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Ontogenes and the Problem of Speciation

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Abstract

The existing hypotheses on speciation rely on Mendelian genes and mutations in them. However, genome-wide sequencing demonstrates that the Mendelian genes account less than one-tenth of the entire genome DNA. This means that a greater part of the genome has not yet been subject to large-scale evolutionary consideration. This paper deals with the conditional mutations in drosophila, which are mutations of the genes belonging to a special category (ontogenes) controlling the program of individual development. The ontogenes presumably reside in the DNA of intergenic spaces and introns. Conditional mutations display a number of properties absent in the mutations of Mendelian genes. These specific properties allow three key problems in speciation to be solved: (1) the possibility of emergence of new traits as a result of sequential mutagenesis; (2) selection of mutants; and (3) establishment of isolation. We have shown that (1) the mutations in ontogenes are able to form new multigenic regulatory blocks that escape selection during their creation; (2) mutations in ontogenes allow for existence of constantly acting zygotic selection, which is by no means less important for speciation than Darwinian selection; and (3) owing to their conditionally lethal effect, the mutations in ontogenes are able to create biological isolation barrier. This gives the grounds for assuming that the emergence of mutations in ontogenes is a necessary condition for speciation.

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Introduction

The classical period in development of genetics gave birth to the genetic foundations of ontogenesis and phylogenesis, bringing the corresponding areas of knowledge to a higher level. However, genetics have encountered difficult questions. The first question is how it is possible to explain the obligate similarity of individuals within a species with the help of changeable (those that form viable mutant variants) genes [1]. The second question is how it is possible to explain the existence of common and unchangeable program of individual development within a species with the help of the concept of changeable gene [2]. Finally, the third question is whether it is possible to explain establishment of biological isolation of a new species, one of the fundamental phenomena in speciation, with the help of mutations in Mendelian genes, which, as a rule, do not interfere with fertility [3].

The attempts to answer these and other questions have suggested existence of different genes, other than the Mendelian ones [4, 5, 6, 7, 8, 9, 10]. These assumptions have not been experimentally confirmed and the classical idea of a universal gene remained valid. Nonetheless, the range of problems associated with speciation served as a launch pad in the search for new genes [11].

We have assumed that the genes responsible for the species-level program of individual development are obligately homozygous; hence, the mutations that lead to speciation should look a sort of paradoxically. They should be lethal in a heterozygous state and not lethal as homozygotes [11]. This hypothesis formed the basis for devising the new methods to recover mutations. Thus, the drosophila mutations later named conditional mutations were discovered [12, 13].

The very fact that conditional mutations were found in drosophila [12, 13] together with the fact that these mutations display a set of unusual properties [14, 15] has allowed us to infer that the genome contains a special category of genes distinct from the Mendelian ones. These genes got the name *ontogenes* [1, 16, 17, 18, 19]. Further elaboration of the concept of ontogenes has led to most important inferences on the process of individual development [2] as well as opened new prospects for solving the problems in phylogenesis [3, 20, 21, 22, 23]. The very opportunity of advancing in the field of ontogenesis and phylogenesis demonstrates that revisiting the concept of a universal unit of heredity is reasonable and promising, making relevant an extensive research into ontogenes.

The goal of this work was to explicate reasoned conclusions (decisions) on three pivotal problems in phylogenesis. The first problem is the possibility of a multistep speciation. The assumption of stepwise speciation looks justified, even the only possible, but its implementation with the help of Mendelian genes alone faces serious obstacles. The second problem is the role of selection in speciation, formulated by Darwin and still debated. The third problem is the mechanism underlying the isolation during speciation, which is among the most important in this field.

All these problems have a deep history, long lists of the papers that have attempted to resolve them, and the generally accepted fact that the solutions are yet absent. The postulates formulated here are based on analysis of the unusual properties of ontogenes earlier discovered in experiments. This paper is a kind of a *travel into the evolutionary issues* with the data on conditional mutations in *D. melanogaster* and the concept of ontogenes.

Ontogenes and Conditional Mutations (Based on Results of Earlier Experiments)

The research into ontogenes has passed through several stages. The first stage consisted in theoretical prediction of the earlier unknown genes and formulation of the search rules allowing the mutations in these genes to be found [1, 11, 24]. This stage yielded a collection of conditional mutations. A conditional mutation (typically, a lethal) manifests itself under certain genetic conditions (a restrictive genotype) and fails to do it under other genetic conditions (a permissive genotype) [1, 12, 13, 25].

