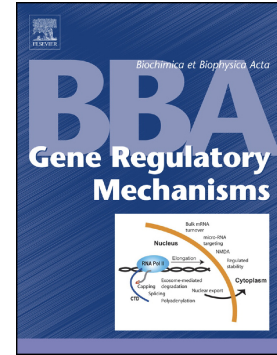


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**Polycomb/Trithorax group-dependent regulation of the neuronal gene *Lim3*
involved in *Drosophila* lifespan control**

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Abstract

Molecular mechanisms governing gene expression and defining complex phenotypes are central to understanding the basics of development and aging. Here, we demonstrate that naturally occurring polymorphisms of the *Lim3* regulatory region that are associated with variation in gene expression and *Drosophila* lifespan control are located exclusively in the Polycomb response element (PRE). We find that the Polycomb group (PcG) protein Polycomb (PC) is bound to the PRE only in embryos where *Lim3* is present in both repressed and active states. In contrast, the Trithorax group (TrxG) protein absent, small, or homeotic discs 1 (ASH1) is bound downstream of the PRE, to a region adjacent to the *Lim3* transcription start site in embryos and adult flies, in which *Lim3* is in an active state. Furthermore, mutations in *Pc* and *ash1* genes affect *Lim3* expression depending on the structural integrity of the *Lim3* PRE, thus confirming functional interactions between these proteins and *Lim3* regulatory region. In addition, we demonstrate that the evolutionary conserved *Lim3* core promoter provides basic *Lim3* expression, whereas structural changes in the *Lim3* PRE of distal promoter provide stage-, and tissue-specific *Lim3* expression. Therefore, we hypothesize that PcG/TrxG proteins, which are directly involved in *Lim3* transcription regulation, participate in lifespan control.

Key words: lifespan; transcription; embryonic development; Polycomb/Trithorax proteins; Polycomb/Trithorax response element; *Drosophila melanogaster*

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