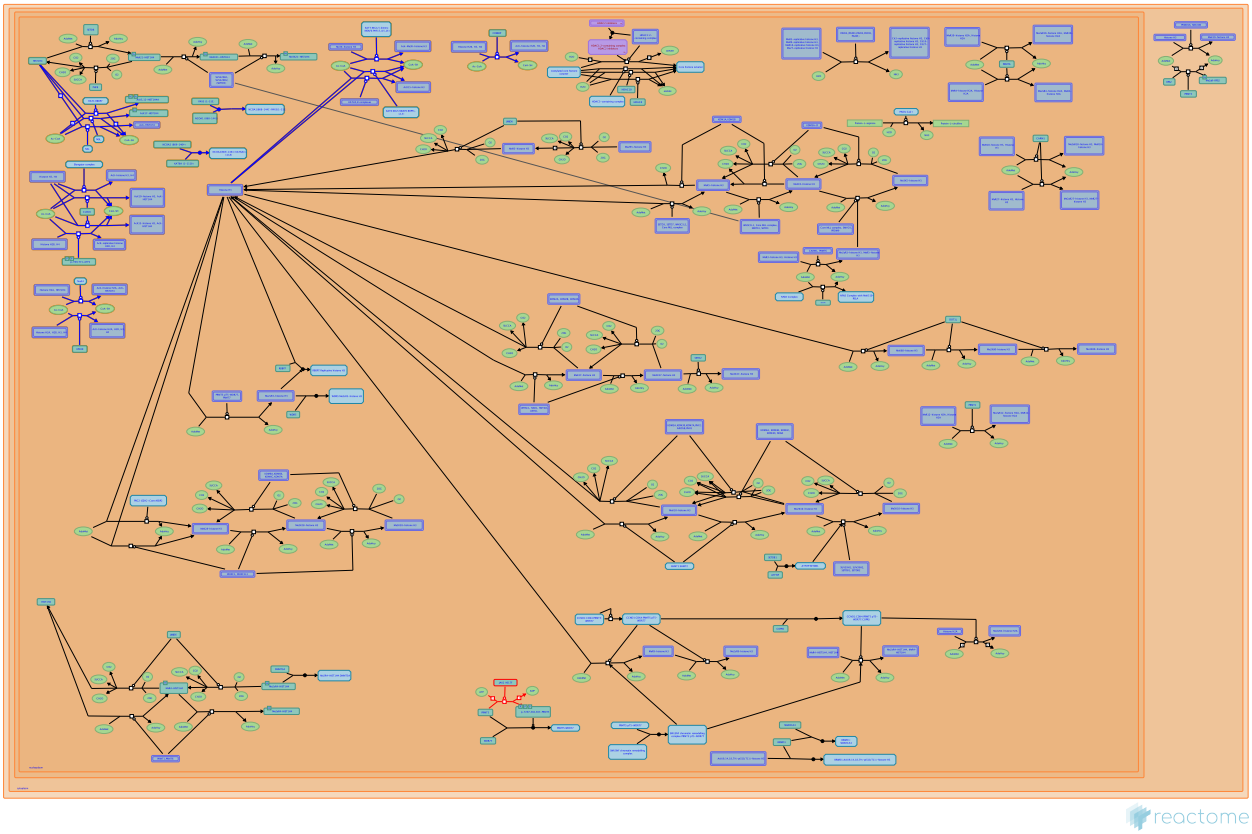
# HATs acetylate histones



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07/09/2021

# 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. ↗

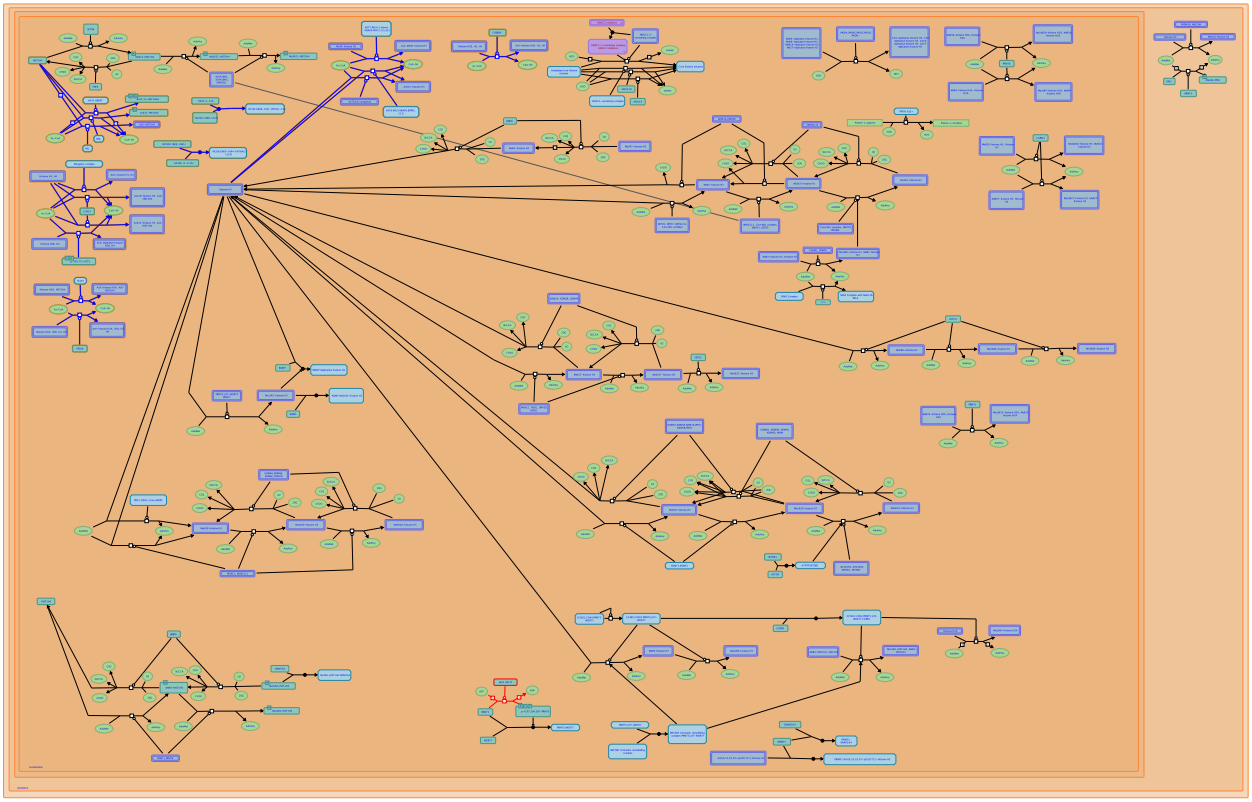
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

## HATs acetylate histones ↗

**Stable identifier:** R-HSA-3214847



Histone acetyltransferases (HATs) involved in histone modifications are referred to as A-type or nuclear HATs. They can be grouped into at least four families based on sequence conservation within the HAT domain: Gcn5/PCAF, MYST, p300/CBP and Rtt109. The p300/CBP and Rtt109 families are specific to metazoans and fungi respectively (Marmorstein & Trievel 2009). Gcn5/PCAF and MYST family members have no significant sequence homology but share a globular alpha/beta fold with a common structure involved in acetyl-Coenzyme A (ACA) binding. Both use a conserved glutamate residue for the acetyl transfer reaction but may not share a common catalytic mechanism (Trievel et al. 1999, Tanner et al. 1999, Yan et al. 2002, Berndsen et al. 2007). The p300/CBP HAT domain has no homology with the other families but some structural conservation within theACA-binding core (Liu et al. 2008). In addition to histone acetylation, members of all 3 human HAT families have been shown to acetylate non-histones (Glozak et al. 2005).