The second stage consisted in the description of how these mutations manifested themselves in permissive genotypes. This manifestation pattern drastically differed from the pattern characteristic of Mendelian mutations [14, 15, 26, 27, 28, 29]. The results obtained in two stages independently of one another demonstrated existence of certain genetic units other than Mendelian genes. The third stage of this research was focused on the development of the concept of the genes underlying conditional mutations.

These genes were named *ontogenes* [1, 16, 17, 18, 19] owing to the characteristic abnormalities observed in the progeny of mutant individuals [28]. One of the most vivid manifestations of these mutations in an ontogene is an abnormality of individual development appearing as morphoses (deformities) [28].

The method for obtaining conditional mutations itself suggests that these mutations are damages in DNA (DNA genes) [30]. The response of these mutations to the presence of chromosomal rearrangements in the genome excludes the possibility that protein is an interface product. The intranuclear RNA is the only remaining putative variant [19]. The unalterable dominance of the effects of conditional mutations suggests that the acting DNA is a duplex [2, 19, 31].

The parental effects of a paternal type and the parental effect of "prohibition on daughters" [32] demonstrate that the ontogenes are active in the germline [2]. The developmental abnormalities (morphoses) appearing in flies [28, 33] suggest impairments in the program of ontogenesis [2, 34].

Table 1 summarizes the properties of ontogenes observed in experiments as compared with the properties of Mendelian genes, long known in genetics. Both are similar in that they are represented by discrete units and these units are DNA regions. However, Mendelian genes and ontogenes are completely opposite in genetic respect: (1) Mendelian genes in their manifestation and inheritance are independent from each other, whereas ontogenes are dependent on each other and the overall genome; (2) Mendelian genes in their manifestation do not depend on their position within the nucleus, whereas ontogenes depend on their positions; (3) Mendelian genes are permitted to change (mutate), whereas any mutations in ontogenes is "prohibited", since the mutations of in ontogenes lead to lethality, i.e., elimination of mutant ontogenes from population together with the genome carrying the mutant variants; and (4) the manifestation of parental ontogenes in the progeny depends not only on the gene composition of a parent, but also on the genome of the mate in cross (this dependence is unobservable among the Mendelian genes). All this suggests that the genome is a two-component system rather than a single-component one and comprises the genes of two categories—Mendelian genes and ontogenes.

The combination of the effect of a chromosomal rearrangement and the phenomenon of parental inheritance [32, 35] allowed us to hypothesize the pattern for function of the genome part composed of ontogenes. The initial stage is DNA transcription

Table 1. Similarities and differences of two gene types

Specific features in gene structure and function	*Mendelian gene*	*Ontogenes*	*Reference*
Template	DNA region	DNA region	[2, 30]
Mechanism of implementation	DNA–mRNA–protein	DNA–nRNA–DNA	[19]
Site of gene activity	Soma	Germline and soma	[2, 34]
Time of activity	The entire period of soma development	Gametogenesis to meiosis and soma	[2]
Final product	Polypeptide	nRNA	[19]
Allelic state	Two products	One product (duplex)	[2]
Status in genome	Unique	Multiplied	[31]
Pattern of interaction in genome	Independent	Dependent	[3]
Typical gene function	Structural	Regulatory	[31]
Dependence of gene function on position in the nuclear	Independent	Dependent	[40, 23,19]

according to the principle of discreteness, stated by Mendel for the classical genes, followed by an "epigenetic" mechanism at the next stage. Ontogenes form nuclear RNA (nRNA) duplexes, which change the conformation of DNA template. The changed DNA template is transferred with gametes to the zygote. This particular conformation initiates ontogenesis with involvement of Mendelian genes [2, 34]. This epigenetic mechanism is another way for deployment of genetic information, which supplements the known method of coding with the help of nucleotides (DNA → mRNA → ribosome → polypeptide).

Thus, the living organism is under a double control of the Mendelian genes and ontogenes, the latter being the most stringent. The effect of ontogenes is of a systemic character, since it depends on the ontogenes of both the own genome and the genome of the partner in cross. The ontogene is manifested in a dominant manner excluding any changes. Any change in the ontogene in one dose, as a rule, leads to death at the earliest embryonic stage. A mutation in an ontogene can be saved from death only if this ontogene loses its activity. The control by ontogenes relies on two entities—nucleotide code of DNA and conformation of DNA molecule.

