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GENERAL GENETICS

Peculiarities of Mutation Process in X Chromosome of *Drosophila melanogaster* Z^{3314} Line from Zvenigorodka (Ukraine) Natural Population

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Abstract—The *Drosophila melanogaster* Z^{3314} line isolated from a Zvenigorodka (Ukraine) natural population is characterized by the manifestation and emergence of a wide spectrum of molecular aberrations. Among them, two types (the wing venation anomaly and violation of the leg segmentation) were the most represented. It was demonstrated that the frequency of manifestation (penetrance) and the expressiveness of these phenotypic aberrations increase with an increase in the temperature. When the Z^{3314} line is bred in the laboratory, autosomal visible *rase* (*ra*: 3 – 97.3) mutation, which leads to reduction of a part of dorso-central and scutellaria macrochaetae, was detected (isolated and identified). A number of genetic peculiarities that determined the consistency and prospects of the study were found during the mutation process study in the Z^{3314} line. The Z^{3314} line is characterized by a high frequency of the emergence of visible mutations in the X-Z^{3314} chromosome, which persisted for a long time of the breeding under laboratory conditions (from 2003 to 2011). Locus-specific high genetic instability in the *singed* locus in the X-Z^{3314} chromosome persisted from the moment of emergence of the first mutant alleles in 2006 until the end of the study. The emergence of mutations was observed both during the line breeding "inside" (in the case of brother–sister crossings) and after the crossings of the X-Z^{3314} chromosome carrier males with females of the C(1)DX,*ywf*/Y laboratory line with linked X chromosomes.

Keywords: chromosomes, mutation, mutability, genetic instability, *Drosophila melanogaster*

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INTRODUCTION

Beginning in the middle of the last century, different visible and lethal mutations were found in significant concentrations during the study of natural *Drosophila melanogaster* populations [1–5]. The average frequency of spontaneous visible and lethal mutations for *Drosophila* is about 10^{-5}–10^{-4}. A highly mutable (or unstable) state, the mutation frequency of which can be significantly higher as compared with the spontaneous level, was found for a number of alleles of some genes [2, 4–11]. Isolated unstable alleles of one gene could differ in the nature of the phenotypic expression of a trait, mutation frequencies, and mutation properties in generative and somatic cells [12–16]. The genetic instability of the alleles could persist in a number of generations for decades of maintaining of the lines under laboratory conditions [10, 16–18], and the question "How long can this state persist?" remains for each specific case.

The study of the mutation process in its different manifestations for several years using the example of one unstable line from nature allows the researchers to clarify experimentally those phenomena and processes that are inherent in natural populations. The Z^{3314} line, isolated from a natural *Drosophila melanogaster* population from Zvenigorodka (Ukraine, 2003) and studied in the Laboratory of Population Genetics of the Institute of Cytology and Genetics (Siberian Branch, Russian Academy of Sciences), refers to one of such models. A number of genetic peculiarities that determined the consistency and prospects of the study were found during the study of the mutation process in the Z^{3314} line.

MATERIALS AND METHODS

Inbred line breeding and family analysis of X-Z^{3314} chromosome mutability. Isofemale Z^{3314} line is a brother–sister progeny of a female from a natural *Drosophila melanogaster* population from Zvenigorodka, 2003 (Ukraine).

Fifteen fertilized females (which were founders of 15 sublines) were taken after several years of the Z^{3314} line maintenance in the collection of the Genetics of Populations Laboratory (Institute of Cytology and Genetics, Siberian Branch, Russian Academy of Sciences). Phenotypic and genotypic analysis in the sublines was conducted in 15 generations. All 15 sublines were homozygous for the recessive autosomal visible mutation, which leads to the reduction of a part of dorso-central and scutellari macrochaetae. The mutation was localized and identified as *rase* (*ra*: 3 – 97.3).

The *D. melanogaster* line breeding was performed under standard laboratory conditions, in vials on "raisin feed" with periodic phenotype analysis by means of an MBS-9 binocular microscope.

