

NoRC:intergenic spacer:Hdac:Dnmt complex deacetylates histone H4 and dimethylates lysine-9 of histone H3 in main promoter of the rRNA gene

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https://reactome.org

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

- 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 data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

Reactome database release: 88

This document contains 1 reaction (see Table of Contents)

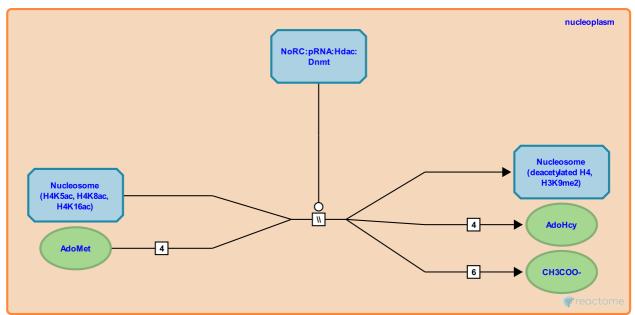
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NoRC:intergenic spacer:Hdac:Dnmt complex deacetylates histone H4 and dimethylates lysine-9 of histone H3 in main promoter of the rRNA gene **→**

Stable identifier: R-MMU-573376

Type: omitted

Compartments: nucleoplasm



Histones in silenced rRNA gene copies are deacetylated by Hdac1 (and possibly Hdac2), which is part of the SIN3-HDAC complex bound to NoRC (Santoro et al. 2002, Zhou et al. 2002). The PHD domain of the Tip5 (Baz2a) component of NoRC binds acetylated lysine-16 of histone H4 (Zhou and Grummt 2005). The residues of histone H4 that are deacetylated are lysine-5, lysine-8, and lysine-12 (Zhou and Grummt 2005).

In the main promoters of silenced rRNA gene copies, histone H3 is methylated on lysine-9 (H3K9) by an unknown histone methyltransferase (Santoro and Grummt 2005). H3K9 methylation is still observed when deacetylation is inhibited, therefore histone methylation does not depend on deacetylation (Santoro and Grummt 2005). However, histone deacetylation is required for DNA methylation. Significantly more H3K9 dimethylation than trimethylation is observed (Santoro and Grummt 2005).

It is unknown if deacetylation precedes methylation or vice versa.

Literature references

Zhou, Y., Santoro, R., Grummt, I. (2002). The chromatin remodeling complex NoRC targets HDAC1 to the ribosomal gene promoter and represses RNA polymerase I transcription. *EMBO J, 21*, 4632-40.

Zhou, Y., Grummt, I. (2005). The PHD finger/bromodomain of NoRC interacts with acetylated histone H4K16 and is sufficient for rDNA silencing. *Curr Biol*, 15, 1434-8.

Santoro, R., Grummt, I. (2005). Epigenetic mechanism of rRNA gene silencing: temporal order of NoRC-mediated histone modification, chromatin remodeling, and DNA methylation. *Mol Cell Biol*, 25, 2539-46.

Santoro, R., Grummt, I., Li, J. (2002). The nucleolar remodeling complex NoRC mediates heterochromatin formation and silencing of ribosomal gene transcription. *Nat Genet*, 32, 393-6.

Editions

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