Biotechnology*, **12**, 1-9. https://doi.org/10.4236/abb.2021.121001

[65] Blyumenfel'd, L.A. (1959) Abnormal Magnetic Properties of Nucleic Acids. *Biofizika*, **4**, 515-519. (In Russian)

[66] Arnold, A.R., Grodick, M.A. and Barton, J.K. (2016) DNA Charge Transport: From Chemical Principles to the Cell. *Cell Chemical Biology*, **23**, 183-197. https://doi.org/10.1016/j.chembiol.2015.11.010

[67] Holmlin, R.E., Dandliker, P.J. and Barton, J.K. (1997) Charge Transfer through the DNA Base Stack. *Angewandte Chemie International Edition*, **36**, 2714-2730. https://doi.org/10.1002/anie.199727141

[68] Polesskaya, O., Guschin, V., Kondratev, N., *et al*. (2018) On Possible Role of DNA Electrodynamics in Chromatin Regulation. *Progress in Biophysics and Molecular Biology*, **134**, 50-54. https://doi.org/10.1016/j.pbiomolbio.2017.12.006

[69] Savelyev, I.V., Zyryanova, N.V., Polesskaya, O.O. and Myakishev-Rempel, M. (2019) On the Existence of the DNA Resonance Code and Its Possible Mechanistic Connection to the Neural Code. *NeuroQuantology*, **17**, 56-71. https://doi.org/10.14704/nq.2019.17.2.1973

[70] Savelev, I. and Myakishev-Rempel, M. (2020) Possible Traces of Resonance Signaling in the Genome. *Progress in Biophysics and Molecular Biology*, **151**, 23-31. https://doi.org/10.1016/j.pbiomolbio.2019.11.010

[71] Chadov, B.F., Fedorova, N.B., Chadova, E.V., Khotskina, E.A., Moshkin, M.P. and Petrovski, D.V. (2010) Genetic Mutation Affects Energy Status of *Drosophila*. *Russian Journal of Genetics*, **46**, 1062-1066. https://doi.org/10.1134/S1022795410090127

[72] Fedorova, N.B. and Chadov, B.F. (2016) Genetics: The Energy Aspect. *Regional Interdisciplinary Conference—Humboldt Kolleg "Energy Conversion: From Nature to Technology"*, 28 August-2 September 2016, Novosibirsk, Russia.