NELF promotes RNA polymerase II pausing at ecdysone-dependent genes in Drosophila melanogaster

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Ecdysone response plays a crucial role in development of *Drosophila melanogaster*. A number of genes which are induced in *Drosophila* cells under the influence of an ecdysone hormone were described long time ago. But exact molecular mechanism causing transcription induction upon ecdysone treatment remains largely underinvestigated. We have recently described some novel molecular partners interacting with ecdysone receptor (EcR) [1]. One of them, subunit A of Negative Elongation Factor (NELF A), we have investigated in detail [2]. NELF A subunit was found to co-immunoprecipitate with ecdysone receptor both in S2 Schneider cells and pupal extract. The knockdown of NELF A by RNA interference in *Drosophila* S2 cells were shown to decrease an inducible transcription of several ecdysone-dependent genes. ChIP-Seq analysis of NELF A demonstrated presence of this protein on EcR-bound sites in Drosophila genome. It is known that ecdysone-dependent genes (at least in *Drosophila* S2 cells) is characterized with a high level of RNA polymerase II pausing: the level of promoter-bound RNA polymerase II several times exceeds the level detected in a gene body. Usually, genes regulated via RNA polymerase II pausing mechanism show a high level of abortive transcription which can be detected in promoter-proximal regions. Using previously published Gro-Seq data (Core et al, Cell reports (2012)), we have demonstrated a presence of abortive transcription at the promoter-proximal regions of the most of ecdysone-dependent genes. Moreover, the level of this abortive transcription was found to decrease upon knockdown of NELF subunits, demonstrating that NELF complex indeed regulates promoter-proximal pausing at the ecdysone-dependent genes. The work was supported by the Russian Science Foundation [grant 18-14-00219].

1. Mazina, M. Y., et al. Sci. Rep. 10, 4793 (2020).
2. Mazina, M. Y., et al. Sci. Rep. 11, 172 (2021).