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Title: COMPETITION FOR H2A.Z BETWEEN GENES AND REPETITIVE ELEMENTS SENSITIZES DEVELOPING EMBRYOS TO INNATE IMMUNE STIMULATION

Abstract: The histone variant H2A.Z plays a critical role in early embryonic development, establishing transcriptional competency through chromatin regulation of developmental gene promoters and enhancers. We find this role to be compromised in zebrafish embryos during innate immune response. Stimulation of interferon response causes H2A.Z to exit developmental gene promoters, which undergo silencing, and to accumulate at a subset of evolutionarily young repetitive elements, including DNA transposons, LINEs, and LTRs. Remarkably, this epigenetic rewiring is greatly influenced by the abundance of total H2A.Z, and developmental consequences of interferon stimulation are mitigated by H2A.Z over-expression. Our study reveals that H2A.Z levels determine sensitivity to innate immune activation, and repetitive elements can function as a nuclear sink, imparting influence over total transcriptional output. These findings uncover general mechanisms whereby competition between counteractive biological processes underlies phenotypic outcomes.