HATs and histone deacetylase (HDAC) enzymes generally act not alone but as part of multiprotein complexes. There are numerous examples in which subunits of HAT or HDAC complexes influence their substrate specificity and lysine preference, which in turn, affect the broader functions of these enzymes (Shahbazian & Grunstein 2007).

N.B. The coordinates of post-translational modifications represented and described here follow UniProt standard practice whereby coordinates refer to the translated protein before any further processing. Histone literature typically refers to coordinates of the protein after the initiating methionine has been removed. Therefore the coordinates of post-translated residues in the Reactome database and described here are frequently +1 when compared with the literature.

## Literature references

Marmorstein, R., Trievel, RC. (2009). Histone modifying enzymes: structures, mechanisms, and specificities. *Biochim. Biophys. Acta, 1789*, 58-68. ↗

## Editions

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|---|---|---|
| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-01 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

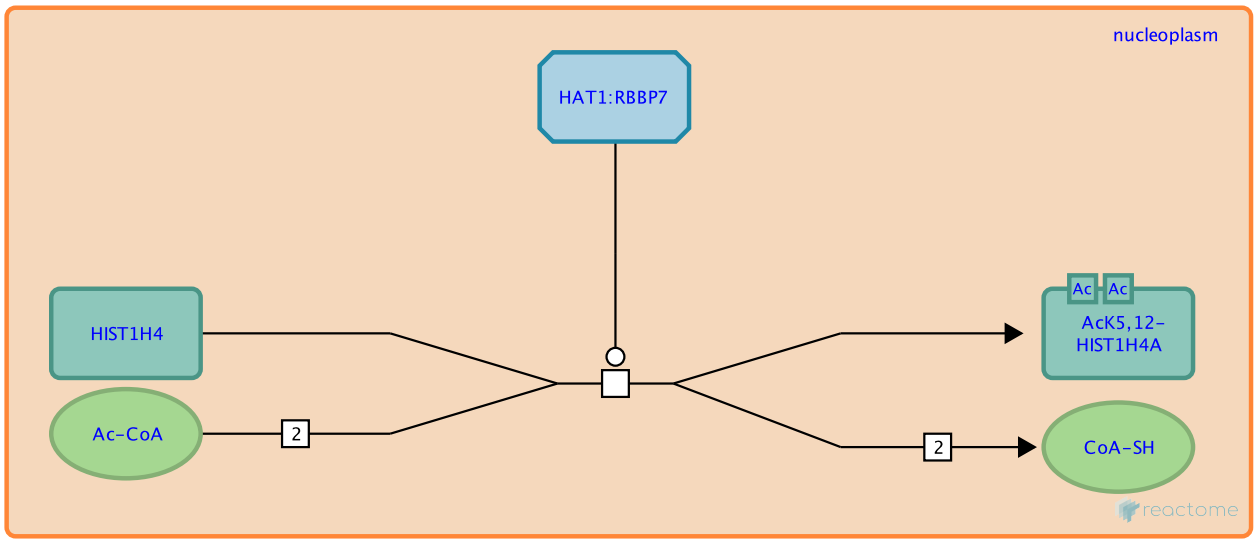
## Type B histone acetlytransferase complex acetylates histone H4 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3662318

**Type:** transition

**Compartments:** nucleoplasm




In humans, newly synthesized histone H4 is acetylated by the cytoplasmic Type B histone acetyltransferase (HAT) complex, which is composed of RBBP7 and HAT1. This interacts with histones H4 and H2A, acetylating soluble but not nucleosomal histone H4 at lysine-6 (H4K5) and lysine-13 (H4K12) and to a lesser extent lysine-6 of histone H2A (H2AK5) (Verreault et al. 1996). The HAT1:RBBP7 complex is part of the sNASP complex, a chaperone for H3-H4 (Campos et al. 2010). HAT1 also has a role in homologous recombination repair, probably as part of a larger complex, facilitating the enrichment of H4K5/K12-acetylated H3.3 to double-strand breaks thereby marking the damaged area for subsequent recruitment of key repair factors (Yang et al. 2013).

N.B. Coordinates of post-translational modifications described here follow UniProt standard practice whereby coordinates refer to the translated protein before any further processing. Histone literature typically refers to coordinates of the protein after the initiating methionine has been removed. Therefore the coordinates of post-translated residues in the Reactome database and described here are frequently +1 when compared with the literature.

### Literature references

Verreault, A., Kaufman, PD., Kobayashi, R., Stillman, B. (1998). Nucleosomal DNA regulates the core-histone-binding subunit of the human Hat1 acetyltransferase. *Curr. Biol., 8*, 96-108. ↗

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## KAT2 complexes acetylate histone H3 ↗

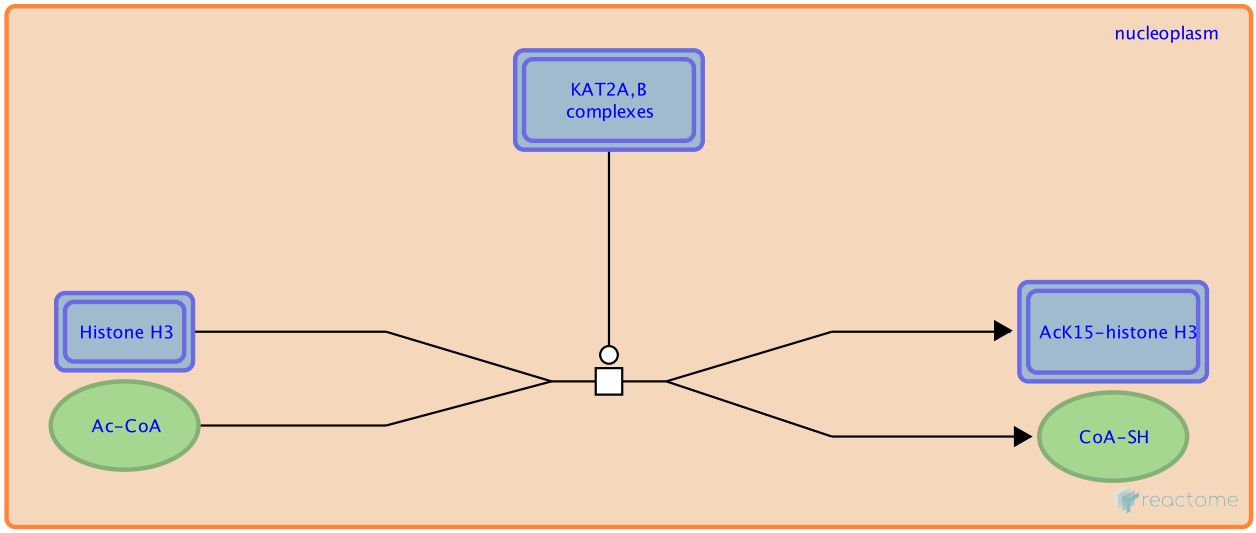
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3301237

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** KAT2A acetylates replicative histone H3 (Homo sapiens)




KAT2A (GCN5) and KAT2B (PCAF) are histone acetyltransferases (HATs) that act as part of large multimember complexes to facilitate transcription by acetylating histones H3 and H4. In eukaryotes the SPT-ADA-GCN5 acetyltransferase (SAGA) complex has 19 subunits including TRRAP, ENY2, USP22 and subunits belonging to the ADA, SPT, TAF, and SGF group of proteins (Nagy et al. 2009). The ADA2A-containing (ATAC) complex shares with SAGA a core composed of KAT2A-TADA3 (ADA3)-CCDC101 (STAF36, SGF29) and either TADA2A (ADA2a) in ATAC, or TADA2B (ADA2b) in SAGA. ATAC complexes contain a second putative HAT, called CSRP2BP (ATAC2), and five other subunits; YEATS2, ZZZ3, MBIP, WDR5, and DR1 (NC2-Beta) (Guelman et al. 2009). CSRP2BP has weak HAT activity in vitro but it's main function is to maintain the structural integrity of ATAC (Guelman et al. 2009). At present, the biological function of the ATAC complex is not well understood. In vitro GCN5 acetylates mainly histone H3K14 (lysine-15 in the UniProt peptide which retains the initiating methionine), but when incorporated into the SAGA complex GCN5 becomes more efficient as an H3K14 acetylase and can also acetylate H3K9 and H3K18 (Brand et al. 1999, Grant et al. 1999), H3K23, and H3K27 (Kuo et al. 1996, Kuo & Andrews 2013). Drosophila ATAC mainly acetylates histone H4 (Ciurciu et al. 2006, Suganuma et al. 2008), suggested to be due to the presence of CSRP2BP in the complex (Suganuma et al. 2008) but different human ATAC preparations have exhibited a range of specificities with no clear difference between SAGA and ATAC (Guelman et al. 2009, Wang et al. 2008, Nagy et al. 2010). SAGA and ATAC complexes from mouse and human contain either GCN5 or PCAF in a mutually exclusive manner (Nagy et al. 2010, Krebs et al. 2010, Spedale et al. 2012).

