Биомика, 2012, Том 4, №1, 20-23

БИОМИКА/BIOMICS
http://biomics.ru

THE LIFE SPAN AND OVERACTIVITY OF TRANSPOSON *HERMES* IN *MUSCA DOMESTICA* STRAINS

Yu.M. Nikonorov, G.V. Benkovskaya

Institute of Biochemistry and Genetics, Ufa Scientific Center of RAS, Ufa, Russia, bengal2@yandex.ru

Abstract

The results showed in the paper concerned to the determination of copy number of transposon *Hermes* DNA in somatic tissues of house fly *Musca domestica.* Reducing of transposon copy number established in the strain S, original for selected on the reduced (strain *Sh 28*) or prolonged (*L 2*) strains, comparing to the data by natural populations of *M. domestica*. The significant exceeding of *Hermes* copy number showed in the strain *Sh 28* characterized by reduced life span. The probable variants of events with transposon *Hermes* participation occurring in the house fly strains examined. Authors discussed the opportunity of positive effect of transposon overactivity appearing as the maintenance of viability of the individuals and the populations as a whole under the stress situations including inbreeding.

Keywords: life span, *Musca domestica* transposon *Hermes*

Disastrous perturbations of population's number seem to be the likely events in respect of animal species characterized by fast synchronous ontogenetic development and high fecundity. Prevention of crucial situations and maintenance of effective species number is possible due to developing of autoregulatory mechanisms which realize their actions by means of average life span control in the separate populations. Within the populations of species investigated the natural polymorphism of life span existing and preserving. It is determined by quantitative trait loci (QTL) representing the polymorphic genes charged with the rate of species ageing [Flatt T., 2004]. Variability of genes copy number (CNV, copy number variation) considering now as one of the reasons of predisposition to many diseases reducing the life span [McCarrol and Altshuler, 2007]. Copy number variability of protein coding genes is lesser than one of ribosomal RNA genes (rDNA) and DNA of transposable elements (TE). High variability of the distribution patterns of separate copies of TE in the genome revealing also. The eukaryotic genomes contain 30-80% of repetitive DNA with TE or their fragments as the considerable part of it [Charlesworth, Barton, 2004]. TE are divided into two classes in respect of mechanisms of reproduction and spreading in the genome. TE assigned to class I, or retrotransposons use RNA intermediate involved by the mechanism described as "copy and paste". Transposons of class II move owing to excision from one site of the genome following by insertion into the other site utilizing the mechanism "cut and paste". Transpositions of TE are extremely mutagenic and toxic to somatic cells. Somatically active DNA transposons can reduce significantly the life span, sexual and locomotive activity in drosophila [Belyaeva et al., 1982; Gong et al., 2006]. Insertion of retrotransposons and DNA transposons into the coding regions of the genome leads to insertional mutagenesis and causes their dysfunctions; therefore in the native populations of drosophila the copy number of TE balanced by the natural selection [Charlesworth and Charlesworth, 1983]. The evident toxic effect of intensive transposons reproduction allowed supposing their participation in ageing processes [Murray, 1990]. Appreciable decrease of demographic values under the transformation by means of transposons some of insect disease vectors keep an interest to transposons like as the tool of biological control [Irvin et al., 2004].

However, whether the role of intensive activity of transposons is always negative for individual and the whole population? Some of investigators consider manifestation of TE activity in the species genome the adaptive trait [Gonzalez, Petrov, 2009]. Spreading in population of individuals with increased resistance to viral infections and insecticides in some cases are bounded up to transposon insertion and consequent

duplication of target gene [Magwire et al., 2011]. The examples of development of different patterns of TE localization in the chromosomes under the selection of quantitative traits with different directions evidence the different functions of TE forming of new phenotype [Pasyukova et al., 2004; Vasilyeva et al., 2007].

The kind of TE is induction of their reproduction as the response to different stressors. Causing dysfunctions and defects in many genes, transposons create the source of genetic variability of the genome which can play key role in adaptation of populations to stressful conditions [Ratner, Vasilyeva, 2000]. Strong inductive stimulus caused by inbreeding. Any quantitative sign selection based on close inbreeding followed the choice of parent pairs with different life span should be connected with genomic stress, developing in consequence to inbreeding and with probable increase of DNA injuries. Can we assume the positive effect of transposons overactivity under the selection? Dysfunctions in separate genes caused by introductions of transposons into their regulatory regions not necessarily would be lethal: these changes if the gene overexpression under the stress suppressed, can enable the effect of internal resources economy and effect of life span prolongation. One more positive effect is "healing" of two-stranded breaches of DNA with increased frequencies under the stresses. DNA of transposons inserting into the breach gaps [Khesin, 1985] realize the defense function; at the same time the opportunity is high to fix the unique pattern of transposons localization during differently directed selection [Pasyukova et al., 2004; Vasilyeva et al., 2007].

