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ABSTRACT

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Short talk: "Histone H3.3 is Required for Interstitial Heterochromatin in Mouse Embryonic Stem Cells"

Recent studies have demonstrated that imprinted genes and a subset of interstitial heterochromatin (confined heterochromatic islands within euchromatic regions), such as endogenous retroviral elements (ERVs) containing long terminal repeats (LTRs), are silenced through trimethylation of histone H3 on lysine 9 (H3K9me3) by ESET (also known as SETDB1 or KMT1E) and a co-repressor complex containing KRAB-associated protein 1 (KAP1; also known as TRIM28) in mouse embryonic stem cells. We discovered that the replacement histone variant H3.3 is also enriched at KAP1-regulated sites. Deposition at a subset of these elements is dependent upon the H3.3 chaperone complex containing α-thalassaemia/mental retardation syndrome X-linked (ATRX) and death-domain-associated protein (DAXX). We demonstrate that recruitment of DAXX, H3.3 and KAP1 to ERVs is co-dependent and occurs upstream of ESET, linking H3.3 to KAP1-dependent H3K9me3. Importantly, H3K9me3 is reduced at ERVs and imprinted genes upon H3.3 deletion, resulting in derepression. Our study identifies a unique heterochromatin state marked by the presence of both H3.3 and H3K9me3, and establishes an important role for H3.3 in control interstitial heterochromatin in embryonic stem cells.

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