The SAGA complex consists of KAT2A (hGCN5), TADA1 (STAF42), TADA2B (ADA2b), TADA3 (STAF54, ADA3), SUPT3H (SPT3), SUPT7L (STAF65G), TAF5L (PAF65B), TAF6L (PAF65A), TAF9 (TAFII31), TAF12 (TAFII20), TAF10 (TAFII31), TRRAP, SAP130 (Martinez et al. 2001), CCDC101, ATXN7, a factor termed STAF55 that cannot be identified, two further factors described as probable members that cannot be identified STAF46 and STAF60 (Nagy & Tora 2007) plus ATXN7L3, USP22, ENY2 (Zhao et al. 2008) and SUPT20H (Nagy et al. 2009).

N.B. Coordinates of post-translational modifications described here follow UniProt standard practice

whereby coordinates refer to the translated protein before any further processing. Histone literature typically refers to coordinates of the protein after the initiating methionine has been removed. Therefore the coordinates of post-translated residues in the Reactome database and described here are frequently +1 when compared with the literature.

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

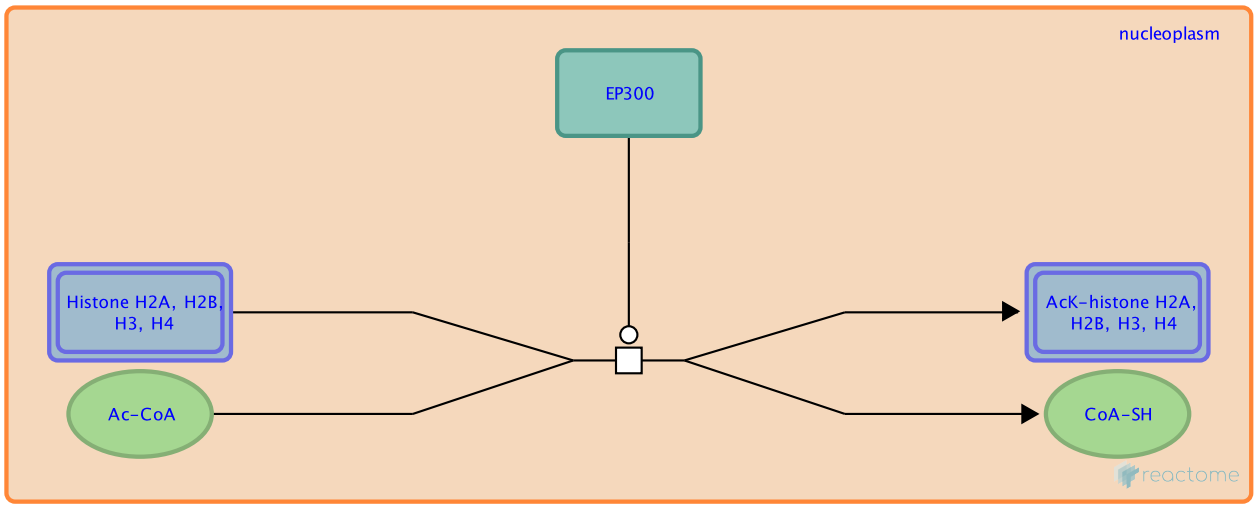
## EP300 acetylates histone H2A, H2B, H3, H4 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3662335

**Type:** transition

**Compartments:** nucleoplasm




EP300 and the related CREBBP are transcriptional regulators that interact with many other proteins. They have overlapping functions but also unique properties, particularly in vivo (Kalkhoven 2004). CREBBP and EP300 proteins are able to form a physical bridge between DNA-binding transcription factors and the RNA polymerase II complex. Histones are believed to be their main acetylation targets, but their ability to acetylate and thereby regulate transcription factors such as p53 (Gu & Roeder 1997) is also believed to be crucial (Kasper et al. 2006). EP300 can acetylate lysine-6 of histone H2A (H2AK5), lysines-12 (H2BK11), 15 (H2BK14) and to a lesser extent 5 and 20 of histone H2B, but preferentially acetylates lysines 14 and 18 of histone H3 and lysines 5 and 8 of histone H4 (Ogryzko et al. 1996, Schiltz et al. 1999). Heterozygous knockout of Ep300 is embryonic-lethal (Yao et al. 1998). Conditional knockouts have a phenotype that overlaps with that of conditional CREBBP knockouts (Kasper et al. 2006).

### Literature references

Schiltz, RL., Mizzen, CA., Vassilev, A., Cook, RG., Allis, CD., Nakatani, Y. (1999). Overlapping but distinct patterns of histone acetylation by the human coactivators p300 and PCAF within nucleosomal substrates. *J. Biol. Chem., 274*, 1189-92. ↗

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## CREBBP acetylates histone H2B, H3, H4 ↗

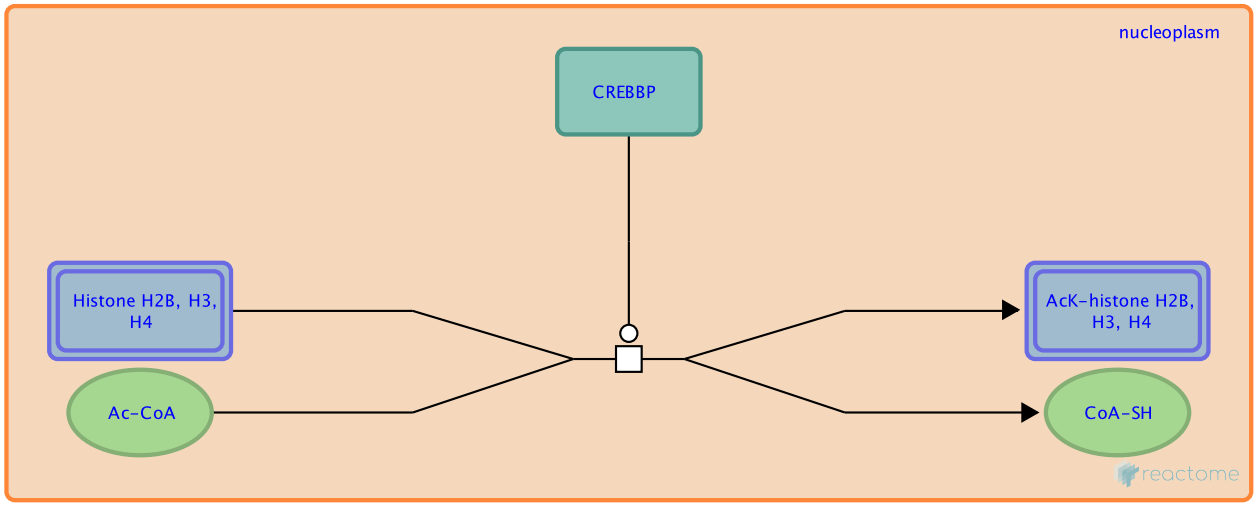
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3697008

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** Crebbp acetylates replicative histone H2B, H3, H4 (Mus musculus)




CREBBP (CBP) is named after its interaction with the CRE-binding protein CREB, though it interacts with many other proteins. It is thought to act as an integrator of signals from various pathways (Goodman & Smolik 2000), which compete for a limited amount of nuclear CREBBP. CREBBP and EP300 (p300) are closely related and have overlapping functions but also unique properties, particularly in vivo (Kalkhoven 2004). Both proteins form a physical bridge between DNA-binding transcription factors and the RNA polymerase II complex. Histones are believed to be the main acetylation targets of CREBBP and EP300, but their ability to acetylate and thereby regulate transcription factors such as p53 (Gu & Roeder 1997) is considered significant additional function (Kasper et al. 2006).