Direct accounting of emerging visible mutations in X chromosome. During the individual crossing of the male with the C(1)DX,*ywf*/Y female with linked X chromosomes, their sons receive the X chromosome and half of the autosomes from the father, while the other half of the autosomes and the Y chromosome come from the mother. Linked X chromosomes are marked by three recessive visible mutations: *yellow* (*y*: 1 – 0.0)—yellow body, brown bristles; *white* (*w*: 1 – 1.5)—eyes and Malpighian tubule system are white; *forked* (*f*: 1 – 56.5)—forked bristles and hairs are thickened. Each descendant male (obtained as a result of the crossing with such females) is an exact copy of the set of the father's genes relative to the allele composition of the X chromosome genes. If sex-linked visible mutation emerged in the father's gametes, we have an opportunity to detect it already among its sons by the emerging exclusive descendants.

Localization of mutations. Identification and localization of mutations were conducted according to standard methods of genetic analysis: (1) by means of the allelism test; (2) by the method of dominant visible mutations with lethal recessive effect; and (3) by means of linked X chromosomes [19].

Estimation of penetrance and expressiveness of phenotypic aberrations and rase mutation at different temperatures of development. The emergence of different morphological anomalies (phenocopies) was observed during the line cultivation. It was not possible to isolate the lines with 100% penetrance of the trait. Two out of such "incomplete-inherited" traits (the wing venation anomaly and violation of the leg segmentation) were studied on the dependence between their manifestation (penetrance and expressiveness) and the development temperature (at 18, 22, 25, and 30°C). The dependence between the degree of expressiveness of the *rase* mutation and the temperature of development was also estimated.

RESULTS

Family Analysis of Z^{3314} Line

Fifteen fertilized females were taken from the *Drosophila melanogaster* Z^{3314} line, and family analysis of phenotype of descendants was carried out in 15 generations (nonconsecutive!). A list of the types of detected/emerging visible aberrations and mutations and their frequencies is given in Table 1. In total, 8695 descendants were viewed. In this experiment, three independently emerged sex-linked mutations were isolated: "cherry eyes," *white-cherry* (one of the *white* gene alleles (1 – 1.5)); *lozenge* (*lz:* 1 – 27.7), diminished eyes, irregular facets; *Notch* (*N*: 1 – 3.0), notches on the wings. In addition, three *yellow-1* (*y*: 1 – 0.0) males were found in a separate family. A mutation in the *white* locus occurred in the progeny of one of the y^1 males when crossing with the C(1)DX,*ywf*/Y females (the y^1w male was obtained).

The aberration "absence of a part of leg segments" typical of the Z^{3314} line persisted in 14 out of 15 studied derivatives (Table 1). The Z^{3314} line was characterized by the emergence of a fraction of flies with phenotypic anomalies, the heritability of which we could not establish owing to a sterility or strong decrease in the viability of their carriers. For example, males with "rotated penis" trait (a change in the copulative organ location (its turn by 90°) were sterile. The fly with diminished head had a decreased viability.

Estimation of Mutability in X-Z^{3314} Chromosome

The estimation of the mutation spectrum and frequency in the *D. melanogaster* Z^{3314} X chromosome was conducted in both individual and mass crossings between males and C(1)DX,*ywf*/Y females with linked X chromosomes (the line 1-163 of the collection of the Genetics Populations Laboratory of the Institute of Cytology and Genetics (Siberian Branch, Russian Academy of Sciences)).

