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Title: EARLY HETEROCHROMATIN FORMATION ON REPETITIVE ELEMENTS IS ESSENTIAL FOR PRECISE DEVELOPMENTAL TIMING

Abstract: After fertilization, the maternal and paternal genomes come together and undergo epigenetic reprogramming to prepare for zygotic genome activation (ZGA) during the maternal-to-zygotic transition (MZT). Epigenetic mechanisms are crucial for ensuring that the initially transcriptionally silent zygotic genome becomes transcriptionally active at the precise developmental time point during MZT. However, few studies have investigated pre-ZGA transcriptional control of non-protein coding regions of the genome, such as repetitive elements. To investigate transcriptional control of repetitive elements, we treated zebrafish embryos with an epigenetic inhibitor of chromatin silencing factors G9a, which deposit H3K9me2, at fertilization. Strikingly, we observed significantly increased mortality and prolonged developmental delays in zebrafish embryos after only transient G9a inhibition during the first 30 minutes of development following fertilization. Our findings suggest that G9a-dependent heterochromatin formation may suppress pre-ZGA repetitive element transcription, which may be an essential aspect of precise early developmental timing control. We postulate that repetitive elements can regulate developmental gene expression by modulating the demand on the transcriptional machinery.