CREBBP has intrinsic histone acetyltransferase (HAT) activity on lysine-13 of H2B, lysine-15 of H3 and lysine-9 of H4 (Bannister & Kouzarides 1996, Rekowski & Giannis 2010, Barrett et al. 2011).

Homozygous knockout of CREBBP results in embryonic lethality (Tanaka et al. 1997). Focal deletion of CREBBP demonstrates that it is critical for the in vivo acetylation of lysines on histones H2B, H3 and H4, and cannot be compensated for by the p300 (Barrett et al. 2011).

Genomic aberrations in CREBBP are associated with Rubinstein-Taybi syndrome (Torress et al. 2013).

N.B. Coordinates of post-translational modifications described here follow UniProt standard practice whereby coordinates refer to the translated protein before any further processing. Histone literature typically refers to coordinates of the protein after the initiating methionine has been removed. Therefore the coordinates of post-translated residues in the Reactome database and described here are frequently +1 when compared with the literature.

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## Elongator complex acetylates replicative histone H3, H4 ↗

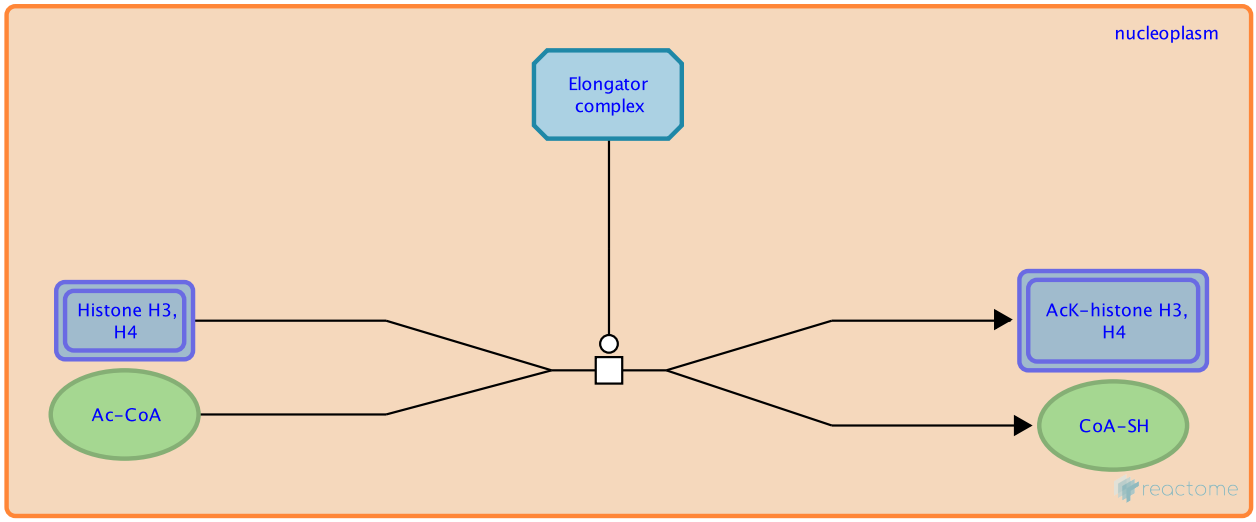
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3301345

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** Elongator complex acetylates H3, H4 (Homo sapiens)




Elongator Protein 3 (ELP3, KAT9) is the catalytic subunit of the highly conserved Elongator complex (Winkler et al. 2001, Hawkes et al. 2002, Li et al. 2005). This unstable six-subunit complex consists of two discrete three-subunit subcomplexes (Winkler et al. 2001). The core Elongator complex (Otero et al. 1999) contains IKBKAP, ELP2 and ELP3. ELP3 has motifs characteristic of the GCN5-related GNAT family of histone acetyltransferases (HATs), but the core Elongator complex has no intrinsic HAT activity, requiring the presence of a complex of Elp4, Elp5, and Elp6 proteins (Winkler et al. 2001).

The Elongator complex is directed specifically toward the N-terminal tails of histones H3 and H4, favouring acetylation at lysine-14 (K14) of histone H3 and lysine-8 (K8) of histone H4 (Winkler et al. 2002).

Yeast Elp3 nulls exhibit slow activation of certain genes and defects in histone H3 acetylation patterns essential for gene activation (Kristjuhan et al. 2002, Winkler et al. 2002, Kristjuhan & Svejstrup 2004). Elp3 is essential for the association of Elongator with nascent RNA in vivo (Petrakis et al. 2004; Svejstrup 2007).

Misregulation of ELP3 is implicated in human disorders that affect neuronal function, including familial dysautonomia (FD), an autosomal recessive neurodevelopmental disease characterized by degeneration of the sensory and autonomic nervous system (Slaugenhaupt & Gusella 2002, Simpson et al. 2009), and the motor neuron degenerative disorder amyotrophic lateral sclerosis (ALS) (Wallis et al. 2008). In mammalian cells Elp3 is essential for promoting transcription-activating histone H3 acetylation in the coding regions of certain neuronal cell motility genes (Close et al. 2006).

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

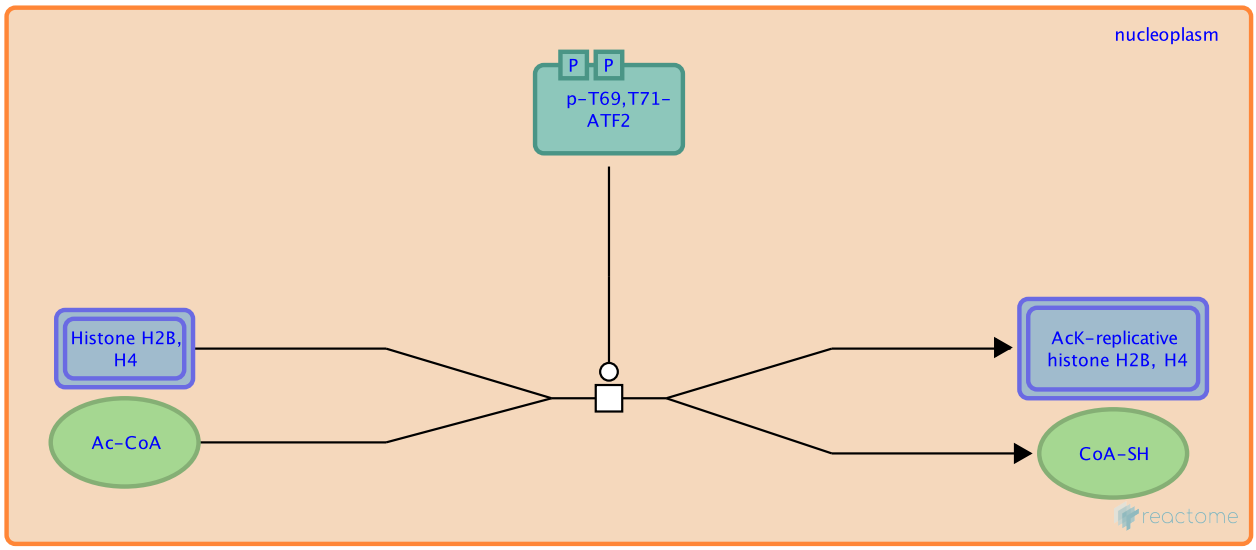
## ATF2 acetylates histone H2B, H4 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3318415

**Type:** transition

**Compartments:** nucleoplasm




ATF2 (activating transcription factor 2) is a basic leucine zipper (bZIP) protein and member of the activator protein-1 (AP-1) family (Wagner et al. 2001). The basic region of ATF2 binds DNA while the leucine zipper region allows dimerization with partners. ATF2 is a histone acetyltransferase (HAT), which specifically acetylates histones H2B and H4 in vitro. ATF2 is sequentially phosphorylated on threonine residues T69 and T71 by protein kinases ERK1/2 and p38 (van Dam et al. 1995, Livingstone et al. 1995, Ouwens et al. 2002, Baan et al. 2009). This phosphorylated form has increased HAT activity (Kawasaki et al. 2000).