Two descendant males with newly emerged *singed bristles* mutation were found in one family in the first series of individual crossings of the Z^{3314} line males with C(1)DX,*ywf/Y* females with linked X chromosomes (in December 2006). Two more independent cases of the *singed* mutation emergence were found subsequently. The allele designated as $sn^{Z\text{-}1\text{-}1}$ was unstable and reverted to the norm with a frequency 1.7×10^{-3} (12 independent mutation events, 7071 $sn^{Z\text{-}1\text{-}1}$ X chromosomes were analyzed). The instability of $sn^{Z\text{-}1\text{-}1}$ X chromosome persisted for 5 subsequent years of observation (Table 2, Fig. 1). We emphasize a peculiarity of the X-Z^{3314} chromosome *singed* locus: a chain of mutation events of $sn^+ \rightarrow sn$ type and *vice versa* was

Table 1. Mutations and anomalies found in 15 families/derivatives of Z^{3314} line

Detected trait (mutation, anomaly)	Number of families in which descendants with anomalies were detected	Descendants with anomalies	
		number	detection frequency,* %
Diminished eyes with uneven surface (*lozenge* mutation)	1	12	0.28 ± 0.08
Cherry eye color (*white-cherry* mutation)	1	6	0.14 ± 0.06
Notches on wings (*Notch* mutation)	1	2	0.04 ± 0.03
Diminished head	1	1	0.01 ± 0.01
Diminished eyes	3	23	0.26 ± 0.06
Spotted eyes	1	1	0.01 ± 0.01
Anomalous thorax (hemithorax)	4	6	0.07 ± 0.03
Normal amount of macrochaetae on scutellum	3	9	0.10 ± 0.03
Crimped bristles	2	10	0.12 ± 0.04
Violation of abdomen segments (abnormal abdomen)	3	7	0.08 ± 0.03
Rotated penis	5	6	0.07 ± 0.03
Improperly developed segments of legs or absence of part of them	14	69	0.79 ± 0.10
Rudimentary wings	1	1	0.01 ± 0.01
Diminished wings	1	1	0.01 ± 0.01
Additional first transverse vein	2	5	0.06 ± 0.03

Total amount of viewed flies (4409♀ + 4286♂) = 8695.
* For sex-linked recessive *white* and *lozenge* mutations, the frequencies were calculated on the set of viewed sons; for dominant mutation with recessive lethal *Notch* effect, they were calculated on the set of daughters.

observed for a 5-year study period (Fig. 1). The mutability of isolated different *singed* alleles in the direction $sn \rightarrow sn^+$ was observed in a range of frequencies from 1.8×10^{-4} to 1.7×10^{-3}; in the direction $sn^+ \rightarrow sn$, from 6.7×10^{-5} to 1×10^{-3}.

The newly emerging *lozenge* mutation in the X-Z^{3314} chromosomes (Table 1) was genetically unstable. Three independent mutation events were detected when crossing the lz^Z line males with the C(1)DX,*ywf*/Y line females: the emergence of two phenotypically normal alleles ($lz^{+Z\text{-}1}$ and $lz^{+Z\text{-}2}$) and one with weak manifestation of the trait ($lz^{Z\text{-}weak}$) with the frequencies 1.6×10^{-3} and 5.6×10^{-4}, respectively.

In 2009, we detected sex-linked dominant *Beadex* (*Bx*: 1 – 59.4) mutation (notches on the wing). The expressiveness of this mutation varied. We allocate at least three phenotypic variants of this mutation manifestation: (1) notches on the wings; (2) notches and bubbles on the wings; (3) notches on not spread wings.

In 2011, sex-linked "dark eyes" mutation was detected in the line with the $sn^{+Z\text{-}1\text{-}2}$ mutation. In the same year, one male with the *yellow-2* mutation was detected in the $sn^{+Z\text{-}1}$ line mass culture. Another, independent case of mutation in the *yellow* locus was associated with the emergence of *yellow-2* mutation in the sn^{+Z}*Beadex*-X^Z chromosome.

Thus, 25 mutation events in the X^Z chromosome were detected by a method of linked X chromosomes from the beginning of the study through 2011; most of them (15 mutation events) were associated with the *singed* locus.

In the scheme presented in Fig. 1, attention should be paid to the difference of the mutation spectrum for the *yellow* and *white* genes in the X^{Z3314} chromosome at different types of crossings: (1) the *yellow-1* and *white-cherry* alleles emerged in the sublines ("inside," without the crossing with laboratory lines), and (2) only alleles of *yellow-2* and *white*$^-$ type emerged when crossing X^{Z3314} males with C(1)DX,*ywf*/Y females.

