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Research Article

Ontogenes and Heterochromatin of D. Melanogaster

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ABSTRACT

Mutations in Drosophila melanogaster ontogenes sharply increase the rate of X-chromosome nondisjunction in meiosis, suggesting that ontogenes are active in meiosis. The activity of homologous ontogenes drives homologs together (to pair); however, ontogenes interact at a distance without any contacts or chemical mediators. The meiotic chromosomes involved in pairing have the appearance of densely compacted chromatin, suggesting that the active ontogenes themselves have a heterochromatin nature.

Incomplete penetrance of the mutations in ontogenes generated in experiment also favors a heterochromatin nature of ontogenes. Incomplete penetrance can be regarded as a consequence of position-effect variegation (mosaicism), characteristic of heterochromatin but taking place in the germline cells of the mutants for ontogenes rather than in somatic cells. Thus, both the meiotic effect of mutations in ontogenes (chromosome nondisjunction) and their incomplete penetrance are two consequences stemming from the same root, namely, the fact that they belong to heterochromatin.

The cytogenetic association of ontogenes with heterochromatin supplements and concretizes the earlier proposed concept of elementary event in development.

Keywords

Ontogene, Heterochromatin, Penetrance, Position-effect variegation, Drosophila.

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Introduction

Mendelian genes and ontogenes are present in the same genetic structures, namely, chromosomes; however, Mendelian genes are known since the advent of genetics, whereas ontogenes have only recently been known [1]. That is why the behavior of chromosomes and the corresponding genetic phenomenology are to this day interpreted solely and exclusively based on the knowledge about Mendelian genes. Some inferences do not lose their value because of this fact but others become invalid.

Here, we consider two genetic phenomena discovered at the dawn of genetics: chromosome nondisjunction in meiosis and incomplete penetrance of genes. Both phenomena have played an outstanding role in the development of genetic knowledge: chromosome nondisjunction in the establishment of the chromosomal theory of heredity [2,3] and incomplete penetrance, in the establishment of phenogenetics, that is, the implementation of a gene into the trait [4]. We encountered both phenomena when studying ontogenes [1] but the uniqueness of the picture observable for ontogenes suggests that these phenomena have been formed according to

another scenario differing from the classical one.

The chromosome nondisjunction and incomplete penetrance are united by the mechanism involving heterochromatin and ontogenes. The cytogenetic specifics of heterochromatin manifestation and the specific genetic features of ontogenes add up to a single picture. This may be determined by that the ontogenes belong to heterochromatin. Here, we consider the experimental data on the chromosome nondisjunction and incomplete penetrance in the *D. melanogaster* mutants for ontogenes. These data allowed us to develop the arguments favoring the involvement of heterochromatin in the considered phenomena. This is the first step in linking the genetic manifestation of an ontogene to cytogenetic manifestation of heterochromatin.

Many traits that are the subject of research in human genetics and medical genetics, despite their genetic nature, do not follow the rules of inheritance of Mendelian genes. They are also characterized by low penetrance, mosaicism, dependence of expression on the sex of the individual, and a link to aneuploidy. There is every reason to believe that all this uniqueness is due to ontogenes [5]. In this case, studying these features in ontogene mutations in Drosophila could shed light on the etiology of certain forms of pathology in humans.

Experimental part

This paper is a conceptual synthesis of part of our data on the study of *Drosophila melanogaster* ontogenes obtained from the 2000 to 2025 [1]. Once we generated the mutations in ontogenes, the attention was focused on the matching of mutation manifestations to the expectations and the dissimilarity of these mutations from classical Mendelian mutations. Further studies outlined the contours of the specific features in the manifestation of the new gene type and revealed the novel meanings. This paper reports the data of two large experiments on generation of the mutations in ontogenes [6,7]. In addition, we brief here the results of the experiment (with the highest information content in this area) [8] that demonstrate the X-chromosome nondisjunction induced by one of the mutations in ontogenes. At first, these data together with the other results on nondisjunction illustrated the ability of ontogene mutations to cause a high rate of chromosome nondisjunction having no analogs in the vast array of data on the point mutations in Mendelian genes.

Find below a comprehensive analysis of the data and the hypothesis on the cause relating the high nondisjunction rate and the phenomenon of incomplete penetrance in the mutants for ontogenes. Discussion provides in detail the arguments favoring the assumption on a putative heterochromatin nature of ontogenes.

Ontogenes

Genetics commenced with the experiments on alternative traits by Gregor Mendel. Alternative traits belong to the category of the traits of intraspecific difference. In addition to these traits, a living organism has the traits of intraspecific similarity. These traits are the same in all representatives of a species. The goal was set to generate the mutations in the drosophila genes responsible for the traits of intraspecific similarity. We assumed that these mutations should manifest in a certain specific manner, namely, they should be viable in a homozygous state and lethal in a heterozygote [9,10].