The control by Mendelian genes is milder. The genes act autonomously (independent inheritance and manifestation) and, as a rule, in a recessive manner (at a double dose). The trans-alleles of Mendelian genes act independently and their mutations are typically not lethal. The Mendelian genes control only material aspect of the living matter, i.e., protein.

The idea of genome inhomogeneity with respect to its composition has been repeatedly posed in genetics. The two components of the genome in terms of cytogenetics are euchromatin and heterochromatin [36]; in molecular genetics, unique and repetitive DNA sequences [37]; and in developmental genetics, the two-component nature appears in the idea of master genes [38 for references]. However, the hereditary units in none of these cases are fundamentally different according to the most important genetic parameters, namely, pattern of inheritance and pattern of manifestation. The crucial differences in inheritance and manifestation were the reason for dividing the hereditary units into the categories of genes and ontogenes.

Hypothesis of the Formation of New Species by Successive Mutagenesis in Ontogenes

Starting from the works by Korzhinsky [39] and de Vries [4], who were the first to raise the question of mutations in living organisms, genetics does not know any other pathways for evolutionary transformation of organisms except for mutations. The problem consists in that many genes are responsible for a single trait of an organism; correspondingly, emergence of a new trait requires that mutations in many genes coincide. This coincidence is extremely improbable at low frequencies of spontaneous mutagenesis. One can assume a sequential mutagenesis extended in time, but this hypothesis creates a new problem. The previous mutation by the moment when the next mutation appears must be somehow retained. However, an individual mutation without a set of mutations that form the corresponding trait as a rule decreases the viability of the organism and its fate is to be eliminated by selection. Thus, a mutation in one gene will disappear from population before another necessary mutation would emerge in some other gene.

Trying to bypass this difficulty, it was proposed that a putative gene duplication took place before the corresponding mutation [41, 42]. The presence of a normal copy of the gene allows elimination of its mutant variant to be avoided. The hypothesis of evolution by gene duplications is most comprehensively described by Susumi Ohno [43]. According to Ohno, the event of multiplication preceding the event of mutation is the condition for evolution. Keeping in mind that the traits are multigenic and the frequency of spontaneous mutations is low, the assumption on the necessity of preliminary duplication of each gene in question does not seem too realistic.

The mentioned assumptions were made with respect to traditional Mendelian mutations and Mendelian genes. Genetics has not known any other genes and mutations. We believe that this is why the idea of sequential mutagenesis is inconsistent. On the contrary, conditional mutations of ontogenes, which are considered here, may represent the particular material for origination, spreading, and retention of a set of mutationally altered genes that represent a new species. The idea of speciation via sequential mutagenesis is quite realistic if it is considered with respect to ontogenes.

Table 2 lists the progeny of the wild-type *D. melanogaster* males mated to *yellow* females. The males carry conditional mutations in their X chromosome. A "conditional" character of mutations consists in that these mutations do not manifest in males. The males have a wild-type phenotype, are viable, and fertile. However, the mutations manifest themselves as dominant lethals in the daughters of these males, which die in this cross failing to appear at all. As is evident from Table 2, the lethality of these mutations is well reproducible. The absence of daughters is observable both when the mutants are detected (cross 2♀ y × ♂+) and in their progenies in laboratory stocks of mutants (cross 6♀ y × ♂+).

The mutations in males led not only to the lethality of daughters, but also to partial lethality of the sons. This is suggested by the ratio of the eggs laid by *yellow* females and the number of adult progenies. In the case when all daughters die, the share of undeveloped eggs should be 50%; however, the number of undeveloped eggs was larger. This demonstrates that part of sons also dies at the stage of egg.

The question arises on how we can explain the absence of lethal effect of mutation in male (father) once it is present in its daughters. There is the only answer: the mutant gene is inactive in male. *Its function is fulfilled by another (the same but not mutant) gene or some other genes able to take on this function.* Thus, duplication of the function in the genome is characteristic of the studied category of genes (ontogenes). This is a normal situation for ontogenes, which makes it unnecessary to assume a special operation of gene duplication for speciation as S. Ohno did.

It is evident from the example with conditional mutations in the drosophila X chromosome that the mutations in ontogenes are able to escape elimination

Table 2. Progenies and fecundity of mutant (+) males crossed to *yellow* females [32]

Mutant male stock no.	Cross: 2♀ y × ♂+		Cross: 6♀ y × ♂+		Fecundity of male*
	Total number of progenies	Share of daughters in progeny	Total number of progenies	Share of daughters in progeny	
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
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
26	92	0.03	89	0.01	–
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

* The ratio of adult progenies to the number of laid eggs.

by selection. The mutant variants of ontogenes can be preserved in special genomes over infinitely large number of generations. If so, a network of mutant regulators forming the basis for a new trait can be constructed involving the mutations in ontogenes generated as a result of sequential mutagenesis [44, 45, 46].

