

# **SETD3, SETD7 (KMT7), WHSC1L1 (KMT3F), Core MLL complex methylate lysine-5 of histone H3 (H3K4)**

Jupe, S., Motamedi, M.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/licenses/).

30/04/2024

## 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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 88

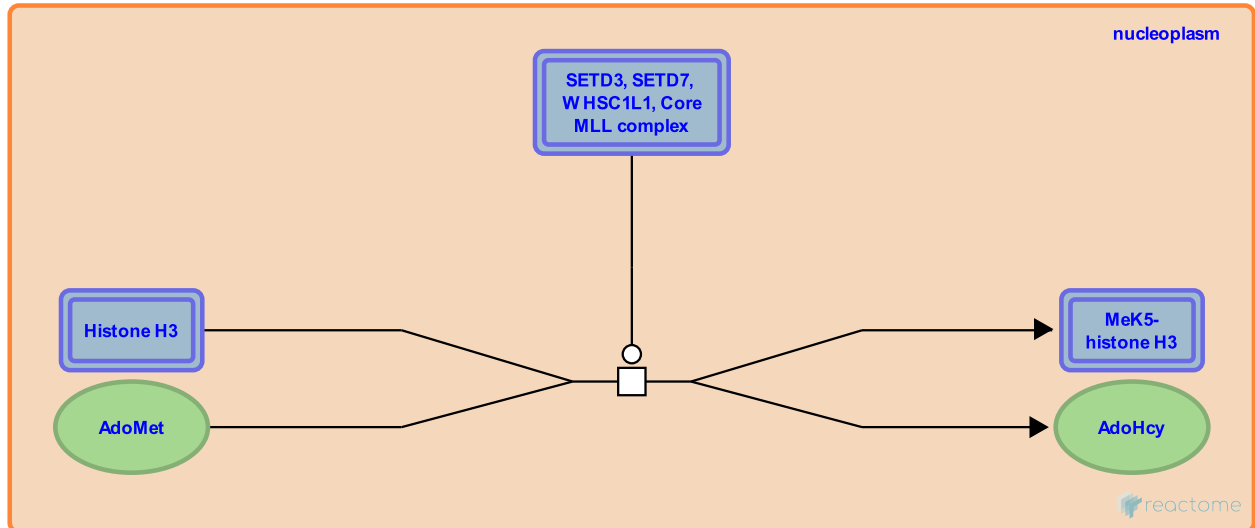
This document contains 1 reaction ([see Table of Contents](#))

## SETD3, SETD7 (KMT7), WHSC1L1 (KMT3F), Core MLL complex methylate lysine-5 of histone H3 (H3K4) ↗

**Stable identifier:** R-HSA-5159245

**Type:** transition

**Compartments:** nucleoplasm



Tri-methylation 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 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).

SETD7 (KMT7, SET9, SET7/9) is an H3K4 mono-methyltransferase (Wang et al. 2001, Xiao et al. 2003, Hu & Zhang 2006) that can also methylate a wide range of non-histone proteins (Dhayalan et al. 2011). SETD3 can mono- and di-methylate H3K4 and H3K36 (Eom et al. 2011).

### Literature references

- Laherty, CD., Myers, MP., Eisenman, RN., Herr, W., Wysocka, J. (2003). Human Sin3 deacetylase and trithorax-related Set1/Ash2 histone H3-K4 methyltransferase are tethered together selectively by the cell-proliferation factor HCF-1. *Genes Dev.*, 17, 896-911. ↗
- Aebersold, R., Demers, C., Dilworth, FJ., Morle, F., Lai, P., Ranish, JA. et al. (2007). Activator-mediated recruitment of the MLL2 methyltransferase complex to the beta-globin locus. *Mol. Cell*, 27, 573-84. ↗
- Kelly, G., Walker, PA., Vasisht, N., Gambelin, SJ., Wilson, JR., Taylor, IA. et al. (2003). Structure and catalytic mechanism of the human histone methyltransferase SET7/9. *Nature*, 421, 652-6. ↗
- Ge, K., Guo, H., Hong, S., Hong, T., Yu, H., Copeland, TD. et al. (2007). PTIP associates with MLL3- and MLL4-containing histone H3 lysine 4 methyltransferase complex. *J. Biol. Chem.*, 282, 20395-406. ↗
- Kee, HJ., Kim, SK., Kim, SM., Choe, NW., Kook, H., Kim, YS. et al. (2006). Characterization of a novel WHSC1-associated SET domain protein with H3K4 and H3K27 methyltransferase activity. *Biochem. Biophys. Res. Commun.*, 345, 318-23. ↗

**Editions**

2013-03-12	Authored	Jupe, S.
2014-09-10	Edited	Jupe, S.
2014-11-17	Reviewed	Motamedi, M.