Description of Mutations and Their Alleles Emerging in Z^{3314} Line

The Z^{3314} initial line proceeds from a female caught in a natural population of *D. melanogaster* in Zvenigorodka.

Alleles of singed bristles (sn: 1 – 21.0) mutation. The *singed bristles* mutation determines different forms of

Table 2. Mutation in X chromosome of Z^{3314} line and its derivatives

Year of study	Initial Z^{3314} line and its derivatives	Number of viewed male descendants	Detected variant emerging with mutation/number of exclusive male descendants*	Number of "bundles" (families)**	Mutation frequency***
2003, 2004, 2005	Z^{3314} ****	8695 (♀ + ♂)	N^{3314}/2	1	4.6×10^{-4}
			$w^{ch\text{-}3314}$/6	1	1.4×10^{-3}
			lz^{3314}/12	1	2.8×10^{-3}
	Z^{3314} (fund)	Not counted	$y^{1\text{-}3314}$/1	1	–
	$y^{1\text{-}3314}$	1000	$y^{1}w^{3314}$/1	1	1×10^{-3}
	$y^{1}w^{3314}$	1000	0	0	0
2006	Z^{3314}	4348	sn^{3314} (1-1)/2	1	4.6×10^{-4}
2007	Z^{3314}	7067	0	0	0
	lz^{3314}	1775	lz^{+3314}/3	1	1.6×10^{-3}
			$lz^{sl\text{-}3314}$/1	1	5.6×10^{-4}
	sn^{3314} (1-1)	2243	sn^{+3314} (1-1, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10)/10	5	4.4×10^{-3}
	sn^{+3314} (1-1)	5863	sn^{3314} (2-1)/1	1	1.7×10^{-4}
	sn^{3314} (2-1)	4416	sn^{+3314} (2-1)/1	1	2.3×10^{-4}
	sn^{+3314} (2-1)	Not counted	sn^{3314} (3-1)/1	1	–
2009	Z^{3314}	2179	sn^{3314} (1-2, 1-3)/3	2	1.4×10^{-3}
			Bx^{3314}/1	1	4.6×10^{-4}
			"Dark eyes"/1	1	4.6×10^{-4}
	sn^{3314} (1-1)	1828	sn^{+3314} (1-11 1-12, 1-13)/3	3	1.6×10^{-3}
2010	sn^{3314} (1-1)	Not counted	sn^{+3314} (1-14)/1	1	–
2011	sn^{+3314} (1-14)	Not counted	$y^{2}sn^{+3314}$ (1-14)/1	1	–
	Bx^{3314}	Not counted	$Bx\, y^{2\text{-}3314}$/1	1	–

* Index numbers assigned to detected exclusive male descendants (founders of derivatives) are indicated in brackets.
** Number of families in which exclusive descendants were found.
*** Mutation frequencies for lines were obtained in a series of individual crossings like 1♂ × ♀♀ C(1)DX,*ywf*/Y.
**** Data obtained according to the results of intralinear crossings like 1 ♀ Z^{3314} × ♂ Z^{3314} (see also Table 1). For sex-linked recessive *white* and *lozenge* mutations, the frequencies were calculated here on the set of viewed sons; for dominant *Notch* mutation, they were calculated on the set of daughters.

bristles and hairs on the fly body and the presence or absence of sterility in homozygous females.

