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Title: COMPETITION FOR H2A.Z BETWEEN GENES AND REPETITIVE ELEMENTS ESTABLISHES RESPONSE TO ANTI-VIRAL IMMUNE ACTIVATION

Abstract:

Activation of endogenous retroviruses leads to widespread transcriptional reprogramming, affecting innate immune activation, metabolic control, and development. We find that the histone variant H2A.Z plays a central role in orchestrating these responses. Stimulating retroviral expression in zebrafish embryos by exposure to either DNA hypomethylating drug 5Aza-dC or environmental toxin TDCIPP, causes H2A.Z to exit developmental gene promoters, which become silent, and to accumulate specifically at 'primed' repetitive elements, which are pre-marked by H3K27ac and H3K9me3. Remarkably, this rewiring is greatly influenced by total H2A.Z abundance, and developmental consequences of retrovirus activation are mitigated by H2A.Z over-expression. Taken together, our results uncover mechanisms whereby H2A.Z levels determine sensitivity to retroviral activation, and repetitive elements function as a nuclear sink to dramatically influence total transcriptional output.