Emergence of a new trait will look as a "sudden" although this is a result of a long-term changes in the genome. If a particular combination of mutations is beneficial, nothing prevents it from becoming homozygous since it is contained in the genomes of sibs in a heterozygous state. Something similar takes place in the long-term stocks of the mutants in the X chromosome (Table 2); namely, individual cases of emergence of homozygotes for the previously lethal mutations are observed.

The recovered mutations in the X chromosome were maintained in the stocks heterozygous for the In (1) Muller-5 inversion [14, 15]. The progeny in such stocks comprises two types of females, In (1) Muller-5/ In(1)Muller-5 and In(1)Muller-5/mutation, and two types of males, In(1)Muller-5 and <+>. No (+) females homozygous in the mutation are produced. The obtained mutations were also maintained in the stocks with attached -X chromosomes [14, 15].

The loss in lethal manifestation of some mutations was accidentally discovered in 2001 in the experiments on determining the level of dominant lethality. Males from stocks nos. 1, 3, 5, 27, and 33 (attached -X stocks) commenced to give female progenies (daughters) when crossed to *yellow* females. Later, lethality was tested using more representative samples of progenies. As was shown, five of the mentioned mutations tested in 2002 and 2004 actually lost their lethal character.

Three additional mutations (nos. 29, 38, and 41) lost their lethality in 2002 and another one (no. 35), in 2004. Some stocks displayed a decrease in lethality rather than its complete loss. Daughters started to appear in progeny although their rate did not reach the normal level of 50% (nos. 7 and 9–11). In total, nine mutations of the 22 mutant stocks completely lost their lethality over 2000–2004 and five mutations become semilethal. This phenomenon was named "loss of lethality" (see [22]) for more comprehensive description).

Note that the mutant X chromosome does not lose its recessive lethal manifestation in the stock despite the cases when the conditional lethality is lost in the test with *yellow* females. The females homozygous in a conditional mutation still do not appear in stocks. This suggests that it is not the chromosome defects that lead to formation of conditional mutations that are changed but rather the alternative regulatory pathways able to take on the function of mutant ontogenes. The latter variants become more numerous and lead to an increase in the number of daughters among the progenies. (Table 3)

Natural Selection of Adult Organisms and Natural Selection of Zygotes

The current theory of evolution relies on Darwinian selection. This selection implies elimination of the individuals poorly fit to environmental conditions and a decrease in fecundity, which reduces its genetic contribution to the next generation. Darwinian selection acts among the adult progenies, i.e., among the organisms in the postnatal period. The concept of environment is relevant to these particular individuals.

Note that the age of the organism that is subject to selection is very important. This information allows us to understand which particular genes are potentially involved in selection under the influence of environment. Naturally, these are the genes becoming active from the moment the zygote is formed. Until recently, all genes of an organism have been regarded as such genes. Thus, *it has been no doubt that all genes of a living organism are in the focus of Darwinian selection.*

The discovery of ontogenes made it clear that the Mendelian genes are by no means the only genes of the organism. There is another kind of genes, ontogenes. They are no less but rather more abundant than the Mendelian genes. Ontogenes commence their activity earlier, during the maturation of gametes in parental organisms [1, 19 32, 34]. They can be also subject to selection but this is quite different kind of selection. The latter selection takes place when the zygote is formed, i.e., before most organisms come into being. Correspondingly, this kind of selection has nothing to do with the impact of environment.

Table 3. Loss in lethal manifestation of mutation recovered in 2000 [22]

