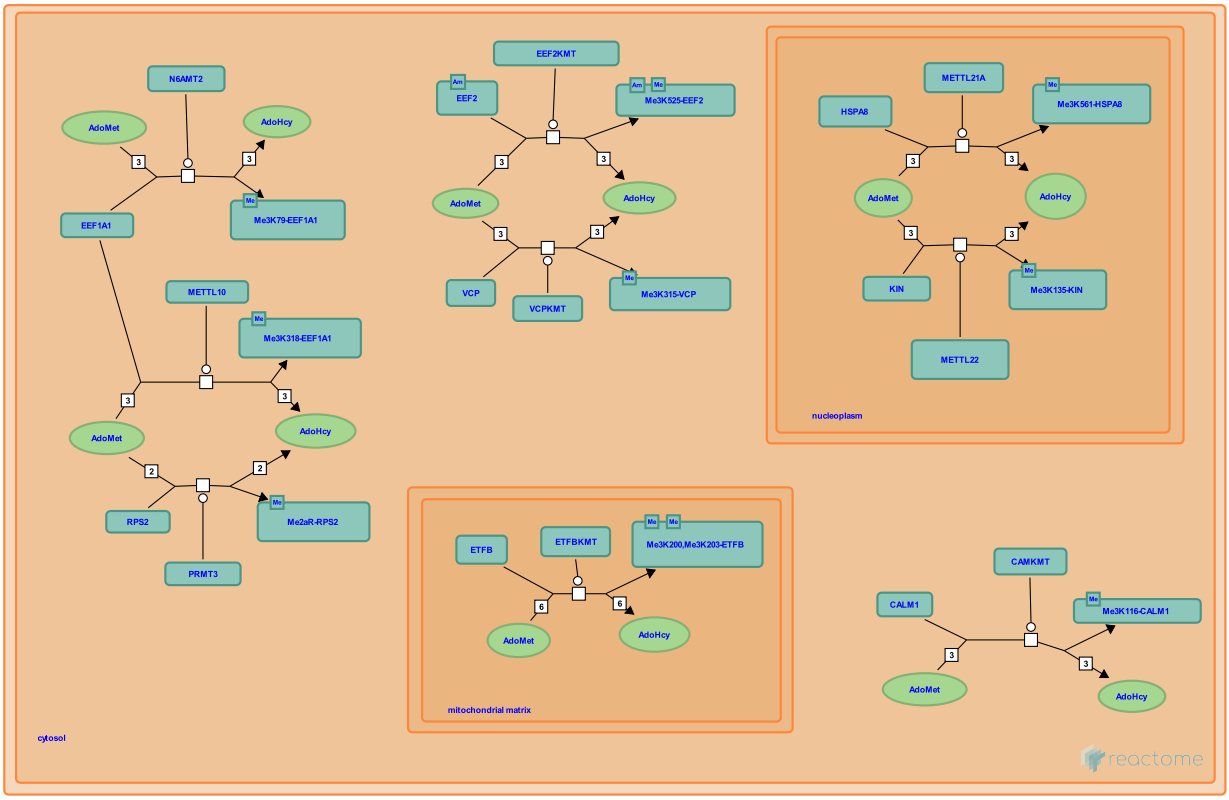
Protein methylation



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

26/04/2024

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. ↗

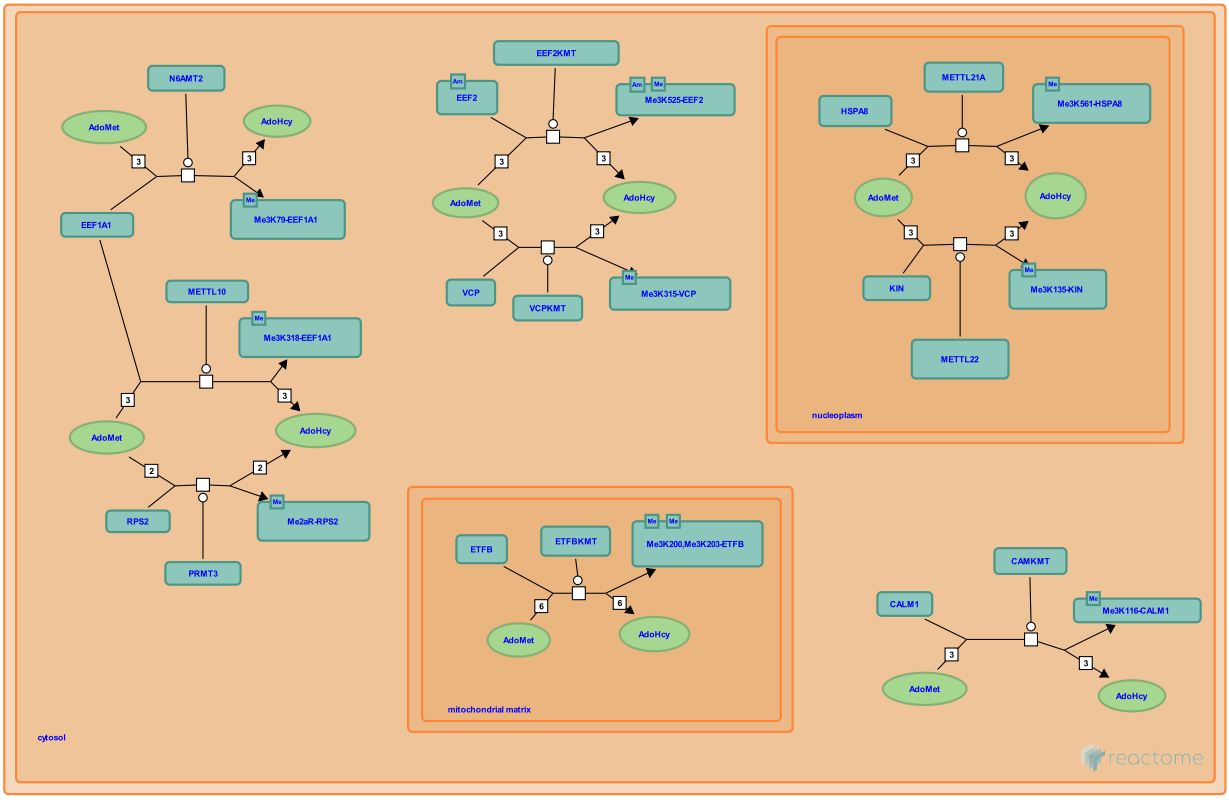
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 88