## Literature references

Kawasaki, H., Schiltz, L., Chiu, R., Itakura, K., Taira, K., Nakatani, Y. et al. (2000). ATF-2 has intrinsic histone acetyltransferase activity which is modulated by phosphorylation. *Nature, 405*, 195-200. ↗

## Editions

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |
| 2013-11-20 | Edited | Shamovsky, V. |

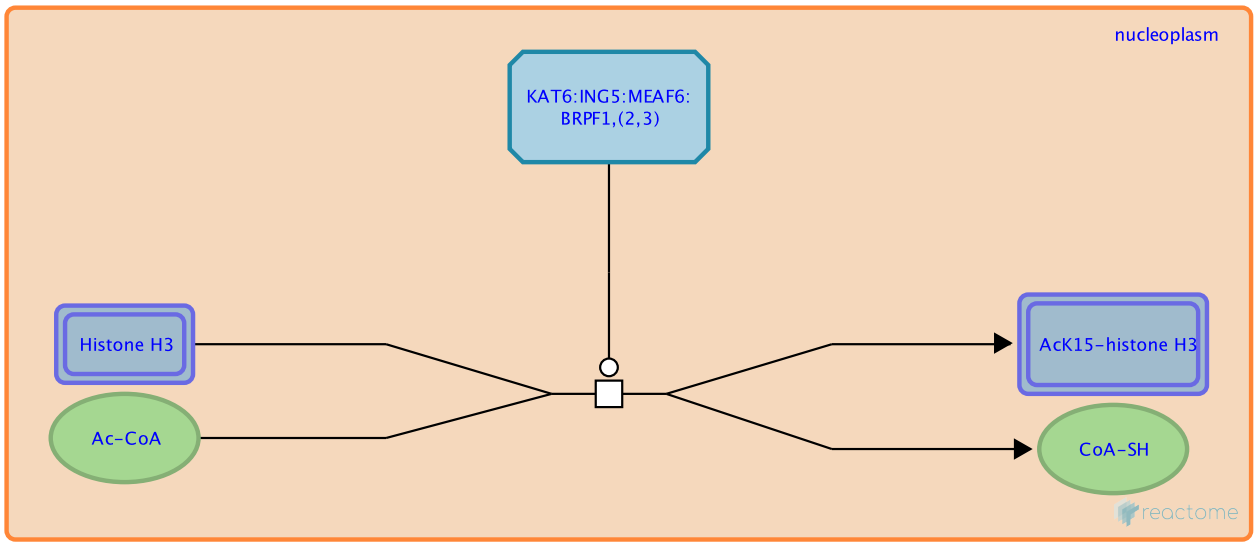
## KAT6A, KAT6B-containing ING5 complexes acetylate replicative histone H3 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3318486

**Type:** transition

**Compartments:** nucleoplasm




KAT6A (Monocytic leukemia zinc finger protein, MOZ) and KAT6B (Monocytic leukemia zinc finger protein-related factor, MORF) are member of the MYST family of histone acetyltransferases, named after the founding members MOZ, Ybf2/Sas3, Sas2 and TIP60 (Borrow et al. 1996, Reifsnyder et al. 1996). The presence of a MYST domain is the only common structural motif in this family. MOZ and MORF are highly homologous (overall amino-acid sequence identity, 60%; similarity, 66%) but distinct from other family members (Yang & Ullah 2007).

KAT6A and KAT6B have intrinsic histone acetyltransferase activity (Champagne et al. 1999, 2001). Both can form tetrameric 'ING5' complexes with BRPF1 (possibly BRPF2 and 3), EAF6 and ING5. BRPF1 and EAF6 drastically stimulate the acetyltransferase activities of KAT6A/B against nucleosomal histone H3 (Doyon et al. 2006, Ullah et al. 2008). ING5-MOZ/MORF complexes acetylate only histone H3 at lysine-14.

KAT6A homozygous mice die at birth, with reduced hematopoiesis and profound defects in the stem cell compartment. These mice have no long-term repopulating stem cells and display substantial reduction in the number of multipotent cells able to form spleen colonies (Thomas et al. 2006). Chromosomal rearrangements of the KAT6A gene are associated with acute myeloid leukemia (AML), uterine leiomyomata and therapy-related myelodysplastic syndromes (Yang & Ullah, 2007).

Mutations in KAT6B are the cause of the Say-Barber-Biesecker variant of Ohdo syndrome and Genitopatellar syndrome (Campeau et al. 2012, Szakszon et al. 2013).

## Literature references

Doyon, Y., Cayrou, C., Ullah, M., Landry, AJ., Côté, V., Selleck, W. et al. (2006). ING tumor suppressor proteins are critical regulators of chromatin acetylation required for genome expression and perpetuation. *Mol. Cell, 21*, 51-64 . ↗

## Editions

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

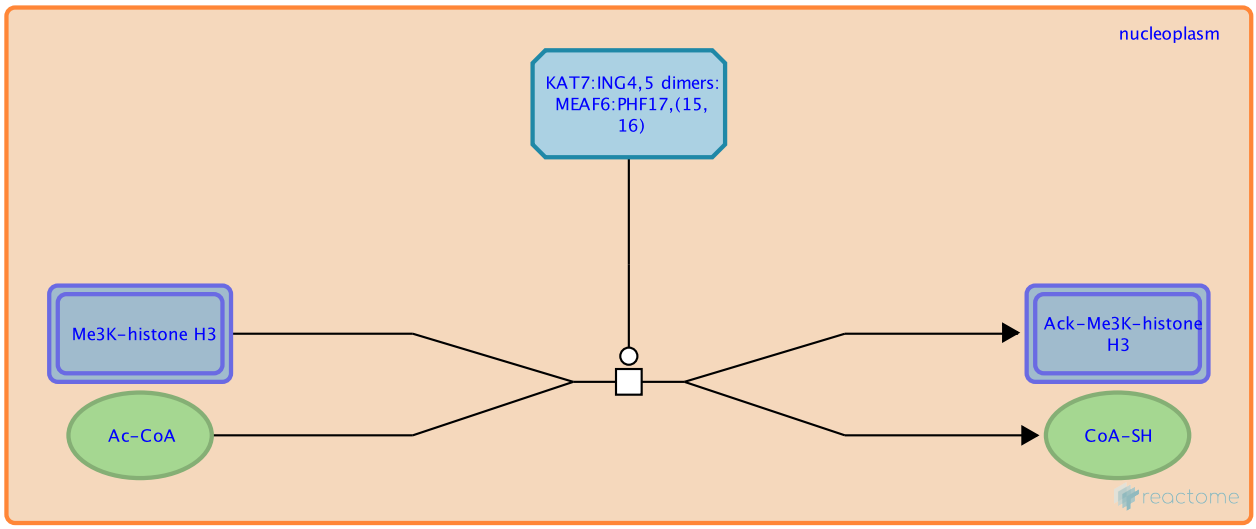
## KAT7-containing ING4/5 complexes acetylate Me3K-histone H3 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3318413

**Type:** transition

**Compartments:** nucleoplasm




The Inhibitor of Growth (ING) family are growth regulators, present in all eukaryotes, with five human proteins ING1 to ING5. ING genes are mutated or downregulated in many forms of cancer. They have roles in chromatin modification and remodeling, gene-specific transcription regulation, and DNA repair, recombination, and replication (Saksouk et al. 2008, Awakumovv et al. 2012).

