

# Core MLL complex, SMYD3, PRDM9 methylate dimethyl-lysine-5 of histone H3 (H3K4)

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## Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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## Literature references

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Reactome database release: 75

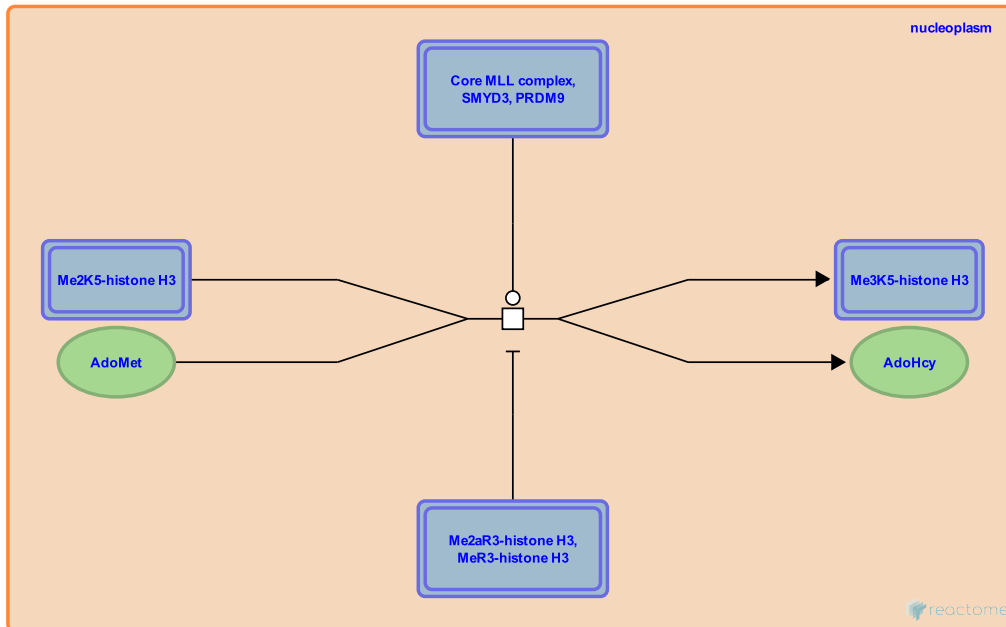
This document contains 1 reaction ([see Table of Contents](#))

## Core MLL complex, SMYD3, PRDM9 methylate dimethyl-lysine-5 of histone H3 (H3K4) ↗

**Stable identifier:** R-HSA-5244692

**Type:** transition

**Compartments:** nucleoplasm



Trimethylation of lysine-5 of histone H3 (H3K4) has been linked to transcriptional activation in a variety of eukaryotic species (Ruthenberg et al. 2007). Several H3K4 methyltransferases have been identified in mammals, predominantly members of the Mixed Lineage Leukemia (MLL) protein family. Five of these, KMT2A (MML1), KMT2D (MLL2), KMT2C (MLL3), KMT2B (MLL4) and SETD1A (KMT2F) have been shown to display H3K4 mono-, di- and tri-methyltransferase activity (Milne et al. 2002, Hughes et al. 2004, Cho et al. 2007, Wysocka et al. 2003). KMT2G (SETD1B) is believed to have similar activity on the basis of sequence homology (Ruthenberg et al. 2007). MLLs are a component of large multiprotein complexes that also include WDR5, RBBP5, ASH2 and DPY30, assembled to form the core MLL complex (Nakamura et al. 2002, Hughes et al. 2004, Dou et al. 2006, Tremblay et al. 2014). The WD40 domain of WDR5 recognizes and binds the histone H3 N-terminus, presenting the lysine-4 side chain for methylation by one of the catalytically active MLL family (Couture et al. 2006, Ruthenberg et al. 2006). Histone H3 recognition by WDR5 is regulated by the methylation state of the adjacent arginine (H3R2) residue. H3R2 methylation abolishes WDR5 interaction with the H3 histone tail (Couture et al. 2006); H3K4 di-/trimethylation and H3R2 methylation have an inverse relationship (Guccione et al. 2006).

SMYD3 (KMT3E) and PRDM9 (KMT8B) are able to tri-methylate H3K4 (Hamamoto et al. 2004, Hayashi et al. 2005, Koh-Stenta et al. 2014).

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## **Editions**

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