The *singed* gene alleles are divided into two types by the bristle form: sn^{+3314} (wild type bristles of normal length and form) and sn^{3314} (mutant phenotype); the first numeral after the allele designation means the allele origin, the second (after the hyphen) means the "bundle" number or the time of origin (for example, the first numeral in the sn^{3314}1-1 allele means the origin from the initial 3314 line; the second means the fact that this allele was obtained from this line the first). According to the phenotype, the *singed* gene mutant allele was determined as *singed-strong*.

sn^{3314}1-1 and sn^{3314}1-2, mutant alleles obtained from the initial Z^{3314} line.

sn^{+3314}1-1, sn^{+3314}1-2, sn^{+3314}1-3, sn^{+3314}1-4, sn^{+3314}1-5, sn^{+3314}1-6, sn^{+3314}1-7, sn^{+3314}1-8, sn^{+3314}1-9, sn^{+3314}1-10, sn^{+3314}1-11, sn^{+3314}1-12, sn^{+3314}1-13, and sn^{+3314}1-14, wild type alleles obtained as a result of the reversion of mutant sn^{3314}1-1 allele.

sn^{3314}2-1, mutant *singed-strong* allele obtained during the mutation of normal sn^{+3314}1-1 allele.

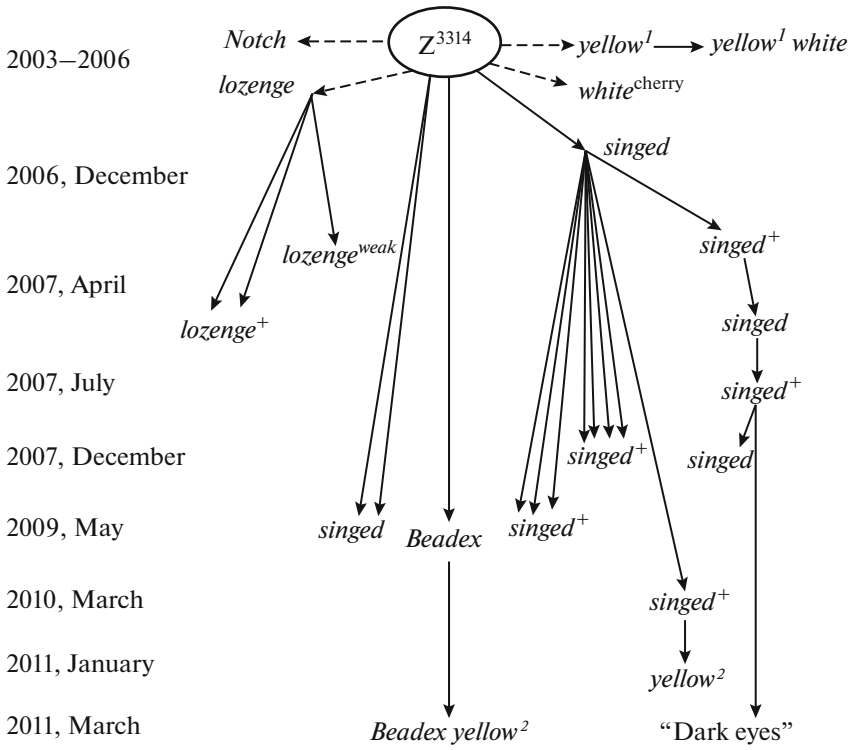

Fig. 1. Scheme of emergence of visible mutations in X^{Z3314} chromosome. Mutation in the X^{Z3314} line ("inside," without crossing with laboratory lines) is designated by dotted lines; mutation in sublines when crossing X^{Z3314} males with C(1)DX,*ywf*/Y females, by dotted lines.

sn^{+3314}2-1, normal allele obtained from mutant *sn*^{3314}2-1 allele.

sn^{3314}3-1, mutant allele obtained from normal *sn*$^{+3314}$2-1 allele.

Alleles of yellow (y: 1 – 0.0) mutation, yellow body color:

y$^{1\text{-}3314}$, *yellow-1*, yellow body, brown hairs and bristles.

y$^{2\text{-}3314\text{-}1}$, *yellow-2* (*y*^{2}), yellow body, black bristles. The derivative was obtained from the *sn*$^{+3314}$1-14 subline.

y$^{2\text{-}3314\text{-}2}$, *yellow-2* (*y*^{2}), yellow body, black bristles. The derivative was obtained from the *Bx*^{3314} subline.

The latter two alleles are phenotypically indistinguishable from each other.

Alleles of white (w: 1 – 1.5) mutation, eyes and Malpighian tubule system are white:

w—white, white eyes;

w^{ch}*—white-cherry*, cherry eye color.

