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PRC1 nano-structures compact Polycomb-associated chromatin during Drosophila embryogenesis.

Regulation of gene expression during cell differentiation is a complex process involving several levels of chromatin organization. Transcription factors such as promoters and enhancers act on discrete elements whose accessibility can be controlled by nucleosomes. Polycomb grouped proteins (PcG) are key factor required to maintain silenced chromatin state. Although PcG proteins bind discrete elements, their associated histone mark H3K27me3 spreads over chromatin domains large of several tens of kb, which evidences a higher-order organization at the linear genomic scale. In 3D nuclear space, PcG proteins and H3K27me3 accumulate in structures named Pc foci. Though, the relationship between the linear distribution of PcG proteins and their 3D organization in the cell nucleus still remains poorly understood, mainly because optical microscopy lacks resolution. In this work, we use STED, a super-resolution microscope allowing observations of embryos, to study the architecture of the most intense Polycomb foci which corresponds to repressed Hox clusters. In Drosophila embryos, the biggest Polycomb foci are composed of several sub-structures of about 70 nm in diameter. We confirm their existence using Airyscan microscopy and show that they move rapidly compare to each other in living embryos. Immuno-FISH experiments indicate that chromatin associated to repressed Hox clusters also displays substructures in STED microscopy. Although PRC1 and chromatin substructures mostly co-localize, they form distinct assemblies. Noticeably, discrete elements bound by PcG proteins within Hox clusters are more associated to the PRC1 sub-structures than the rest of chromatin marked by H3K27me3. In null mutant for Polycomb, the only subunit of PRC1 which can bind to H3K27me3, both discrete elements bound by PcG proteins and chromatin only covered by H3K27me3 are less associated with PRC1 substructures. Taken together, we evidence new higher-order PRC1 structures organizing Polycomb associated chromatin and explaining why H3K27me3 is distributed within genomic domains of several tens of kb and the effect of PRC1 on chromatin compaction and long-range interactions.

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