Human INGs can be divided into three groups: ING1/2, ING3, and ING4/5, based on their association with three distinct types of protein complexes (Doyon et al. 2006). All regulate chromatin via histone acetylation and deacetylation. The catalytic histone acetyltransferase (HAT) subunits of ING complexes are members of the MYST family, KAT5 (Tip60), KAT7 (HBO1) KAT6A (MOZ), KAT6B (MORF), and KAT8 (MOF). ING4 exists in vivo as a dimer, binding two lysine-4 trimethylated histone H3 (H3K4me3) modifications (Palacios et al. 2010). Homology modeling suggests that other INGs are likely to be dimers (Culurgioni et al. 2012).

KAT7-ING4/5 complexes interact with lysine-4 trimethylated histone H3 (H3K4me3), acetylating surrounding histone tails to stimulate local transcription (Palacios et al. 2008, Champagne et al. 2008, Hung et al. 2009, Saksouk et al. 2009).

### Literature references


Hung, T., Binda, O., Champagne, KS., Kuo, AJ., Johnson, K., Chang, HY. et al. (2009). ING4 mediates crosstalk between histone H3 K4 trimethylation and H3 acetylation to attenuate cellular transformation. *Mol. Cell, 33*, 248-56. ↗

Palacios, A., Muñoz, IG., Pantoja-Uceda, D., Marcaida, MJ., Torres, D., Martín-García, JM. et al. (2008). Molecular basis of histone H3K4me3 recognition by ING4. *J. Biol. Chem., 283*, 15956-64. ↗

Champagne, KS., Saksouk, N., Peña, PV., Johnson, K., Ullah, M., Yang, XJ. et al. (2008). The crystal structure of the ING5 PHD finger in complex with an H3K4me3 histone peptide. *Proteins, 72*, 1371-6. ↗

## Editions

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|---|---|---|
| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

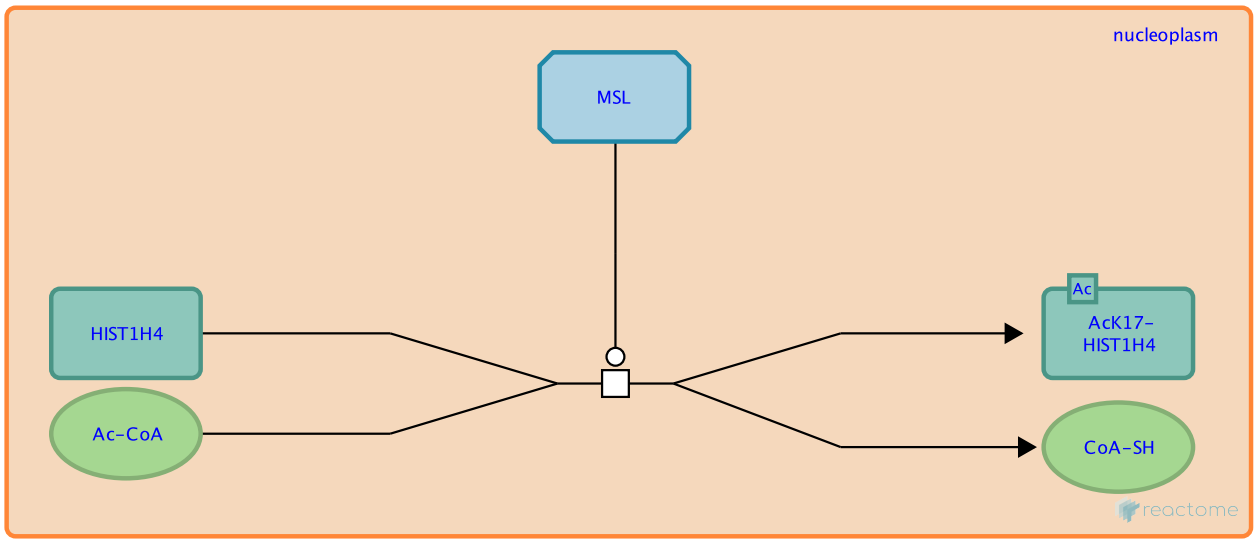
## MSL acetylates histone H4 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3321883

**Type:** transition

**Compartments:** nucleoplasm




The MSL complex has histone acetyltransferase (HAT) activity with a high specificity for histone H4 lysine-17 (H4K16) (Smith et al. 2000, 2005, Conrad et al. 2012). The subunit responsible for this activity is KAT8 (Males Absent on the First, MOF) a member of the MYST (named for yeast and human members MOZ, YBF2, SAS2, and Tip60) HAT family. In Drosophilla, the MSL complex associates at hundreds of sites along the X chromosome in somatic cells, resulting in the hyperacetylation of H4K16 (Lavender et al. 1994, Smith et al. 2000). In humans MSL is responsible for the majority of H4 acetylation at lysine-17 in the cell. KAT8 is a component of other complexes (Smith et al. 2005, Mendjan et al. 2006, Cai et al. 2010).

## Literature references

Neal, KC., Pannuti, A., Smith, ER., Lucchesi, JC. (2000). A new human member of the MYST family of histone acetyl transferases with high sequence similarity to Drosophila MOF. *Biochim. Biophys. Acta, 1490*, 170-4. ↗

## Editions

| | | |
|---|---|---|
| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

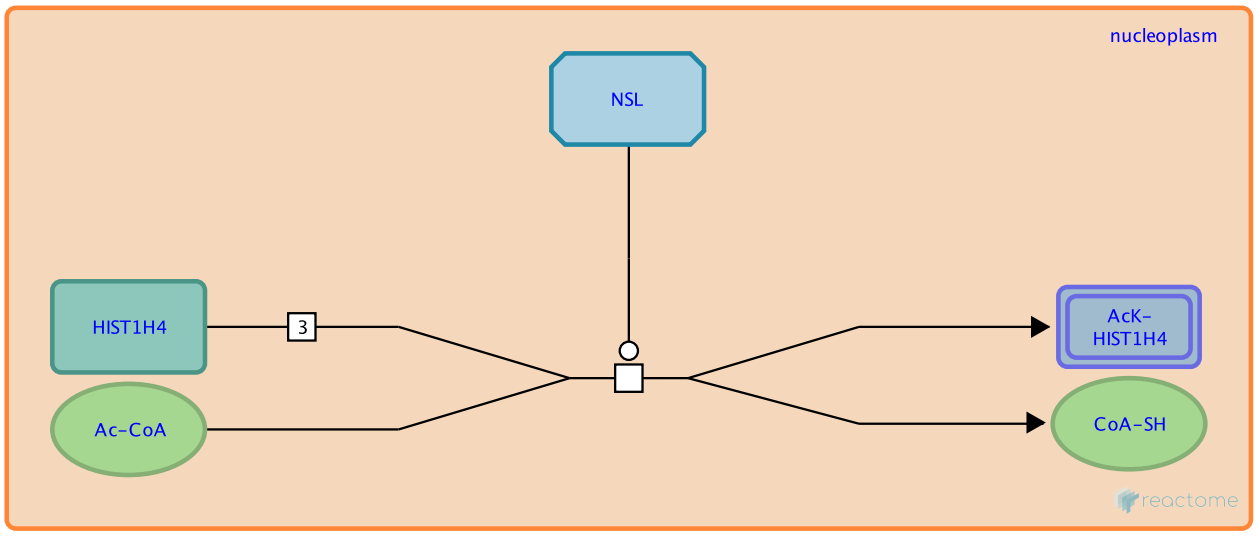
## NSL acetylates histone H4 ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3321805

**Type:** transition

**Compartments:** nucleoplasm




KAT8 (MOF, MYST1) is a member of the MYST (Moz-Ybf2/Sas3-Sas2-Tip60) family of histone acetyltransferases (HATs). KAT8 is the catalytic component of the nine-subunit non-specific lethal (NSL) complex (Mendjan et al. 2006, Cai et al. 2010).

