UMEÅ UNIVERSITET

JACK OF ALL TRADES, MASTER OF NONE

The multifaceted nature of H3K36 methylation

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Akademisk avhandling

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Abstract
Post-translational modifications of histones enable differential transcriptional control of the genome between cell types, developmental stages and as a response to environmental factors. The methylation of Histone 3 Lysine 36 (H3K36) is one the most complex and well-studied modifications and has been shown to be involved in a wide range of molecular processes. Commonly associated with active genes and transcriptional elongation, H3K36 methylation is also a crucial factor in DNA repair, repression of cryptic transcription and as a guide for additional post-translational modifications to histones, genomic DNA and RNA. In *Drosophila melanogaster*, methylation of H3K36 has also been linked to dosage compensation of the single male X chromosome. There is an additional system of chromosome specific gene regulation in *D. melanogaster* where transcription from the small heterochromatic fourth chromosome is increased by Painting of fourth (POF), a protein specifically binding nascent RNA on the fourth chromosome. The fourth chromosome is thought to have been an ancestral X chromosome that reverted into an autosome.

Using immunofluorescent stainings of polytene chromosomes together with RNA and ChIP sequencing in disrupted H3K36 methylation mutants we show that methylation of H3K36 is vital for the maintained high transcriptional output from the *D. melanogaster* fourth chromosome but not for the single male X-chromosome. Instead, we show that the SET domain containing 2 (Set2) methyltransferase is required for dosage compensation of the X-chromosome independent from its function as a H3K36 histone methyltransferase, suggesting the existence of additional Set2 substrates. Furthermore, we also show that methylation of H3K36 plays an important role in the suppression of transposable element activity in somatic cells, potentially through heterochromatin formation at transposon loci. These findings together add to the already complex network of processes dependent on H3K36 methylation.

Keywords
H3K36, histone methylation, dosage compensation, chromosome-specific gene regulation, transposable elements, PIWI/piRNA biosynthesis, Set2, Ash1, NSD, Histone 3.3

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