In our experiments with the strains of *Musca domestica* selected for increased and reduced life span we investigated possible participation of transposon *Hermes* in development of these signs. Transposon *Hermes* isolated from *M. domestica* assigned to class II of TE. Flies from native populations contain in their genomes 20-30 copies of transposon DNA [Warren et al., 1994]. It is considering that presence of specific mechanism regulating mobility of *Hermes* based on co-suppression by defect copies coding mutant forms of transposase prevents from more wide expansion of transposon in the *M. domestica* genome [O'Brochta et al., 1996]. Episomic forms of transposon produced due to excision of element can be passed on from maternal line [O'Brochta et al., 1999]. From polymorphic origin strain S derived from strain Cooper we got the strain Sh28 characterized by early reproductive effort and shortened life span of adults (on average 23-25 days) and strain L2 with late reproductive effort and prolonged life span (47-52 days). Simultaneously with the selected traits these strains acquired some distinctions both between each other and from origin strain S in resistance to temperature and toxic stresses and in reactions to the change of photoperiod [Benkovskaya, 2010; Benkovskaya et al., 2011; Benkovskaya, Mustafina, 2012]. *Hermes* DNA copy number in larval muscle tissues (12 larvae from each strain), puparium (also 12 from each strain), and thoracic imaginal muscles (24 females and males from each strain) we detected using quantitative real time PCR. At the same time we determined the copy number of ribosomal RNA genes (rRNA) and mitochondrial DNA (mtDNA).

The least variations of *Hermes* copy number observed in pupal DNA from all the strains: there were on average near about 8 copies per haploid genome or about 16 copies per whole genome. This value apparently can be considered resident for all mentioned congenetic strains. In larval DNA copy number excluded the obtained value 8 (1.5-fold higher in the strains S and L2 and almost twofold higher in the strain Sh28). About 20-25% of all progeny in the selected strains can not survive two transformations (larva-pupa and pupa-adult) during their ontogenesis. Among the reasons of these losses may be the elimination of carriers of "genetic load" such as *de novo* originated lethal mutations including mutations induced by the *Hermes* displacement. There are rarely appear adults with very high copy number of Hermes (maximal value vas 35 copies per haploid genome in the strain Sh28, 13 and 16 copies in the strains S and L2 accordingly) as a possible consequence of such a "selection".

Evaluating the copy number of transposon DNA in adults muscle tissues we revealed the excluding of copy number in the selected strains against to pupal stage (9-16 copies in the strains) and the excluding of copy number in the muscle tissues of adults from strain Sh28 (15-16 copies) as compared to the origin strain S (8-9 copies) and to the strain L2 (9-11 copies). A minimum of copy number, 5-6 copies per haploid genome, was recorded in the separate adults from the strain S. It is possible that in the genome of flies from strain L2 some copies of transposon localized in the regulatory regions of genes which not necessarily must overexpressed for normal vital functions of house flies in the laboratory conditions and the most part of resident copies keep their previous localization. It would lead to decrease the whole metabolism level and accordingly to reduce the volume of nascent toxic metabolites. In favor of this assumption evidenced the presence in adults from strain L2 relatively long postreproductive period [Benkovskaya et al., 2011]. Some additional quantity of copies (1-3 per haploid genome) detected in the muscle tissues DNA suggested the low level of transposition activity in somatic tissues of adults from this strain.