The target mutations in *D. melanogaster* were generated using γ-irradiation and a special selection procedure [6,7]. These mutations were named conditional [11-14,]. Table 1 illustrates the progeny of a batch of the males, mutant for the X chromosome obtained early as 2000 [14]. The males were crossed with *yellow* females. The obtained mutations look as *conditional (facultative) dominant lethals*. Daughters were absent in the progeny of mutant males. The conditionality of these mutations consists in the fact that *yellow*/+ daughters died (restrictive genotype), whereas the mutant male itself is viable and fertile (permissive genotype). The genes responsible for the mutations (mutant genes) were named ontogenes [15,16] because of their ability to induce the formation of monstrosities (morphoses) [17-19]. For the comprehensive results of the study of ontogenes see [1].

Table 1: Progenies and fecundity of mutant (+) males crossed to *yellow* females [14].

Mutant male stock no.	Cross: 2♀ *y* × ♂ +		Cross: 6♀ *y* ×♂ +		Fecundity of males*
	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	65	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.

Mutations of ontogenes differ in their penetrance

The majority of experiments with ontogenes were conducted with the mutations in the X chromosome manifested as facultative dominant lethals with a high penetrance. Table 1 lists these mutations. The number of daughters in the progeny indicates the

level of penetrance of a lethal. In the case of a complete (100%) penetrance, daughters are absent at all. However, the facultative dominant lethals generated with the help of γ-irradiation contained numerous lethals with an incomplete penetrance. The lower the penetrance of a lethal mutation, the larger is the number of daughters in the progeny of a mutant male. Tables 2 and 3 show the progenies of the mutants selected using the test for the absence of daughters (two experiments with irradiation). As is evident from Tables 2 and 3, the progeny of selected males differed in the number of daughters. The mutants were divided into groups according to this characteristic. The groups were formed based on the similarity in the trait "share of daughters in the progeny" in the cross 2 ♀*y* × ♂+. The difference between groups is evident when comparing the mean values for the groups. The first group comprised the mutants with the highest penetrance of lethals (complete or almost complete absence of daughters in the progeny); the penetrance was lower (more daughters) in the second and third groups. As for the fourth group of the selected mutants, it contained the highest possible share of daughters (about 50%) making it impossible to decide on the presence of mutation (the share of daughters in the crosses of individuals lacking mutation is 50%).

Noteworthy that the share of daughters in the progeny (according to groups) is reproducible in repeated experiment. Correspondingly, this suggests that the level of penetrance is the characteristic of mutation of ontogene. An important feature of the manifestation of ontogenes is the dependence of the level of penetrance on the genome of the mutant itself and the genome of the partner, which is evident from Table 3. The mutations with a high penetrance identified in the cross of a mutant male with *yellow* females displayed other (lower) levels of penetrance in the crosses with the females of other genotypes (*Muller-5, Berlin wild,* and *Barnaul*). In general over the experiment, the cross with *Barnaul* females is the most effective in decreasing the level of penetrance.

In general, the mutations in *D. melanogaster* ontogenes generated using a single protocol differ in the level of penetrance. The penetrance changes with the genetic conditions under which it was determined. This specific feature (among others) fundamentally distinguishes the mutations in ontogenes from Mendelian mutations, which have a relatively stable and uniform manifestation.

Ontogenes are active in germline cells

1. Activity of ontogenes in gonial cells (parental type of inheritance in the manifestation of mutant ontogenes.

The mutations in ontogenes demonstrate a whole bunch of manifestations that are inherited according to a parental type [13,20]. This type of inheritance consists in that the progeny receives the trait independently of whether it acquires the mutant gene with gamete or not. For example, a mutant parent can produce the progenies with the mutant parental phenotype but lacking the parental chromosome carrying the mutation. The parental effect of inheritance can be both maternal and paternal depending on the gender of the mutation carrier. The ontogene mutations of this type were also recorded; they displayed a maternal effect when mother was the carrier of mutation and a paternal effect when the carrier was the father.

Maternal and paternal effects have been observed in the cases of (1) interaction of conditional mutations with one another; (2) interaction of a conditional mutations with the Y chromosome; (3) interaction of conditional mutations with chromosome rearrangements; (4) inheritance of a visible manifestation of one of the conditional mutations; and (5) development of morphoses (monstrosities) in the progenies of mutants. As is mentioned above, the maternal and paternal effects are not mutually exclusive: one and the same mutation can display both maternal and paternal effects. This phenomenon indicates that ontogenes are active in germline cells before they undergo meiosis; moreover, ontogenes are active in both genders.

2. Activity of ontogenes in meiosis (X-chromosome nondisjunction in the mutants for ontogenes)

Meiotic abnormalities in the mutants for ontogenes have been repeatedly observed as the emergence of the sons patroclinous for the X chromosome [8]. The X-chromosome nondisjunction was comprehensively studied in the mutants carrying the *l*(1) ontogene mutation [8]. Table 4 lists the data on the X-chromosome nondisjunction in the females of three genotypes heterozygous for this mutation. In females *l*(1)/*w,* the second X chromosome had a normal structure; in females *l*(1)/*In*(1), it contained an inversion in the X chromosome; and females *l*(1)/*In*(1)/*Y* carried the inversion in the X chromosome and an additional Y chromosome.