Stock no.	2000		2001		2002		2004	
	Total number of progenies	Share of daughters	Total number of progenies	Share of daughters	Share of daughters	Total number of progenies	Share of daughters	Total number of progenies
1	191	0.00	13	*0.46	199	*0.42	77	*0.52
2	435	0.00	4	0.00	259	0.02	36	0.03
3	180	0.00	20	*0.45	311	*0.43	95	*0.50
5	303	0.02	33	*0.45	265	*0.60	83	*0.41
6	283	0.02	2	0.00	111	0.02	39	0.05
7	100	0.00	3	0.00	44	**0.27	63	**0.40
8	216	0.07	5	0.00	90	0.09	49	**0.14
9	529	0.00	7	0.00	169	**0.21	81	0.04
10	297	0.04	7	0.00	69	**0.30	57	**0.26
11	409	0.06	4	0.00	82	**0.18	55	**0.16
26	89	0.01	–	0.00	175	0.07	40	0.02
27	161	0.00	29	*0.69	113	*0.56	92	*0.49
29	76	0.00	4	0.00	171	*0.54	80	*0.51
30	115	0.00	8	0.00	109	0.02	71	0.00
31	189	0.00	8	0.00	138	0.01	70	0.03
32	198	0.00	4	0.00	74	0.00	53	0.02
33	234	0.00	23	*0.52	214	*0.56	88	*0.51
34	198	0.00	–	0.00	62	0.00	54	0.02
35	115	0.04	12	0.00	162	**0.13	83	*0.48
36	110	0.01	5	0.00	106	0.02	54	0.07
38	84	0.01	3	0.00	80	*0.56	51	**0.33
41	100	0.01	5	0.00	331	*0.49	106	*0.52

* Loss of a lethal effect of mutation.

** Reduction in a lethal effect of mutation.

Zygotic selection or "genome incompatibility". Zygotic selection or genome incompatibility implies the death of zygotes immediately after they are formed. This is caused by certain problems in the interaction between the parental genomes that meet in the zygote. Certain deviations from the norm in the genomes lead to death; however, these deviations cannot be regarded as a direct cause of the death. The direct cause is the *abnormal interaction between the genomes caused by these deviations.* The deviation in one of the parents itself does not lead to death. Much depends on the other parent. The phenomenon of zygotic selection or genome incompatibility has its specific characteristics. Let us consider this in more detail.

The death takes place immediately after the zygote is formed. As has been earlier demonstrated, the mating of mutant males to *yellow* females leads to the death of daughters and part of sons (Table 2). The lethality rate in some stocks approaches 100% (Table 2, nos. 1 and 7). A special experiment was conducted to find out the stages when the progeny dies (Table 4). This experiment demonstrated that the progenies died at the earliest embryonic stages of zygote development (Table 4): the lethal cases at the stages of white and brown eggs accounted for 90% of the total lethality [2].

Zygotic lethality results from an impaired interaction between the genomes that met in the zygote rather than particular alterations in the genomes. Catastrophic death of the progeny in the crosses of mutant males with *yellow* females does not mean that either conditional mutations or *yellow* mutation are the cause of the death. The *yellow* females mated to males of other strains display a high fecundity. In turn, the males carrying conditional mutations in the X chromosome can have daughters in the progeny when crossed with the *yellow* females carrying chromosomal rearrangements. Table 5 demonstrates that the rearrangements in the X chromosome of *yellow* females remove the phenomenon of "prohibition of daughters in the progeny". Table 6 shows that the presence of rearrangements in autosomes 2 and 3 of *yellow* females (inversions *Curly, Plum,* and *Dichaete*) gives the same result. This suggests that the cause of zygotic lethality is created when the male and female pronuclei meet in the

Table 4. Death of zygotes in crosses of *yellow* females with the males carrying conditional mutations in the X chromosome [31]

Male mutant strain	Total number of laid eggs	Lethality (%) at the stage of				Live imagoes (%)
		White egg	Brown egg	Larva	Pupa	
1	50	92	2	–	–	6
2	50	81	13	2	–	4
3	50	76	18	-	–	6
5	100	65	28	3	–	4
6	50	80	8	–	–	12
7	50	52	32	6	2	8
8	50	90	6	–	–	4
10	50	68	20	6	–	6
11	50	56	30	2	-	12
27	50	72	8	6	–	12
29	50	92	6	–	–	2
30	50	96	2	1	–	–
31	50	90	4	2	-	4
32	50	46	32	8	–	14
33	50	50	28	6	2	14
36	24	33	54	–	6	7
38	40	68	22	5	–	5
41	50	90	6	–	–	4
Average	51	72	18	3	0.6	7

Table 5. Removal of the lethal effect of conditional mutations in the X chromosome of male by rearrangements in the X chromosome of *yellow* female [40]