In adults from the strain Sh28 we detected 1200-1300 copies of rRNA genes per haploid genome while in the strains S and L2 detected 600 and 800 copies. At the larval stage in the strain Sh28 the content of mtDNA was twofold higher than in the other strains. However, then at the puparium stage the value became approximately equal – about 700 copies per cell in the all strains. In the three-days adults muscle tissues in the strain Sh28 the content of mtDNA doubled as compared to the strains S and L2, and this ratio raised until 14 days. The data are consistent with the typical for flies from this strain phenomenon of realization of their reproductive potential in a short time. For this strain is too big probability of intensive production of toxic metabolites and their damaging effect on the

genomic DNA. In the somatic cells of flies from strain Sh28 increased transposition activity probably provoked by appearance of breaks and breaches in DNA molecule. The consequences of such excess activity bear most likely negative nature, manifests as decrease of life span. But it is very possible that in some individuals from this strain positive effect manifests caused by intense transposon activity since new copies of transposon inserting into the breaks of genomic DNA thereby "reparating" these injuries and prolonging the life of damaged cells.

We assume that expansion of transposon *Hermes* in the genome which is accompanied by increase of its copy number, can be realized according to scheme (fig.1, B) supplemental to the existent canonical mechanism of transposition, supposed existence of intermediate episomic form (fig.1, A).

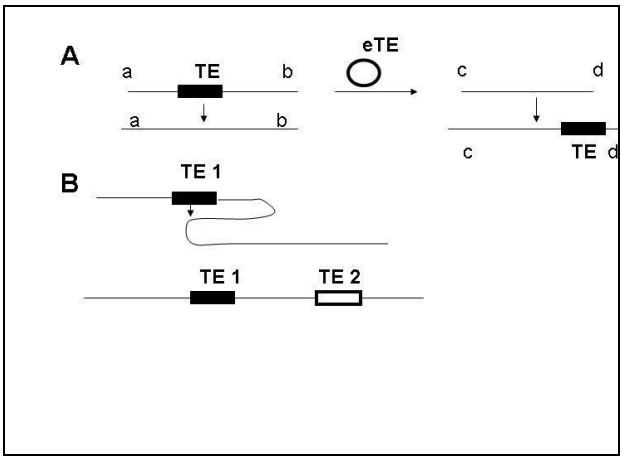

Figure 1. Mechanism of transposition of *Hermes* DNA: A – canonical, B – putative.
TE 1 – origin copy of transposon. TE 2 – new copy of transposon. eTE – episomic form of transposon.

The incision of recipient DNA can be realized at different distances including large ones from the site of initial contact with transposase. I.e., proposed the phase of "scanning" by the transposon – transposase complex of adjacent regions of chromosome for the purpose of appropriate site of insertion. During the meeting of complex with DNA region having the one-stranded or two-stranded break the initiation of cascade of reactions takes place, the final result of which is the insertion of new copy of transposon at some distance from initial copy in the same chromosome. Under the localization of resident copy of transposon not far from the "hot" region of chromosome, distinguished from other regions by the heightened sensibility to damage, formation of the whole "nest" of new copies is possible.

Thus, as a result of selection we got two strains of *M. domestica* differ significantly by the life span. During over than 30 generations of inbreeding in the strains remained the increased activity of *Hermes* manifests as the self-excited generation of individual variability of transposon copy number in the set of generations. We presume to propose that under the stress situations the positive effect can be observed concerned with maintenance of viability of organism in spite of risk of acquisition of unfavorable mutations by the germ line cells due to the increase of transposition activity of transposon.

Acknowledgments. Investigations funded by RFBR 12-04-01450-a and 11-04-97005-r_povolzhye_a.