NSL acetylates histone H4 on lysines 17 (H4K16), 6 (H4K5) and 9 (H4K8) (Cai et al. 2010).

KAT8 is also the catalytic subunit of the male-specific lethal (MSL) complex, which acetylates almost exclusively H4K16 and is responsible for a large fraction of H4K16 acetylation in human cells (Smith et al. 2005).

N.B. Coordinates of post-translational modifications described here follow UniProt standard practice whereby coordinates refer to the translated protein before any further processing. Histone literature typically refers to coordinates of the protein after the initiating methionine has been removed. Therefore the coordinates of post-translated residues in the Reactome database and described here are frequently +1 when compared with the literature.

### Literature references

Cai, Y., Jin, J., Swanson, SK., Cole, MD., Choi, SH., Florens, LA. et al. (2010). Subunit composition and substrate specificity of a MOF-containing histone acetyltransferase distinct from the male-specific lethal (MSL) complex. *J. Biol. Chem., 285*, 4268-72. ↗

### Editions

| | | |
|---|---|---|
| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## NuA4 complex acetylates histone H2A, HIST1H4 ↗

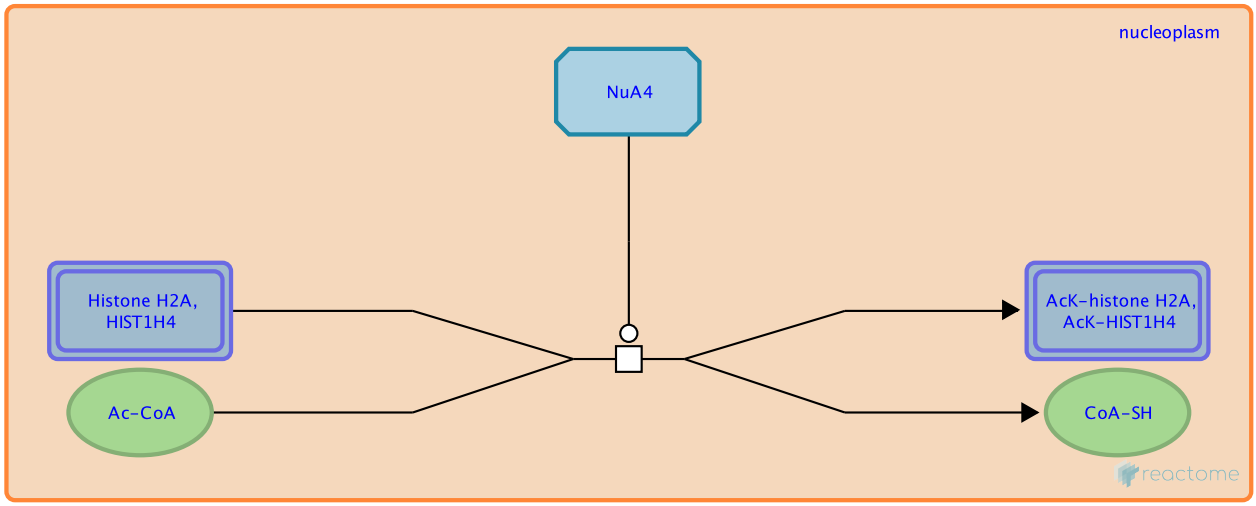
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3321975

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** NuA4 complex actetylates H2A and H4 (Gallus gallus)




The NuA4 complex contains the histone acetyltransferase (HAT) KAT5 (TIP60), a member of the MYST family. The first characterisation of a mammalian NuA4 complex identified the additonal components TRRAP, the Enhancer of Polycomb protein (EPC1), actin-like protein ACTL6A (BAF53a), which is a homolog of yeast Arp4, actin (ACTB), the SNF2-related helicase p400 (EP400) and the AAA ATPases RUVBL1 (TIP49a) and RUVBL2 (TIP49b) (Ikura et al. 2000). Subsequently further copmponents were identified as MRGBP, MORF4L1 (MRG15), MORF4L2 (MRGX), (Cai et al. 2003), BRD8, DMAP1, ING3, MEAF6, YEATS4 (Doyon et al. 2004) and VPS72 (YL1) (Cai et al. 2005).

### Editions

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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## CLOCK acetylates lysine-10 of histone H3, H4 ↗

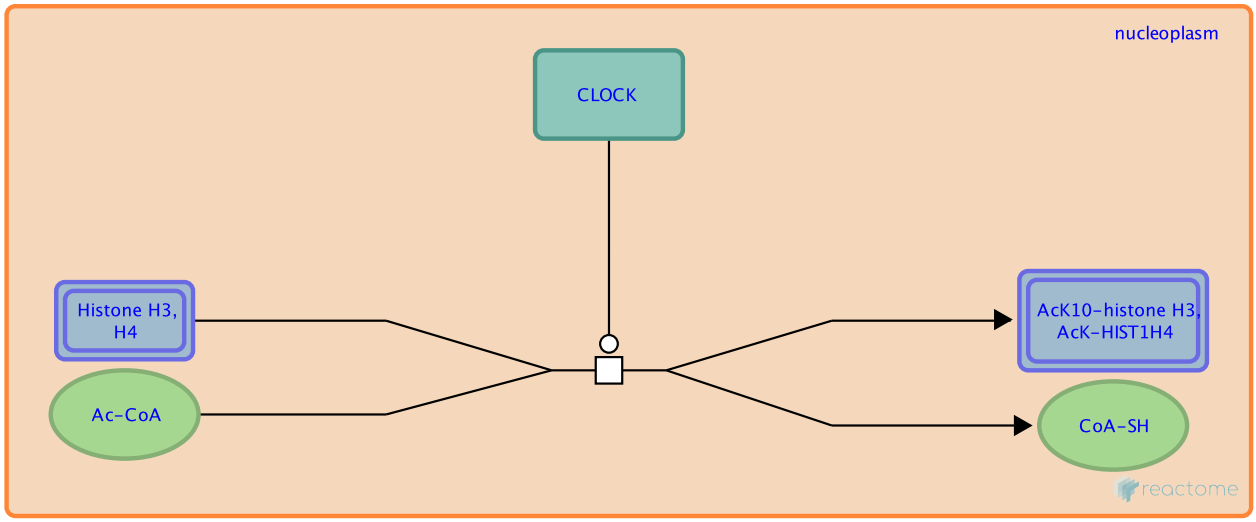
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-3697920

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** Clock acetylates histones H3, H4 (Homo sapiens)




CLOCK is a central element of the core clock mechanism that governs circadian rhythms. It has intrinsic histone acetyltransferase (HAT) activity which regulates the transcription of many clock-controlled genes (Doi et al. 2006, Hirayama et al. 2007). The carboxy-terminal region of CLOCK displays significant sequence homology with the carboxy-terminal domain of NCOA3 (ACTR), which also has intrinsic HAT activity (Chen et al. 1997). CLOCK acetylates histones H3 and H4 with greatest activity at H3K14, lesser activity at H3K9, but does not acetylate H2A and H2B (Doi et al. 2006 and Nakahata et al. 2007).