Alleles of lozenge (lz: 1 – 27.7) mutation, diminished oval eyes, uneven eye surface due to violation in the location of facets:

lz^{s3314}, mutant allele with a strong manifestation of the mutant phenotype (*lozenge-strong*);

lz$^{sl\text{-}3314}$, mutant allele with weak manifestation of the mutant phenotype (*lozenge-slite*);

lz^{+3314}, normal eyes.

Dominant mutation of the notch on the wings, *Beadex* (*Bx*: 1 – 59.4).

Dependence of Manifestation of Developmental Anomalies on Temperature

As a result of the study, it was revealed that the frequencies of manifestation (penetrance) and the degree of expression (expressiveness) of some phenotypic aberrations are increased with an increase in the temperature at which the development occurs (Table 3). An increase in the expressiveness of the *rase* mutation with an increase in the temperature was detected. One or two bristles were absent in each fly among dorsocentral and scutellaria macrochaetae at 18°C; up to half were absent at 30°C.

DISCUSSION

An intense mutation process (the mutation rate about 10^{-3} by the *yellow*, *white*, and *singed* loci) occurred in the X chromosome of Z^{3314} line during the studied period; it had several specific peculiarities:

Table 3. Dependence of frequency of anomalies on developmental temperature

Temperature, °C	Descendant studied	Anomalies of leg segmentation	Anomalies of wing venation*
18	437	1	3 (0)
22	679	2	35 (0)
25	762	3	33 (6)
30	732	8	39 (6)

* Number of cases with strong expression of the mutant trait (development of additional transverse vein on both wings) is indicated in brackets.

(1) High frequency of direct and reverse mutation for several genes (for example, the mutation frequency from lz^Z to lz^{+Z} reached 1.8×10^{-3}).

(2) High number of X chromosome genes affected by the mutation process (*y*, *w*, *Notch*, *lz*, *sn*, *Bx*, and visible "dark eye" mutation).

(3) The mutation process was studied in the X-Z^{3314} chromosome both in the inbred line and in its derivatives when crossing the males of the line with C(1)DX,*ywf*/Y females with linked X chromosomes. Multiple visible mutations emerging in the X chromosome of the line with both breeding variants were recorded during the ten-year period of the study.

We note that the diversity of *de novo* emerging mutant alleles in one of the variants of the experiment differed from the obtained diversity in another variant. Mutations in the same locus occurred in both variants of the experiment, but the emerging mutant alleles differed phenotypically and genetically. For example, by their mutational properties, y^1 emerged in a "pure" line, while y^2 emerged two times in the experiment when crossing the males of the line with the C(1)DX,*ywf*/*Y* females; w^{ch}, in "pure" line; w^-, in the crossing variant with C(1)DX,*ywf*/Y females.

Two periods of increased concentration of mutant alleles were recorded for the *yellow* gene: in 1937–1946, throughout the territory of the Soviet Union [2, 4]; in 1982–1991, for the natural *D. melanogaster* population in Uman (Ukraine) [16, 20]. This phenomenon (figuratively called "fashion on mutation" was also recorded for other genes). A period of the "fashion on mutation" in the *D. melanogaster* populations on the territory of the former Soviet Union was registered and studied for the *singed* gene (1973–1979). The "fashion on mutation" in *D. melanogaster* by sex-linked *yellow* and *singed* genes was accompanied by a highly mutable state in these loci. It was suggested (and then established) that mobile genetic elements (MGE) are a reason for genetic instability of the genes [21–25]. The insertions of the *P* and *hobo* mobile element sequences were demonstrated for some unstable mutations in the *singed* and *yellow* loci in the *D. melanogaster* by molecular genetic methods [24–27].