The X-chromosome nondisjunction in meiosis was assessed by the frequency of exceptional progeny [21]. The exceptional progeny comprises matroclinous daughters and patroclinous sons. The former carry both maternal X chromosomes and the latter, the paternal X chromosome. These chromosome sets emerge in the absence of normal pairing between homologous X chromosomes in the oogenesis and the resulting formation of abnormal XX and X0 egg cells. In other words, the emergence of an exceptional female or an exceptional male indicates a meiotic event lacking a regular pairing of the X chromosomes so that they migrate to the division poles independently of each other. The progeny formed as a result of the normal X-chromosome pairing and segregation is referred to as regular and also consists of daughters and sons.

The frequency of exceptional females is calculated as the ratio of the number of matroclinous daughters to the number of all daughters in the progeny of a female and the frequency of exceptional sons, as the ratio of the patroclinous sons to the number of all sons in the progeny. The number of exceptional individuals in these calculation is doubled to compensate for the death of the half of them in a standard cross (in Table 4, this number is shown in column "With adjustment for lethality").

The nondisjunction rate was very high. The share of matroclinous daughters reached 24.7% of the total progeny and of patroclinous males, 24.9%. The inversion in the opposite X chromosome and

Table 2: Progeny of the males carrying a mutation in ontogene in the crosses with different females [9].

Mutant male stock no.	Cross: 2♀y × ♂ +		Cross: 6♀ y × ♂ +		Cross: 6 ♀ y w f x♂ +		Fecundity of males*
	Total number of progenies	Share of ♀♀	Total number of progenies	Share of ♀♀	Total number of progenies	Share of ♂♂	
27	68	0,00	93	0.00	66	0.24	0.18
29	15	0.00	61	0.00	63	0.57	0.14
30	122	0.07	115	0.00	80	0.50	0.19
31	106	0.00	83	0.00	70	0.21	0.15
32	81	0.00	117	0.00	180	0.48	0.13
33	144	0.00	90	0.00	72	0.54	0.16
34	88	0.00	110	0.00	63	0.52	0.12
Mean for group 1		0.01		0.00		0.44	0.15
26	92	0.03	89	0.01	–	–	–
35	102	0.03	115	0.04	45	0.76	0.17
36	95	0.00	110	0.01	76	0.47	0.35
37	52	0.02	68	0.04	67	0.63	0.14
38	54	0.06	84	0.01	92	0.73	0.14
41	79	0.03	100	0.01	91	0.57	0.10
Mean for group 2		0.03		0.02		0.62	0.17
43	9	0.00	97	0.32	–	–	–
45	13	0.08	–	–	73	0.42	–
48	76	0.42	174	0.38	119	0.60	–
52	70	0.11	97	0.31	–	–	–
Mean for group 3		0.15		0.37		0.51	
46	153	0.44	128	0.45	140	0.56	0.38
47	233	0.45	174	0.47	128	0.61	-
49	137	0.44	175	0.41	187	0.64	-
50	90	0.40	175	0.45	85	0.54	-
54	139	0.43	177	0.41	-	-	-
55	148	0.45	183	0.48	-	=	-
56	139	0.45	190	0.48	-	-	-
Mean for group 4		0.44		0.45		0.58	0.38

*Fecundity of males is the ratio of the number of the imagoes developed from the eggs laid by females to the number of laid eggs.

Table 3: Share of daughters in the progeny of a male carrying mutation in the X chromosome crossed with the females of wild-type laboratory strains [9].

Mutant male stock no.	Female strains							
	Yellow		*Muller-5*		*Berlin wild*		*Barnaul*	
	Total number of progenies	Share of ♀♀	Total number of progenies	Share of ♀♀	Total number of progenies	Share of ♀♀	Total number of progenies	Share of ♀♀
1	191	0.00	–	–	–	–	91	0.02
2	435	0.00	23	0.22	7	0.17	143	0.03
3	180	0.00	36	0.25	18	0.17	146	0.04
4	293	0.00	156	0.31	–	–	135	0.01
5	303	0.02	41	0.34	–	–	143	0.19
6	283	0.02	161	0.50	212	0.31	138	0.03
7	100	0.00	–	–	–	–	–	–
8	216	0.07	–	–	–	–	–	–
9	529	0.04	160	0.55	128	0.29	303	0.28
10	297	0.00	63	0.06	–	–	–	–
11	409	0.06	182	0.53	223	0.38	178	0.22
Mean share of females	0.01		0.35		0.26		0.10	
27	93	0.00	62	0.29	84	0.08	112	0.10
29	61	0.00	53	0.53	64	0.20	113	0.26