### Editions

| | | |
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| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

## CLOCK acetylates lysine-15 of histone H3, H4 ↗

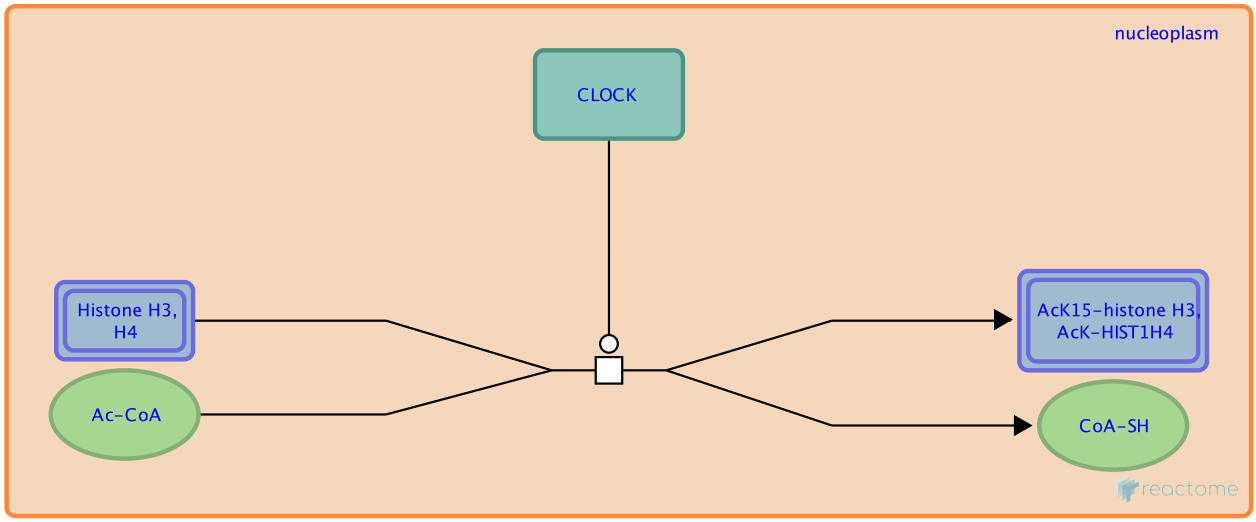
**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-5144542

**Type:** transition

**Compartments:** nucleoplasm

**Inferred from:** Clock acetylates histones H3, H4 (Homo sapiens)




CLOCK is a central element of the core clock mechanism that governs circadian rhythms. It has intrinsic histone acetyltransferase (HAT) activity which regulates the transcription of many clock-controlled genes (Doi et al. 2006, Hirayama et al. 2007). The carboxy-terminal region of CLOCK displays significant sequence homology with the carboxy-terminal domain of NCOA3 (ACTR), which also has intrinsic HAT activity (Chen et al. 1997). CLOCK acetylates histones H3 and H4 with greatest activity at H3K14, lesser activity at H3K9, but does not acetylate H2A and H2B (Doi et al. 2006 and Nakahata et al. 2007).

### Editions

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|---|---|---|
| 2013-03-12 | Authored | Jupe, S. |
| 2013-11-18 | Edited | Jupe, S. |
| 2013-11-18 | Reviewed | Karagiannis, T. |

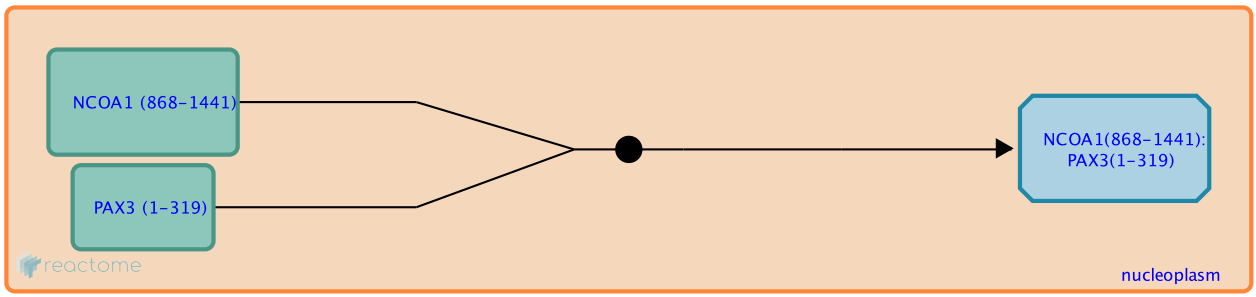
## NCOA1(868-1441) binds PAX3(1-319) ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-5579018

**Type:** binding

**Compartments:** nucleoplasm




A chromosomal aberration involving the nuclear receptor coactivator NCOA1 and paired box protein Pax-3 (PAX3) is a cause of rhabdomyosarcoma (RMS). Translocation t(2;2)(q35;p23) with PAX3 generates the NCOA1-PAX3 oncogene consisting of the N-terminus part of PAX3 and the C-terminus part of NCOA1. The fusion protein acts as a transcriptional activator. RMS is the most common soft tissue carcinoma in childhood, representing 5-8% of all malignancies in children (Wachtel et al. 2004).

### Literature references

Wachtel, M., Dettling, M., Koscielniak, E., Stegmaier, S., Treuner, J., Simon-Klingenstein, K. et al. (2004). Gene expression signatures identify rhabdomyosarcoma subtypes and detect a novel t(2;2)(q35;p23) translocation fusing PAX3 to NCOA1. *Cancer Res., 64,* 5539-45. ↗

### Editions

| | | |
|---|---|---|
| 2014-06-06 | Authored, Edited | Jassal, B. |
| 2015-02-11 | Reviewed | D'Eustachio, P. |

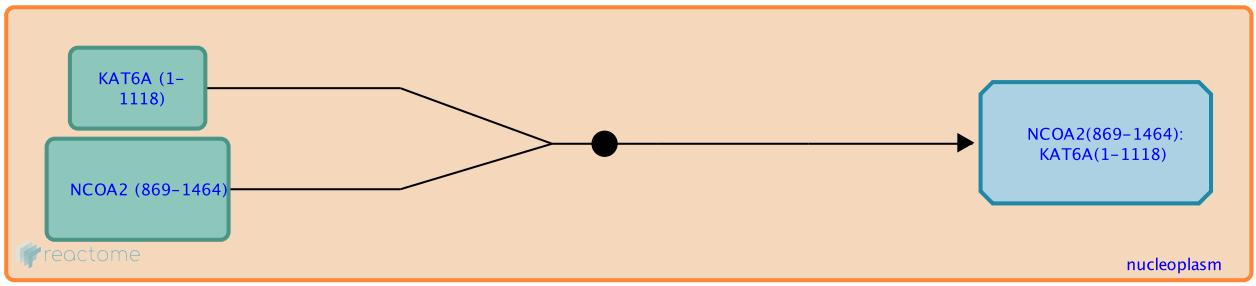
## NCOA2(869-1464) binds KAT6A(1-1118) ↗

**Location:** HATs acetylate histones

**Stable identifier:** R-HSA-5579023

**Type:** binding

**Compartments:** nucleoplasm




Chromosomal aberrations involving nuclear receptor coactivator 2 (NCOA2) and histone acetyltransferase KAT6A (KAT6A aka MOZ) may be a cause of acute myeloid leukemias. Inversion inv8(p11;q13) generates the KAT6A-NCOA2 oncogene, which consists of the N-terminal part of KAT6A and the C-terminal part of NCOA2. KAT6A-NCOA2 binds to CREBBP and disrupts its function in transcription activation (Carapeti et al. 1998).

### Literature references

Carapeti, M., Aguiar, RC., Goldman, JM., Cross, NC. (1998). A novel fusion between MOZ and the nuclear receptor coactivator TIF2 in acute myeloid leukemia. *Blood, 91*, 3127-33. ↗

### Editions

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|---|---|---|
| 2014-06-06 | Authored, Edited | Jassal, B. |
| 2015-02-11 | Reviewed | D'Eustachio, P. |

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