Male stock no.	*Female y/y (control)*		*Female In(1)5, y/y*		*Female In(1)23, y/y*		*Female T(1; 2)12, y/y*		*Female T(1; 2)19, y/y*	
	Total number of progenies	Rate of females	Total number of progenies	Rate of females	Total number of progenies	Rate of females	Total number of progenies	Rate of females	Total number of progenies	Rate of females
1	191	0.00	169	0.06	87	0.01	138	0.01	148	0.03
2	435	0.00	236	0.12	76	0.11	38	0.05	173	0.13
3	180	0.00	469	0.63	190	0.43	128	0.59	331	0.58
4	293	0.00	209	0.08	162	0.04	86	0.00	213	0.08
5	303	0.02	107	0.27	112	0.01	46	0.04	96	0.22
6	283	0.02	136	0.23	106	0.23	64	0.00	112	0.25
7	100	0.00	154	0.36	135	0.21	13	0.23	145	0.39
26	89	0.01	121	0.24	210	0.30	46	0.02	69	0.28
27	93	0.00	123	0.05	117	0.02	79	0.00	79	0.06
29	61	0.00	203	0.49	122	0.57	18	0.00	128	0.55
30	115	0.00	142	0.38	100	0.17	93	0.09	106	0.19
31	83	0.00	118	0.19	123	0.22	121	0.04	195	0.27
32	117	0.00	183	0.13	101	0.19	80	0.14	117	0.35
33	90	0.00	144	0.34	123	0.24	42	0.17	100	0.22
34	110	0.00	115	0.25	71	0.07	31	0.29	41	0.15
36	110	0.01	108	0.25	127	0.20	105	0.01	323	0.46

synkaryon. In some cases, their encounter results in development of the formed zygote and in the others, either synkaryon is not formed or its development is arrested [30, 35]. Unfavorable outcomes in the case of normal individuals are rather rare judging from a high fertility rate of crosses. The presence of mutant ontogenes or chromosomal rearrangements in the genome drastically increases the rate of adverse outcomes.

Zygotic lethality follows the pattern of a parental (maternal or paternal) effect. The death of daughters and sons in the crosses involving *yellow* females (Table 2) follows a paternal pattern. The presence of a conditional mutation in the father leads to the death of not only daughters, which acquired a mutant X chromosome from their father, but also of the sons, which did not got this chromosome. Thus, the property of lethality is passed from the father to all its gametes rather than only to the gametes that got the mutation from it (parental effect, paternal variant).

A maternal variant of zygotic lethality appears in the experiments with autosomal rearrangements (Table 6). The rearrangements *Curly, Plum,* and *Dichaete* allowed daughters to appear in the progeny of *yellow* females. Interestingly, the daughters that appear in the progeny are not only the individuals carrying these chromosomal rearrangements (*Curly, Plum,* and *Dichaete*), but also the ones without these rearrangements. Thus, the ability to neutralize lethality is passed from mother to all its gametes rather than only those gametes that got the corresponding rearrangement.

The above listed specific features of zygotic lethality and, in particular, the parental effect, suggest that zygotic lethality is prepared by the processes that involve the genetic material during maturation of reproductive products in the germline tissue. The processes go on on a regular basis during formation of each gamete [2]. We assume that they lead to epigenetic changes [30,35]. The epigenetic patterns of the genomes that form a zygote are compared to make the decision on whether the zygote is to be further developed or its development should be arrested. The latter means its death [2, 30, 35].

The existence of zygotic selection fundamentally alters the concept of evolutionary development. In addition to Darwinian selection, which involves the adult organisms, the germ cells are selected on a regular

Table 6. Suppression of the "prohibition on daughters", caused by conditional mutations, with rearrangements in chromosomes 2 and 3 [40]

Male mutant stock no.	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

basis. This selection takes place at the stage of synkaryon and zygote formation. The internal factors of the organism are important for this selection rather than external environment. There is no more talk about the adaptation to external environment in the case of zygotic selection.

A regular adjustment of the program of individual development, occurring when each gamete is formed, precedes the zygotic selection [2, 30, 35] and the effectiveness of this fine-tuning is tested when the parental genomes meet in the zygote. Zygotic selection is the reflection of sorting out of misfit variants.

The fact that zygotic selection exists leads to *revisiting of the significance of Darwinian selection,* which Darwin himself and his followers reduced to exclusive adaptation to environment. It is more correct to regard *both forms of selection as a mechanism for assessing the efficiency of morphogenesis,* which takes place in the living world on a regular basis. The efficiency of the interaction between the systems within the organism is constantly tested by zygotic selection and the efficiency of the interaction between the organism as a whole and environmental factors, by Darwinian selection. The adaptation to environment in the latter case is not the cause but rather a consequence of the evolutionary process.