Most of the mutations (stable and unstable) are caused by the processes of MGE introduction and excision [28]. Interallelic transitions of unstable genes can be associated with the excision, change of sites, copy number, and orientation of the introduction inside or in the vicinity of the genes. Different MGE types are characterized by a specificity of its activity (they can differ in the frequencies of introduction in different gene regions or excision). For example, the majority of mutations in a large set of insertion mutant *white* gene alleles are caused by a MGE insertion in two distant gene regions. Thus, for example, it was detected for the *pogo* MGE that as a minimum three independent mutation events occur on a very narrow region of the gene. The insertion of this MGE was found only in one of many morphologically manifested allelic states of the *white* gene ($white^-$, pure white eyes) [29]. The majority of mutation events for the *singed* gene presented and described in the Flybase database [29] are caused by the *P*-element insertion. In addition, unstable *singed* gene alleles caused by the insertion of the *hobo* element are known [24, 30]. When crossing the Z^{3314} line males with the C(1)DX,*ywf*/Y laboratory line females, a change in the composition of genetic material by chromosomes 2 and 3 (as well as cytotype) partially occurs in descendants. As a possible consequence of this, the activity of another MGE system (which can inhibit the activity of initial "natural" MGE composition) is launched.

Effect of Possible MGE Suppressor and Activator Genes during Their Introduction in Studied Line upon Crossing

The mutator genes can affect the character and spectrum of mutation. For example, the character of mutation on specific sites in the X chromosome changed with the introduction of chromosome 2, which carries the MR*12* male recombination factor, to the genome. This change in the mutation frequencies affected the *singed*, *yellow*, and *rasmarine* loci [21]. The *high* mutator gene, localized in *D. melanogaster* chromosome 2, increased the frequency of occurrence of at least one visible mutation (crumpled wings phenotype) in the X chromosome [31]. It is possible that in our case a hypothetical suppressor (probably contained in the C(1)DX,*ywf*/*Y* line) inhibits the activity of the mutability mechanism, which works in the initial line.

The repressing, activating, and neutral effects of the *P*-element were established during the study on the effect of the chromosomes carrying the *P*-elements and the appropriate cytoplasm on the mutation rate of three insertion unstable mutations caused by different MGE [32].

A decrease in the mutation frequency was observed for unstable mutation in the *singed* gene caused by the *mdg3* mobile element during the introduction of full-size *P*-element in the line [33]. On the basis of this, the authors hypothesized a competition of mobile elements for the transcription factor. In our case, hypothetical MGE (contained in the initial line) can also experience competition from the mobile element introduced with the C(1)DX,*ywf*/Y line. Consequently, the frequency of mutations caused by the initial MGE decreases (more precisely, such mutations are not diagnosed). But in our case, we know for sure that the C(1)DX,*ywf*/Y line has an M cytotype, that is, does not carry full-size or deleted *P*-element variants. It is possible that similar interaction of other mobile element systems takes place.

The following model is one of the possible explanations of a change in the character of mutations. There is a large set of genes associated with the processes occurring in DNA, including with the activity of mobile elements. The location of these genes should differ from the location of the sites of manifestation of activity of mobile elements (including the location in different chromosomes). If a substitution of half of the genetic material occurs when crossing two lines, the allelic state changes (and, as a consequence, peculiarities of the activity of such genes). This affects the MGE activity. In particular, the experiment on clarification of the dependence between genetic instability in the y^{+743} line and the presence of the mutant *mus308* gene copy in the genome (in a heterozygous state) was conducted (Yu.A. Koromyslov, S.V. Cheresiz, N.N. Yurchenko, and I.K. Zakharov, unpublished data). It was found that the presence of mutation in the *mus308* gene (chromosome 3) associated with DNA reparation processes leads to a decrease in the instability by the *yellow* gene in the X chromosome. Variations in peculiarities of the work of such genes in the Z^{3314} and C(1)DX,*ywf*/*Y* lines could affect the mechanisms of MGE transposition and, consequently, the mutation spectrum and activity.