30	115	0.00	76	0.36	102	0.33	135	0.17
31	83	0.00	77	0.18	87	0.08	129	0.07
32	117	0.00	62	0.53	140	0.34	80	0.30
33	90	0.00	59	0.39	149	0.28	48	0.27
34	110	0.00	68	0.31	99	0.24	117	0.27
Mean share of females	0.00		0.37		0.22		0.21	
26	89	0.01	69	0.29	100	0.22	111	0.23
35	115	0.04	73	0.33	145	0.27	123	0.15
36	110	0.01	99	0.28	92	0.36	124	0.29
37	68	0.04	67	0.55	89	0.39	119	0.3
38	84	0.01	54	0.61	36	0.5	39	0.38
41	100	0.01	129	0.4	92	0.37	130	0.38
43	97	0.32	30	0.60	–	–	57	0.49
45	–	–	–	–	26	0.58	–	–
48	174	0.38	131	0.67	172	0.53	232	0.57
52	97	0.31	27	0.59	–	–	62	0.24
Mean share of females	0.13		0.48		0.40		0.34	
46	128	0.45	108	0.60	145	0.46	191	0.50
47	174	0.47	130	0.54	194	0.45	237	0.57
49	175	0.41	111	0.55	209	0.59	196	0.51
50	175	0.45	110	0.67	213	0.38	225	0.49
53	111	0.42	43	0.53	60	0.55	79	0.56
54	177	0.41	92	0.52	157	0.50	159	0.52
55	183	0.48	111	0.45	34	0.57	184	0.56
56	190	0.50	83	0.53	134	0.44	189	0.52
25	83	0.55	85	0.48	104	0.30	131	0.47
Mean share of females	0.46		0.54		0.47		0.52	

Table 4: Effect of the *l*(1) mutation in an ontogene on the X-chromosome nondisjunction in the meiosis of drosophila females [8].

Studied female genotype	Regular progeny		X-chromosome exceptional progeny		Total progeny		Rate of exceptional individuals (%)	
	♀	♂	♀	♂	Imago	With adjustment for lethality*	♀	♂
l(1)/*In*(1)	691	380	126	268	1465	2239	11.3	23.9
l(1)/*In*(1)/Y	373	164	109	154	810	1237	17.6	24.9
l(1)/*w*	1132	730	362	149	2423	2934	24.7	10.2
w/*In(1)* (control)	1038	821	10	46	1935	1991	1.0	4.6
w/*In*(1) (external control 1)	946	922	1	23	1902	1926	0.1	2.4
w/*In*(1) (external control 2)	842	749	0	20	1638	1658	0	2.4

* The number of living progenies is supplemented with the number of exceptional females, exceptional males, and dying *l*(1) males (females of genotypes 1–3).

the additional Y chromosome had no effect on the X-chromosome nondisjunction. The balance of XX and X0 cells was disturbed: exceptional daughters were prevalent in the progeny of the females with a normal opposite chromosome and exceptional males, in the progeny of the females with the inverted X chromosome. Approximately 12% of the matroclinous daughters produced by the mothers with a normal opposite X chromosome emerged to be homozygous for the marker of one of the maternal X chromosomes (equational nondisjunction). This was a "fading" parental effect of the mutation in ontogene on the X-chromosome nondisjunction [8]. For more complete data on the nondisjunction in ontogene mutants see [1]. The general conclusion here is that the ontogene mutations sharply interfere with the joining of homologous chromosomes in meiosis. The disturbance of pairing of homologs caused by point mutations in ontogenes unambiguously demonstrates the activity of ontogenes in meiosis.

3. Activity of ontogenes in meiosis and heterochromatin

The phenomenon of the chromosome nondisjunction in drosophila meiosis has been known from the classical works [21], has been studied in detail, and considered in the reviews [2,3]. However, the above data make it possible to look at this phenomenon from a new angle. The following three facts are of interest: (1) The mutations in ontogenes sharply increase the nondisjunction rate versus the

mutations in Mendelian genes, which, as is known from the relevant genetic literature, have no effect on disjunction. It is clear that it is the ontogenes that are active in meiosis rather than Mendelian genes, as has been earlier believed. The previous opinion that it is the Mendelian genes that are involved in pairing stems from the lack of the knowledge about existence of the genes other then the Mendelian genes. However, it is ontogenes that implement pairing; (2) The interaction of ontogenes in homologous chromosomes that leads in the norm to a regular pairing of homologs and disturbs pairing in the mutants for ontogenes takes place at a distance.

Separate location of homologs before the commencement of pairing that only later ends in pairing is a cytological fact requiring no additional evidence. In the case of ontogenes, we for the first time encounter the interaction of genes without a physical contact and chemical intermediaries (see [1] for detailed discussion); and (3) Meiotic chromosomes at the stage when homologs approach one another to pair are tightly compacted. This means that the activity bringing them together comes for the ontogenes in a supercoiled state.

These three positions suggest that ontogenes are a genetic structure with a unique function of interacting at a distance. Noteworthy that ontogenes implement their activity in the state of tight compaction characteristic of heterochromatin. Heterochromatin and heterochromatization are in the range of the phenomena potentially related to ontogenes. Since densely compacted heterochromatin is associated with the meiotic abnormalities caused by mutations in ontogenes, it is reasonable to refer to the properties of heterochromatin and to find out whether some of its properties can explain one more unusual manifestation of ontogenes, namely, the incomplete penetrance of mutations.

