

SIRT1 regulates the histone methyl-transferase SUV39H1 during heterochromatin formation

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In contrast to stably repressive, constitutive heterochromatin and stably active, euchromatin, facultative heterochromatin has the capacity to alternate between repressive and activated states of transcription¹. As such, it is an instructive source to understand the molecular basis for changes in chromatin structure that correlate with transcriptional status. Sirtuin 1 (SIRT1) and suppressor of variegation 3–9 homologue 1 (SUV39H1) are amongst the enzymes responsible for chromatin modulations associated with facultative heterochromatin formation. SUV39H1 is the principal enzyme responsible for the accumulation of histone H3 containing a tri-methyl group at its lysine 9 position (H3K9me₃) in regions of heterochromatin². SIRT1 is an NAD⁺-dependent deacetylase that targets histone H4 at lysine 16 (refs 3 and 4), and through an unknown mechanism facilitates increased levels of H3K9me₃ (ref. 3).

Here we show that the mammalian histone methyltransferase SUV39H1 is itself targeted by the histone deacetylase SIRT1 and that SUV39H1 activity is regulated by acetylation at lysine residue 266 in its catalytic SET domain. SIRT1 interacts directly with, recruits and deacetylates SUV39H1, and these activities independently contribute to elevated levels of SUV39H1 activity resulting in increased levels of the H3K9me₃ modification. Loss of SIRT1 greatly affects SUV39H1-dependent H3K9me₃ and impairs localization of heterochromatin protein 1. These findings demonstrate a functional link between the heterochromatin-related histone methyltransferase SUV39H1 and the histone deacetylase SIRT1.

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