This issue was already considered when discussing Darwinism and orthogenesis [3] but will evidently demand a more comprehensive description. Anyway, we now cannot avoid consideration of two distinct forms of selection when dealing with the driving forces of the evolutionary transformation of genomes.

Speciation with Involvement of Ontogenes Leads to Genetic Isolation of Species

The individuals belonging to different species either do not cross with each other or give infertile progeny. Owing to this property, referred to as isolation, all living matter exists as hereditary separate sets, individual species. From the standpoint of the modern evolutionary synthesis, the genome of a new species is constructed of the mutations in the Mendelian genes of the precursor species. This approach to speciation does not allow the phenomenon of isolation to be explained. Indeed, mutations of Mendelian genes are unable to provide isolation of a newly formed species. The mutants in Mendelian genes are full-fledged members of

the species-level community without any trend of isolation. That is why there are no grounds for isolation of a new species in this case.

On the contrary, mutations in ontogenes are a perfect material for establishment of isolation. Each mutation in ontogene is a lethal with a particular range of action. A mutation in ontogene (= conditional mutation) causes death of the progeny that received the corresponding lethal as well as the progeny that did not get this lethal (parental effect) (Table 2). A class of the progeny can die in full or in part. It is important that these lethals are conditional. To become a factor of isolation, a lethal should act as such in the cross with differing genotypes and be not lethal in the cross with the like genotypes. This is the particular property characteristic of conditional mutations.

The mutations in ontogenes possess a unique pattern of lethal manifestation. They are lethal even in heterozygous state, except for permissive genotypes. We believe that it is the ability of an ontogene to be inactive that allows the mutant ontogenes to escape elimination from population [31]. A mutant ontogene can be retained in the genome of a living individual if it is not involved in the regulation (inactive) whatever the reason is.

Once becoming mutant, an ontogene commences acting as both speciation and isolation factors. The event of new species formation is the event of homozygotization of the mutant ontogenes. It marks creation of a new congruous regulatory system, which is not lethal but rather beneficial from biological standpoint. The fundamental significance of ontogenes in solving the problem of isolation was recognized immediately on appearance of the first data on conditional mutations [47, p. 279].

A lethal effect of mutations in an ontogene displays remarkable features, described above in the section on zygotic selection. The lethal effect depends on both the mutation itself and the gamete of the partner in mating. Mutation can lose its lethal manifestation in the crosses with a certain partner. This has been shown experimentally (Tables 5 and 6). Thus, the lethality can be lost in some cases in homozygotes for a mutation. We have observed individual cases when homozygotes survived after a long-term maintenance of mutant stocks. The cases of homozygotization reproduce the formation of a new species: a clone of individuals is formed and these individuals are fertile when crossing within their group but sterile when crossing to individuals of the initial species (isolation).

This picture resembles the situation with chromosomal rearrangements. As a rule, the chromosomal rearrangements from natural drosophila populations are lethal in a homozygous state [48, 49] but drosophila species genomes carry different rearranged regions in a homozygous state [50]. According to our data, the chromosomal rearrangements in heterozygote manifest their lethality according to the same pattern as conditional mutations. Their lethality is a dominant character; it is conditional (depends on the genotype of the partner in cross); manifests in the progeny; and is inherited according to a parental type [2]. This means that chromosomal rearrangements behave as conditional mutations. Correspondingly, their behavior in speciation [50] suggests that both conditional mutations (mutations in ontogenes) and chromosomal rearrangements (acting as modifiers for the function of ontogenes) are necessary for speciation.

Speciation with Involvement of Ontogenes: New Aspects

The speciation issues considered above were formulated as early as the classical period in development of genetics. The concept of ontogene can enhance their resolution. The last section of this paper discusses the new questions in evolutionary transformation of the living matter. These questions arise with the emergence of the concept of ontogene on the genetic horizon.

A Two-Component Genome: the Genome Components and Their Relationships in Evolution

The emergence of a new genetic unit, an ontogene, transforms the genome from a one-component to two-component entity. The question arises on the similarity and distinction between these components. In molecular terms, these elementary units of the genome are similar, being represented by DNA sequences; however, they code for different processes, namely, regulatory (switching genes on and off) and synthetic (protein synthesis). Changes in the functions of DNA region in the course of evolution cannot be excluded. Both functions—regulatory and synthetic—had sometimes originated from the same structural material (a polynucleotide). *The problem of acquisition of*

functions by DNA regions and change in these functions comes into view. Numerous assumptions appear on the relationships between the sequences in the genome. Some sequences are obligately homozygous, while others can be both homozygous and heterozygous. We have shown that the phenomena of inbreeding depression and heterosis are explainable based on the relationships between genes and ontogenes in the putative two-component genome]. The most important is the fact that the existence of two components gives the free scope to construction of a complex genetic system. The fact of zygotic selection indicates that this two-component system is constantly improved in a living organism.