References

1. Belyaeva E. S., Pasyukova E. G., Gvozdev V. A., Ilyin Y. V., Kaidanov L. Z. (1982). Transpositions of mobile dispersed genes in *Drosophila melanogaster* and fitness of stocks. *Mol. Gen. Genet. 185, 324–328.*
2. Benkovskaya G. V. (2010). Possibilities and limitations of life span changes in laboratory experiment. *Advances in gerontology 1 (3) 442-446.*
3. Benkovskaya G. V., Mustafina R. Sh. New Sex_Linked Mutation of Wings Fragility with Age_Depended Expression (*fw*) in *Musca domestica* L. (2012). *Rus. J. Of Genetics 48(2), 230-233.*
4. Benkovskaya G.V., Nikonorov Y.M., Somova R.Sh, Udalov M.B. (2011). Variants of realization of life programm: model strains of *Musca domestica* L. with different life span. *Appl. Entomol. 2(6), 21-25.*
5. Charlesworth B., Barton, N. (2004). Genome size: does bigger mean worse? *Curr. Biol. 14, 233–235.*
6. Charlesworth B., Charlesworth D. (1983). The population dynamics of transposable elements. *Genet. Res. 42, 1–27.*
7. Flatt T. **(**2004). Assessing natural variation in genes affecting *Drosophila* lifespan. *Mech. Ageing Develop. 125, 155—159.*
8. Gong Y., Thompson J. N. Jr., Woodruff R. C. (2006) Effect of deleterious mutations on life span in *Drosophila melanogaster. J Gerontol A Biol. Sci. Med. Sci. 61(12), 1246-1252.*
9. Gonzalez J., Petrov D.A. (2009). The adaptive role of transposable elements in the Drosophila genome. Gene 448(2), 124-133.
10. Irvin N., Hoddle M. S., O'Brochta D. A., Carey B., Atkinson P. W. (2004). Assessing fitness costs for transgenic Aedes aegypti expressing the GFP marker and transposase genes. *PNAS 101(3), 891-896.*
11. Khesin R.B. (1985). The Instability of the Genome. *M. Nauka, 472.*
12. Magwire M.V., Bayer F., Webster C.L., Cao Ch., Jiggins F. M. (2011). Successive increases in the resistance of *Drosophila* to viral infection through a transposon insertion followed by a duplication. *PLoS Genetics 7(10), e1002337.*
13. McCarrol St., Altshuler D. (2007). Copy-number variation and association studies of human disease. *Nature Genetics Suppl. 39, 37-42.*
14. Murray,V. (1990). Are transposons a cause of ageing? *Mutat. Res. 237(2), 59-63.*
15. O'Brochta D.A., Warren W.D., Saville K.J., Atkinson, P.W. (1996). *Hermes*, a functional

non-drosophillid insect gene vector from *Musca domestica*. *Genetics 142, 907-914.*

16. O'Brochta D.A., Stosic Ch.D., Pilitt K.., Subramanian R.A., Atkinson, P.W. (2009). Transpositionally active episomal *hAT* elements. *BMC Mol. Biol. 10, 108.*
17. Pasyukova E.G., Nuzhdin S.V., Morozova T.V., Mackay, T.F.C. (2004). Accumulation of transposable elements in the genome of *Drosophila melanogaster* is associated with a decrease in fitness. *Journal of Heredity 95(4),284–290.*
18. Ratner V.A, Vasilyeva L.A. (2000). Induction of mobile genetic elements' transpositions by stress treatments. *Soros' Educational Journal 6, 14-20.*
19. Vasilyeva L.A., Antonenko O.V., Vykhristyuk O.V. (2007). The response of genomic pattern of transposable elements TE412 to quantitative trait selection in Drosophila melanogaster. *Journal of General Biology 5, 341-349.*
20. Warren W.D., Atkinson P.W., O'Brochta D.A. (1994). The *Hermes* transposable element from the house fly, *Musca domestica*, is a short inverted repeat-type element of the *Hobo, Ac*, and *Tam 3 (hAT)* element family. *Genet. Res. 64, 82-92.*

ПРОДОЛЖИТЕЛЬНОСТЬ ЖИЗНИ И ПОВЫШЕННАЯ ТРАНСПОЗИЦИОННАЯ АКТИВНОСТЬ ТРАНСПОЗОНА *HERMES* В ЛИНИЯХ *MUSCA DOMESTICA*

Ю.М. Никоноров, Г.В. Беньковская
Федеральное государственное бюджетное учреждение науки Институт биохимии и генетики Уфимского научного центра Российской академии наук, Уфа, bengal2@yandex.ru

Резюме

В статье приведены результаты определения копийности ДНК транспозона *Hermes* в соматических тканях комнатной мухи *Musca domestica*. Установлено снижение числа копий транспозона по сравнению с данными для природных популяций комнатной мухи в линии *S*, исходной для отбираемых на сокращение (линия *Sh 28*) или продление (линия *L 2*) продолжительности жизни чистых линий *M. domestica***.** Показано существенное превышение числа копий транспозона у личинок и имаго линии *Sh 28*, отличающейся сокращенной продолжительностью жизни. Рассмотрены вероятные варианты событий с участием транспозона *Hermes*, происходящих в лабораторных линиях комнатной мухи. Авторы обсуждают возможность проявления позитивного эффекта повышенной транспозиционной активности, выражающегося в поддержании жизнеспособности отдельных особей и популяций в целом, в стрессовых ситуациях (включая инбридинг).

Ключевые слова: продолжительность жизни, *Musca domestica*, транспозон, *Hermes*