

Natural variability in the regulatory regions of longevity genes and ecological adaptation

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Motivation and Aim: The elucidation of the molecular mechanisms underlying the relationship between gene expression and phenotype is a fundamental scientific task that is crucial for understanding the basis of development, life, and aging of living organisms. Transcription, which is the most important step that determines the level of gene expression, depends on the interaction between various regulatory elements localized in noncoding DNA and the regulatory proteins that interact with them. In nature, regulatory elements are characterized by significant structural variability, which can affect the level of transcription and, ultimately, complex phenotypes and adaptation. The aim of our work is a comprehensive analysis of the functional role of natural variability in the regulatory regions of genes controlling longevity.

Methods and Results: The variability of the 5' and 3' regulatory regions of the *shuttlecraft* and *escargot* genes in flies collected in the Alexandrov and Valдай populations (Russia) was characterized: segregating polymorphisms in populations were identified and their frequencies were compared with those observed in populations living in different parts of the world. The association of the identified segregating polymorphisms with the lifespan of flies and environmental conditions of populations was analyzed. It was shown that lifespan is associated with the variability of at least two polymorphic loci located in the 5' regulatory region of the *stc* gene. The variability of the same polymorphic loci is associated with the air temperature in the habitats of the populations. It was shown that the transcription of the *stc* gene and the expression of the reporter gene in *Drosophila* cell culture depend on which nucleotide is located in each of the two polymorphic loci.

Conclusion: This work allowed us to identify functionally important sites of the gene regulatory region and characterize the functional significance of their natural variability for the control of transcription, phenotype, and ecological adaptation.

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