Evolution of Genome Implemented Via Zygotic Selection

The data reported here directly suggest the presence of zygotic selection and demonstrate that the object of selection is variants of regulation implemented by ontogenes. Presumably, this mechanism is used in order to incorporate new regulatory scenarios underlying the new species. This mechanism may represent the long-awaited *method of self-improvements of a genetic system,* which was so long searched for by the advocates of orthogenesis [51]. Most diverse ideas of orthogenesis may be thus implemented [52].

Evolution of Species After the Event of its Isolation

The process of creation of a new species when referring to the constantly going zygotic selection must also continue after the isolation is formed. The organism of a new species now can get rid of some functions and structures of the progenitor species that became needless and energetically unbeneficial. This process can be implemented via both Darwinian and zygotic selections.

Ontogenes and Genome Instability

Experimental data show emergence of gene, chromosome, and genome instabilities in the mutants carrying conditional mutations [14, 22, 29, 53]. As is believed, speciation requires high mutation rates [47]. The discovered instability perfectly fits the formation of new genetic variants.

Substantial, Spatiotemporal, and Energy Aspects of the Evolution of Living

The heading for this section lists the biological aspects in considering a living material object. A genetic view on the evolutionary process as compared with a biological view is evidently narrower. Mendelian genes allow for consideration of only substantial aspect. Indeed, it is possible to explain formation of proteins, the major part of a living organism, using the concept of Mendelian gene. However, Mendelian genes contain no information about when (temporal aspect) and where (spatial aspect) these genes should act.

It is ontogenes that open the road for studies into a spatiotemporal aspect in living objects (ontogenesis and phylogenesis). Ontogenes are involved in construction of the program for individual development of a species [2]. This program specifies the order of gene and ontogene switching and the time intervals for their activities [2, Fig. 7]. The response of ontogenes to the presence of genome rearrangements suggests that these particular genome units are responsible for introducing the factor of "space" in a developing organism. The putative epigenetic mechanism underlying the activities of epigenes represented by genome conformation [30, 35] suggests the same pattern.

Until recently, genetics has not touched the energy aspect of a living organism. However, this aspect quite unexpectedly appeared when studying the ontogenes. The mutants in ontogenes display a higher level of the basal metabolism as well as high locomotor activity [27]. These data may suggest the method for controlling the energy status of mutants, thereby introducing the energy aspect to evolutionary schemes [44, 45, 46, 53].

Conclusions

Molecular analysis of genomic DNA in eukaryotes shows that most of it is not involved in protein synthesis [54, 55]. The genome-wide sequencing has shown that the length of the DNA comprising all protein-synthesizing genes accounts for less than one-tenths of all genome DNA. According to the project" human Genome " at the time of February 13, 2001 coding protein exons account for 1% of genomic DNA, 24% accounted for non - coding introns and 75% - in the intermountain intervals [56]. Just a few percent of the human genome encodes information on protein synthesis [55, 57]. Thus, the current concept of phylogenesis is based on the data related to a small share of the genome. The major part of the genome has

not been examined in a large-scale manner similar to the research into Mendelian genes. It is reasonable to assume that the key to creation of the theory of phylogenesis lies in this fact. The data on ontogenes and their mutations in this case could not have come at a better time. It may happen that ontogenes is the particular part of the genome that has not been so far involved in a large-scale genetic examination.

In this paper, we have analyzed the specific features of the mutations in ontogenes, including (1) their conditional manifestation; (2) lethal effect; and (3) parental effect. These features distinguish ontogenes from the traditional Mendelian genes. Our data demonstrate that the specific features of ontogenes make it possible to resolve some problems in phylogenesis that have emerged because of the classical idea of a single-component genome comprising only Mendelian genes.

It is worth noting that we consider here three evolutionary problems at once although each of them deserves a separate consideration. The chance to simultaneously advance in all three directions demonstrates that the central idea postulating existence of the genome composed of Mendelian genes and ontogenes is an adequate one. This idea forms the background for a new approach to the research into the genetic system.

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