Heterochromatin and the position-effect variegation in somatic cells (a literature digest)

Initiation of the position-effect variegation is one of the noteworthy features of heterochromatin. Gene position effect is the change in gene expression (typically, a decreased activity or silencing) when the gene is transferred from its usual position in the genome to some other site. One of the forms of this effect is a variegated position effect, when a Mendelian gene is transposed from the euchromatin to a heterochromatin region. The transition to heterochromatin causes gene malfunction appearing as the retention of the activity in some cases and its cessation in others. This brings about a mosaic phenotype, that is, different gene manifestation in neighboring cells of the same somatic tissues [22]. The effect of heterochromatin spreads beyond its boundaries and gradually weakens [23]. This suggests that *the emergence of a mosaic pattern of gene expression results from the specific features in DNA functioning within heterochromatin rather than a mere change in the gene position in chromosome.* As has been shown, the wave of supercoiling (compaction) coming from heterochromatin region spreads to the gene in the case of position-effect variegation [23,24].

Ontogenes and position-effect variegation in germline cells (hypothesis about the cause underlying incomplete penetrance of gene)

Drosophila ontogenes (see page 3) are active in the germline cells. If so, *it is expectable that the mutants for ontogenes can induce position-effect variegation in germline cells similar to heterochromatin in somatic cells.* Let us consider in what form in this case the effect will appear to researcher.

The obtained mutations in ontogenes are facultative dominant lethals. In the presence of position-effect variegation, one part of the gonial cells will contain the mutation in an active state, while the other part of the cells will carry the mutation on an inactive state. Both cell types will give gametes and individuals (progenies) after fertilization. The zygotes with the lethal in an active state will not give *yellow*/+ daughters in the progeny, whereas the zygotes with an inactive lethal will give the progeny. At the level of progeny, a pattern of lethal mutation with incomplete manifestation (penetrance) will appear. The degree (level) of incomplete penetrance of mutations will be different. The lethals with both complete penetrance (100%) and incomplete penetrance in a wide range of values (from <100 to 50%) are expectable in our variant of the experiment on selection of lethal mutations. The level of 50% is the threshold when it is impossible to distinguish the event of "mutation nonmanifestation" in this setting of experiment.

The results of conducted experiments on radiation-induced generation of mutants (Table 2) match the expectations. As is evident from Table 2, the mutations with both 100% penetrance of a lethal (complete absence of *yellow*$^+$ daughters) and the mutations with lower penetrance were observable. The level of daughters in the progeny of a mutant female varied from 0 to 50%. The level of 50% in the progeny in this variant of experiment means the absence of dominant lethal in the tested individual. The share of daughters in the progeny of mutant female is preserved in the subsequent generations of the crosses of the same type (column "cross 6♀*y* × ♂+"). As is evident, the pattern of position-effect variegation in somatic cells is well transformable in the pattern of varying penetrance in the mutants for ontogenes.

Discussion

The main part presents the experimental data and the information for their logical connection. The work looks like a problem with the statement and solution. The problem statement comprises two groups of experimental data: (1) a high rate of X-chromosome nondisjunction in meiosis of the mutants for ontogenes and (2) incomplete penetrance of the mutations in ontogenes. The problem solution: *ontogenes are fragments of heterochromatin regions of chromosomes.* The order of reasoning when solving this problem is as follows;

The first set of arguments in favor of the thesis that ontogenes belongs to heterochromatin

(1) A high rate of the X-chromosome nondisjunction in meiosis of the mutants for ontogenes suggests the activity of ontogenes

in the meiotic prophase;
(2) The chromosomes in meiotic prophase are compacted; correspondingly, active ontogenes are compacted as well;
(3) A compacted supercoiled DNA is characteristic of heterochromatin; thus, ontogenes are also heterochromatin regions.

The second set of arguments in favor of the thesis that ontogenes belongs to heterochromatin

(1) Characteristic of heterochromatin is position-effect variegation. It takes place in somatic cells and is referred to as somatic mosaicism;
(2) Ontogenes are active in germline cells. Progeny develops from these cells. The position-effect variegation in germline cells looks different. The cells become gametes differing in the status of the studied ontogene: ontogene will be active in some cells and inactive in the others;
(3) Two types of gametes become the source of two types of progenies. Some progenies will contain an active ontogene and the others, the same ontogene but in an inactive form. This phenomenon is referred to as gene penetrance and its degree is assessed. In our case, the penetrance is incomplete;
(4) Thus, the position-effect variegation at the level of somatic cells leads to cell mosaicism, while the same effect at the level of germline cells leads to the phenomenon of incomplete gene penetrance (position-effect variegation at the level of progeny);
(5) The phenomenon of incomplete penetrance is the characteristic of a heterochromatin nature of a gene to the very same degree as the classical position-effect variegation; and
(6) Since incomplete penetrance is characteristic of the mutations in ontogenes (statement 2 of the problem), ontogenes can be regarded as belonging to heterochromatin.

Thus, we reasoned ***in a classical manner of genetic analysis*** that ontogenes belong to heterochromatin: this is not a direct physical statement of a certified event or a structure but rather the theoretical inference about a high probability of their existence made based on the observations of the events and structures available for a direct observation. This is not yet a fact but the assumption about its existence and indication of the conditions under which it can be more clearly recorded.