The mutation properties of highly mutable genes are usually allele-specific and are caused by the properties of the genes themselves [34, 35]. However, there are exceptions: for example, the X chromosome of the sn^{mZ} line from the population of Zaporozhye, where along with instability in the *singed* locus an increased mutation activity for other genes (*yellow*, *white*, *vermilion*, *garnet eyes*) is also observed and in which the occurrence of lethal mutations was observed with an increased frequency [36]. The Z^{3314} line is very similar in this respect to the sn^{mZ} line. Mutations in a single locus can be caused by different MGE [23]. However, having homologous insertion sites, different mobile elements can have different degree of affinity for the target sites (which can determine a preferential spectrum and values of mutation frequencies) [37].

Depending on which part of the gene MGE is inserted and what rearrangements can emerge as a result of this, a lethal or visible mutation is generated or the molecular event passes without the phenotype change or formation of lethal mutation. Thus, for example, the authors explain the phenomenon of frequent changes of the phenotype by the *yellow* gene to the mutant one or on the contrary in lines of the *D. melanogaster* natural populations from Uman (Ukraine) by multiple inversions and re-inversions of the gene regulatory sequence located between two copies of the *hobo* element [25]. A high instability for the *singed* gene in the case we are considering can also be explained by such activity of mobile element (or elements). We note that they manifest themselves both under conditions of inbred line breeding (four visible mutations were obtained) and when crossing with the laboratory lines (three visible mutations were obtained). In the case of Z^{3314} line, we are probably dealing with different types of MGE, the activity and possible interaction of which explains all the completeness of the mutation process passing in the line. Molecular study of mutations in the Z^{3314} line is required to prove this.

A high frequency of morphological aberrations of two classes (anomalies of the wing venation and leg segmentation) is a characteristic feature of the studied Z^{3314} line. Their penetrance grows with an increase in the temperature (Table 3). An association of manifestation of phenotypic aberrations with a change in the temperature of development typical of some mutants for the heat shock protein genes can be noted [38]. At the same time, an increase in the frequency of morphological anomalies with an increase in the temperature of development is also typical of the P-M hybrid dysgenesis [39]. However, it should be emphasized that a growth in the frequency of manifestation of the anomalies that we studied occurred without any hybrid crossings.

The systems of genetic instability can differ in their abilities of increased mutation in the cells of generative and somatic tissues [10, 13, 15, 17, 34, 40]. The insertion mutations in the cells of generative and somatic tissues can have the same molecular genetic events. For example, reversions to the norm for the $white^{ivory}$ allele in both generative and somatic cells were associated with 29 kb DNA fragment duplication [41]. The transposition activity of MGE in generative and somatic cells can both be controlled by its own properties (or the cell MGE complex) and depend on many genetic and cytoplasmic factors and on the character of the gene expression in the cells of different tissues and organs [32, 33, 42, 43].

In conclusion, we can say that, although the mutability of each specific gene is its specific property, there is no doubt that the genetic surrounding of this gene (either the mutator gene, MGE, or a system of interacting mobile elements) affects this property, decreasing or increasing the mutability for this gene. Although changes occurring in the genome do not predetermine the mutation spectrum, they can strongly modify the frequencies and directions of mutation for different genes.

This work is a logical continuation of the population genetic studies conducted in the Laboratory of Population Genetics of the Institute of Cytology and Genetics (Siberian Branch, Russian Academy of Sciences). Further study in terms of understanding molecular genetic mechanisms of the reasons for mutation and changes in the mutation spectrum is required. Similar works on other lines are required in order to detect both the uniqueness and the universality of detected patterns of mutation and the sources and mechanisms of the maintenance of genetic diversity.

The evolution of populations and the sources and the mechanism of the development of genetic variability in populations constitute a complex process, which depends on many factors [1, 3, 44, 45]. An increase in the concentration of a specific mutation in the population can be a consequence of two processes. First is selection (the advantage of heterozygous carriers). Second is the distribution of the mutator genes in populations, as well as the presence of mutationally active MGE that cause a total and locus-specific mutability (instability). Moreover, a combination of these two factors (increased mutability and the advantage of heterozygotes) can provide a synergistic effect of the continuous increase in the concentration of mutations.

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