DOI 10.18699/SBB-2022-639

Transcription regulation in aging and lifespan control

Rybina O.Y.[1, 2]*, Pasyukova E.G.[1]

[1] *Institute of Molecular Genetics, National Research Centre "Kurchatov Institute", Moscow, Russia*
[2] *Federal State Budgetary Educational Institution of Higher Education "Moscow Pedagogical State University", Moscow, Russia*
** flybee@mail.ru*

Key words: transcription regulation, lifespan, aging, transcription factor

Spatio-temporal regulation of gene expression governs the functioning of the organism, its development and aging. Tissue-specific changes in the activity of embryonic transcription factors have been shown to cause gene expression reprogramming, resulting in a reduction of age-dependent disorders. Thus, the induced change in transcriptional regulation could be one of the mechanisms for direct control of lifespan. In this regard, the study of tissue-specific transcription factors that are responsible for the organism functioning at a young age is of particular interest. Human *Lhx3/4* is a transcription factor which is required for pituitary development and motor neuron specification. *Lhx3/4* is highly homologous to *Drosophila Lim3,* which encodes an RNA polymerase II transcription factor involved in motor neuron specification.
Lim3 has a significant impact on *Drosophila* lifespan while being misregulated ubiquitously in the neuronal system and muscles. However, the strongest *Lim3* effect on fly lifespan is observed when it is down-regulated at an early age of *Drosophila* development and is associated with the alteration of mitochondrial and neuromuscular junction activities, an increase in ATP level and *Drosophila* locomotion activity. To determine the mechanisms underlying the impact of *Lim3* on the lifespan of flies, we studied the natural variability of the *Lim3* regulatory region. We found that naturally occurring polymorphism in *Lim3* promoter that is associated with gene expression variations and lifespan control in *Drosophila* are located exclusively in the Polycomb response element (PRE). We revealed this region to be enriched with Polycomb group (PcG) proteins: *Polycomb (Pc),* Polyhomeotic*,* Pleiohomeotic *proteins.* Furthermore, mutations in *Pc* affected *Lim3* expression, thus confirming functional interactions between this protein and *Lim3* regulatory region. Thus, PcG proteins that are thought to mediate epigenetic silencing are directly involved in the regulation of *Lim3* transcription, which is associated with the control of *Drosophila* lifespan.