This problem solution looks as reliably substantiated. Individual to logically consistent statements (1) and (2), described in detail, this solution is based on the earlier inferences on (1) a regulatory nature of ontogenes [25,26]; (2) control of ontogenes over cell construction [27] and (3) parental type of inheritance of the manifestation of ontogenes [20,28,29].

A "heterochromatin version" of the origin of chromosome nondisjunction and incomplete penetrance proposed in this paper is a new explanation of particular phenomena, namely, meiotic chromosome nondisjunction and incomplete penetrance of mutations. Earlier, chromosome nondisjunction was explained by a defect in the interaction of homologous genes situated in a pair of homologs [30]. As of the moment the explanation appeared, it was clear that it was imperfect: the point mutations of Mendelian genes do not increase the frequencies of nondisjunction of homologs [2]. Now, it is clear that the nondisjunction is undoubtedly caused by the disturbance of the pairing of homologs but this disturbance is the result of an abnormality (mutation) of ontogenes rather than Mendelian genes. The existence of ontogenes has only recently become known [5].

The phenomenon of incomplete penetrance was explained with a polygenic nature of the biological trait [4,32,33]. As in the case with nondisjunction, it was clear that the explanation is not completely adequate at the very moment it was proposed. All biological traits are polygenic but only some of them for some reason display incomplete penetrance. Now, with the discovery of ontogenes, incomplete penetrance is explainable with a mutational damage of the ontogene controlling a particular Mendelian gene [1]. As for the classical Mendelian mutations, they display complete penetrance and are flawlessly inherited according to the rules of Mendel because the mutational damage generating the mutant phenotype is limited to the protein-coding region and does not affect the ontogenes that control the mutant gene.

The conclusion on a heterochromatin nature of ontogenes makes it possible to also revisit some other concepts of classical genetics based on the confidence in the universality of Mendelian gene, in particular, the idea of chemical attraction and repulsion caused by homologous (Mendelian) genes [33,34], and the hypothesis on the origin of quantitative traits [34]. They are numerous and deserve separate consideration.

Let us consider the idea for which the inference on a heterochromatin nature of ontogenes is the impetus for development. This is *the concept of quantization of genetic information during ontogenesis,* described in the paper titled "The Elementary Event of Development" [36]. This work was initiated by the discovery of the nonstandard inheritance of a parental type in different forms in ontogene mutations. It became clear that parental effect was a more significant phenomenon than a mere transfer of certain additional factors with the egg cytoplasm (maternal effect) [20]. Indeed, the parental effect in ontogenes can also follow a paternal pattern, as well as a maternal–paternal pattern, when the transfer of any products with the cytoplasm is out of question [28,29]. We saw the essence of the parental effect in the mechanism of individual development and named it *the elementary event of development (ontogenesis)* [36].

Theoretically, the genetic control of ontogenesis is a chain of sequential activations of some regulatory genes by other regulatory genes. The difficulty in constructing an acceptable scheme of a process is in that the entire genome is present in each cell; correspondingly, it is necessary to assume a stepwise activation of the genome to avoid an absurd situation when the entire genome in active in a zygote. Thus, we proposed the mechanism of *quantized genome activation,* that is, *the activity of one gene of ontogenesis*

(ontogene) is switched to another ontogene with the help of the event of cell division as the obligatory element.

We hypothesize that the meaning of the parental effect of a gene consists in the formation of a regulatory product (or a regulatory impact) that does not act at the site of the active gene but rather acting in another newly formed cell. The discovered property (production of a regulatory product "for export") was used as the basis for the principle underlying the course of ontogenesis. Thus, the regulatory gene of ontogenesis (ontogene) synthesizes an inactive product and initiates cell division. The cell division by activating the product that came with the maternal cytoplasm switches off the previous ontogene and switches on the next one. We named *the transition of activity from one gene controlling ontogenesis (ontogene) to another ontogene via the event of cell division the elementary event of development.* Our hypothesis consists in that this is how the chain reaction of three interconnected ontogenetic processes—activation of genetic information, increase in the cell mass, and distribution of activated information among the cells—emerges and is maintained. The experimental data confirming that ontogenes do control cell divisions [27] confirm the concept of *elementary event of development.*

The data on the association of ontogenes with heterochromatin, briefed above, are the novel and important supplement to the pattern of elementary event of development. The ontogene–heterochromatin concept makes it possible to discern the mechanism underlying the quantization of genetic information into the phenomenon of ontogene mosaicism in germline.

When considering the position-effect variegation, attention is focused on the changes in the activity of the gene transferred from euchromatin to heterochromatin. However, two events rather than one should be considered on closer examination, namely, (1) division of the cell containing the observed target genes and (2) the events occurring with these genes. The former event became apparent when considering the mechanism of ontogene penetrance. Now, keeping the eye on the cell, we can see that the phenomenon of cell variegation is not only the ability of ontogenes to change their activity, but also the ability to coordinate these changes with the event of cell division.

The event of a change in the activity of an ontogene (ontogenes) and the event of cell division are rigidly bound rather than independent of one another. That is why only two types of cells do exist: the cells with an active gene and the cells with an inactive gene. There are no cells in which the gene is at different stages of activation or activity. This is the only way how cell mosaicism—the site composed of the cells contrasting in the gene manifestation—can come into being. If the switch on–switch off event were not linked to the event of somatic cell division, the phenomenon of mosaicism (the formation of a whole from different fragments) would not exist.

