Integration specificity of the mobile element *Tirant* in the *Drosophila melanogaster* genome

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Mobile genetic elements (MGEs) account a significant part of the eukaryotic genome. Their transposition has a wide range of phenotypic expression and proved to be one of the most important mechanisms of the evolutionary process. The genome of the model object *Drosophila melanogaster*, since it contains a wide variety of the MGEs differed by the structure and movement characteristics, is widely used to study the mechanisms of the regulation and the evolutionary significance of transposition.

The choose of target sites for the MGE integration is influenced by a number of factors, including the structure of the target DNA, DNA methylation and transcription status, integrase features and others. It has been found that the transposition of the *D. melanogaster* MGEs of the *gypsy* group occurs to the specific target sites with the determined nucleotide sequence. Among these MGEs, *ZAM* and *Titant* recognize target site 5'-CGCGCG-3' [1]. Besides, the transposition of the *ZAM* element occurs mainly in the heterochromatic regions and is regulated by interaction of its 5'-untranslated region with the heterochromatin protein Hp1a [2]. Since the MGE *Tirant* is close to *ZAM* in phylogenetic terms, we suggested that the regulation of its transposition may also be carried out through the interaction with the Hp1a protein

With use of the sequenced genome of *D. melanogaster*, available in the FlyBase database, we have determined that all transpositions of the MGE *Tirant* occurs in euchromatin and predominantly in introns of genes or in areas adjacent to genes, which are characterized by a high level of transcription in the early stages of development. In the 5'-untranslated region *Tirant* 102 bp tandem repeats are indentified, and their number may vary from 3 to 6. Most of the *Tirant* copies have 5-6 repeats, and this observation allows us to put forward the assumption that copies with the greater number of repeats have the selective

advantage. This assumption is confirmed experimentally. It is noteworthy that the identified repeats form open reading frame and in a hypothetical translation show homology to the tetratricopeptide repeat domain (TRP) detected in the structure of a number of regulatory proteins.

We characterized *D. melanogaster* genes, in which sequences the insertions of *Tirant* were detected, by their ability to interact with protein Hp1a. For this experiment, we used data of the modENCODE project (Genome-wide Chromatin Profiling in Drosophila), performed on Affymetrix microchips. As a result, we found that most of the analyzed genes do not interact with Hp1a on embryonic and larval stages; this corresponds to the data on their expression. On the adult stage, these genes have a very low level of expression or no expression. This fact coincides with the results of microarray analysis detected their interaction with Hp1a on the adult stage. The same pattern of expression and interaction with Hp1a was found for the *aralar* and *cactus* genes, in which introns *Tirant* de novo insertions have been detected in our laboratory.

Thus, the MGE *Tirant* transposes, apparently, on the early stages of *D. melanogaster* development, when the majority of its target sequences are not associated with Hp1a and expressed at high level. The lack of association with the Hp1a protein is a necessary condition for the *Tirant* integration. The presence of tandem repeats in the 5'-untranslated region and the selection toward increasing their number may both indicate the existence of an alternative mechanism of *Tirant* integration using repeats to facilitate contact with the DNA targets either through their inclusion as a part of own proteins or by direct interaction with host proteins.

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1. L.N.Nefedova et al. (2011) Integration specificity of LTR retrotransposons and retroviruses in the *Drosophila melanogaster* genome. *Virus Genes*, **42(2)**:297–306.

2. C.Minervini et al. (2007) Heterochromatin protein 1 interacts with 5′UTR of transposable element *ZAM* in a sequence-specific fashion, *Gene*, **393**: 1–10.