The inference on the transition of activity from one ontogene controlling development to another via the event of cell division was theoretically substantiated in the concept of the elementary event of development. Thus, ontogenes allows us to see how cell division is involved in changing the activity of regulatory genes in the case study of mosaicism phenomenon. The principle of quantization of individual development via cell division is confirmed as an elementary event in the operation of genetic system in ontogenesis.

Conclusions

The genetic theory, after having as if successfully overcome the difficulties in decoding the structure of the gene, came to a dead end when encountering gene function, that is, gene activation in the course of individual development. The discovery of ontogenes clarified the reason of this difficulty. Until recently, an important structural element of the genetic system—ontogene—remained unknown. Because of the inertia of thinking, Mendelian gene, the factor of heredity that was discovered first, was regarded as the only and sufficient unit for implementing all functions of the living organism. The existence of any other hereditary factors was not even considered. However, ontogenes, similar to Mendelian genes, emerged to be the regions of DNA molecule as well [37] but the way they work as regulatory elements of the genome fundamentally differed from that of Mendelian genes. In general, this is understandable [1] but a comprehensive description is to be done in future.

Our work is a step in this direction. The association between the ontogene and the cytogenetic structure referred to as heterochromatin is outlined. Heterochromatin has long been the object of close attention of cytogeneticists; however, its function is vague. "The question arises about the functions of eu- and heterochromatin. While everything is quite obvious regarding euchromatin since it contains the main part of the genes necessary for the development of organisms and vital activities of cells, the functional significance of heterochromatin still remains a subject of debate and speculations among scientists. So far, it has been rather difficult to find reasonable explanations for the existence of heterochromatin. It is only possible to indicate the area that should be searched for this explanation… All this suggests that heterochromatin plays a special role in the life of germline cells" [23].

The association of heterochromatin with ontogenes reveals its significance and adds specifics to ontogenes. Let us consider what the assumption on the association of heterochromatin with ontogenes adds separately to (1) the genetic significance of heterochromatin and (2) genetic significance of ontogenes.

The functional significance of heterochromatin increases owing to the following functions of ontogenes:
(1) Regulation of the work of Mendelian genes;
(2) Control of cell construction;
(3) Arrangement of "quantization" of individual development;
(4) Links between all genes of the genome (a systemic character of the genome);
(5) Activities at all stages of the life activities of an organism; and

(6) Arrangement of a special (biophysical) interaction between ontogenes.

The functional significance of ontogenes increases owing to the following features of heterochromatin:
(1) Arrangement of a special (biophysical) interaction between ontogenes by changing the degree of coiling;
(2) Arrangement of "quantization" of individual development; and
(3) Arrangement of spatial configuration/architecture of genetic structures in the cell.

Thus, the presence of ontogenes within heterochromatin adds to its functional significance. The function of heterochromatin in the genome in some works is highly estimated and regarded as the second system of genetic variation [38]. Ontogenes, since the idea of their existence emerged and further with accumulation of the relevant experimental facts, have been also regarded as the elements of the system regulating genetic activity. The reason why seemingly different structures pretend to fulfill the same function consists in that in both cases we speak about one and the same regulatory system. This system can be formed by *the ontogenes in a special (heterochromatin) design.*

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References

1. Chadov BF. Genetics of intraspecific similarity (experiments with conditional mutations in Drosophila): monograph. 2025; 168.
2. Chadov BF. From the phenomenon of nondisjunction to the problem of chromosome co-orientation (75th anniversary of Bridges' article). Genetika. 1991; 27: 1325-1348.
3. Chadov BF. A genetic model of crossing-over. Vort. Pflanzenzuchtg. 2000; 48: 143-158.
4. Timofeev-Resovsky NV, Ivanov VI. Some issues of phenogenetics / Actual issues of modern genetics / edited by S.I. Alikhanyan. Moscow: Moscow State University Publishing House. 1996; 114-130.
5. Chadov BF, Fedorova NB. Ontogenes and the genetics of intraspecific similarity. Medical Research Archives. 2021; 9.
6. Chadov BF, Chadova EV, Kopyl SA, Fedorova NB. A New Class of Mutations in Drosophila melanogaster. Dokl Biol Sci. 2000; 373: 423-426.
7. Chadov BF. Mutations in the regulatory genes in Drosophila melanogaster. Proc. Intern. Conf. Biodiversity and Dynamics of Ecosystems in North Eurasia. Novosibirsk. 2000; 16-18.
8. Chadov BF, Fedorova NB. Ontogenes and Chromosome Nondisjunction in the D. melanogaster Meiosis. Advances in Bioscience and Biotechnology. 2022; 13: 317-335.
9. Chadov BF. Mutations Capable of Inducing Speciation. Tomsk State University Press. 2001; 138-162.
10. Chadov BF. Features of Intraspecific Similarity and Peculiarities of Mendel's Approach to Study of Heredity. Philosophy of Science. 2005; 26: 94-114.
11. Chadov BF. Conditional dominant lethals — a new class of mutations in Drosophila. Proceedings of BIT Life Sciences' 3-rd Annual World Congress of Gene. 2009.
12. Chadov BF, Fedorov NB, Chadova EV, Khotskina HA. Conditional mutations in Drosophila. Life Sciences. 2011; 5: 224-240.
13. Chadov BF, Fedorova NB, Chadova EV. 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. 2015; 765: 40-55.
14. Chadov BF, Fedorova NB. Conditional Mutations and New Genes in Drosophila. Mutagenesis and Mitochondrial-Associated Pathologies. 2022.
15. Chadov BF, Chadova EV, Kopyl SA, Artemova EV, Khotskina EA, et al. From Genetics of Intraspecific Differences to Genetics of Intraspecific Similarity. Russian Journal of Genetics. 2004; 40: 945-958.
16. Chadov BF. Ontogenes in Drosophila melanogaster: Genetic Features and role in Onto- and Phylogeny. JINR, Dubna. 2007; 80-91.
17. Chadov BF, Chadova EV, Kopyl SA, Khotskina EA, Fedorova NB. Genes Controlling Development: Morphoses, Phenocopies, Dimorphs and Other Visible Expressions of Mutant Genes. Russian Journal of Genetics. 2004; 40: 271-281.
18. Fedorova NB, Chadova EV, Khotskina EA, Chadov BF. Conditional mutations in Drosophila melanogaster: formation of morphosis. Proceedings of the II International Conference "Drosophila in experimental genetics and biology". Odessa (Ukraine). 2010; 104-108.
19. Fedorova NB, Chadova EV, Khotskina EA, Chadov BF. Conditional Mutations: Obtainment by the Method of Morphoses. Kiev. 2010; 78-83.
20. Chadov BF, Fedorova NB, Chadova EV. Parental Effects of Conditional Mutations and Their Explanations. Russian Journal of Genetics. 2013; 9: 141-150.
21. Bridges CB. Nondisjunction as proof of the chromosome theory of heredity. Genetics. 1916; 1: 1-52.
22. Koryakov DE, Zhimulev IF. Chromosomes. Structure and functions. Novosibirsk: Publishing House of the Siberian Branch of the Russian Academy of Sciences. 2009; 69-258.
23. Zhimulev IF. General and molecular genetics. Novosibirsk: Publishing House of Novosibirsk. Univ. 2002; 459.
24. Zhimulev IF. Heterochromatin and the effect of gene position. Novosibirsk: Nauka Publ. 1993; 490.

25. Chadov BF. The "image" of the regulatory gene in experiments with Drosophila. Russian Journal of Genetics. 2002; 38: 725-734.
26. Chadov BF, Chadova EV, Khotskina EA, Artemova EV, Fedorova NB. The Main Effect of Chromosomal Rearrangement Is Changing the Action of Regulatory Genes. Russian Journal of Genetics. 2004; 40: 723-731.
27. Chadov BF, Fedorova NB. Ontogenes and Their Role in Cellular Construction Advances in Bioscience and Biotechnology. 2003; 14: 49-73.
28. Chadov BF, Chadova EV, Fedorova NB. The Genetics of Conditional Mutations and Individual Developmental Program in D. melanogaster. SCIOL Genetic Science. 2017; 1: 3-21.
29. Chadov BF, Chadova EV, Fedorova NB. Conditional Mutations in Drosophila: Concept of Genes That Control Individual Development. Advances in Bioscience and Biotechnology. 2018; 9: 243-272.
30. Sturtevant AH, Beadle GW. The relation of inversions in the X chromosome of Drosophila melanogaster on crossing-over and disjunction. Genetics. 1936; 2l: 554-604.
31. Timofeev-Resovsky NV. On the phenotypic manifestation of the genotype I. Genovariation of radius incompletus in Drosophila funebris. Boil Ser A. 1925; 3: 93-142.
32. Timofeev-Resovsky NV. The relationship between the gene and the external sign // N.V. Timofeev-Ressovsky. Medicine. 1996; 59-84.
33. Dobzhansky T. Studies on chromosome conjugation. I. Translocations involving the second and the Y- chromosomes of Drosophila melanogaster. Vererbungsl. 1932; 60: 235-286.
34. Dobzhansky T. Studies on chromosome conjugation. II. The relation between crossing-over and disjunction of chromosomes/ involving the second and the Y- chromosomes of Drosophila melanogaster. Vererbungsl. 1933; 64: 269-309.
35. Dragavtsev VA. On the problem of genetic analysis of polygenic quantitative characteristics of plants. St. Petersburg. 2003; 35.
36. Chadov BF, Fedorova NB. The elementary event of development. Doklady Biological Sciences. 2003; 89: 183-187.
37. Chadov BF, Fedorova NB. Mutation in Ontogene and Emergence of Secondary Chromosome Damages in Drosophila Germline Cells. Advances in Bioscience and Biotechnology. 2003; 14; 379-398.
38. Panshin IB. The second system of hereditary variation as a consequence of quantitative regularities of heterochromatic gene position effect. Novosibirsk. 1992; 23-98.