This document contains 1 pathway and 9 reactions (see Table of Contents)

Protein methylation ↗

Stable identifier: R-HSA-8876725



Methylation of lysine (Lys) and arginine (Arg) residues on non-histone proteins is a prevalent post-translational modification and important regulator of cellular signal transduction pathways including MAPK, WNT, BMP, Hippo and JAK–STAT. Crosstalk between methylation and other types of post-translational modifications and between histone and non-histone protein methylation is frequent, affecting cellular functions such as chromatin remodelling, gene transcription, protein synthesis, signal transduction and DNA repair (Biggar & Li 2015).

Literature references

Biggar, KK., Li, SS. (2015). Non-histone protein methylation as a regulator of cellular signalling and function. *Nat. Rev. Mol. Cell Biol., 16*, 5-17. ↗

Editions

2016-06-16	Authored	Jupe, S.
2016-10-10	Reviewed	Falnes, PØ.
2016-10-10	Edited	Jupe, S.

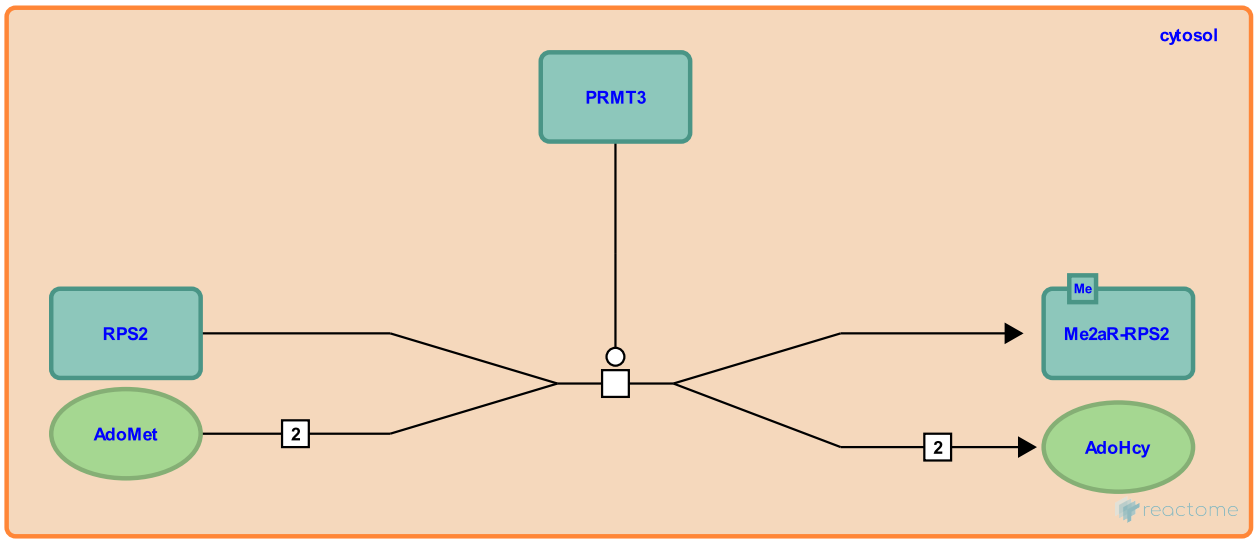
PRMT3 transfers 3xCH3 from 3xAdoMet to RPS2 ↗

Location: Protein methylation

Stable identifier: R-HSA-8879123

Type: transition

Compartments: cytosol



Protein arginine methyltransferase 3 (PRMT3) is a cytosolic enzyme that catalyzes the formation of omega-mono- or asymmetric dimethylarginine (Tang et al. 1998). It has a unique substrate binding N-terminal C2H2 Zn finger domain and a catalytic C-terminal domain that is homologous to other PRMTs (Zhang et al. 2000). PRMT3 associates with ribosomes in the cytosol, which contain its main in vivo substrate, the small ribosomal subunit Ribosomal protein S2 (RPS2). PRMT3 methylates arginines in the RG-rich N-terminal tail of RPS2 forming asymmetric dimethylarginines (Swiercz et al. 2005). Prmt3–null mice show developmental delay during embryogenesis and have embryos that are markedly smaller than wt , though size at birth is normal suggesting that PRMT3 loss can be compensated for in most cell types but may not be in under conditions that demand extremely fast protein synthesis (Swiercz et al. 2007).

Literature references

Herschman, HR., Clarke, S., Tang, J., Gary, JD. (1998). PRMT 3, a type I protein arginine N-methyltransferase that differs from PRMT1 in its oligomerization, subcellular localization, substrate specificity, and regulation. *J. Biol. Chem., 273*, 16935-45. ↗

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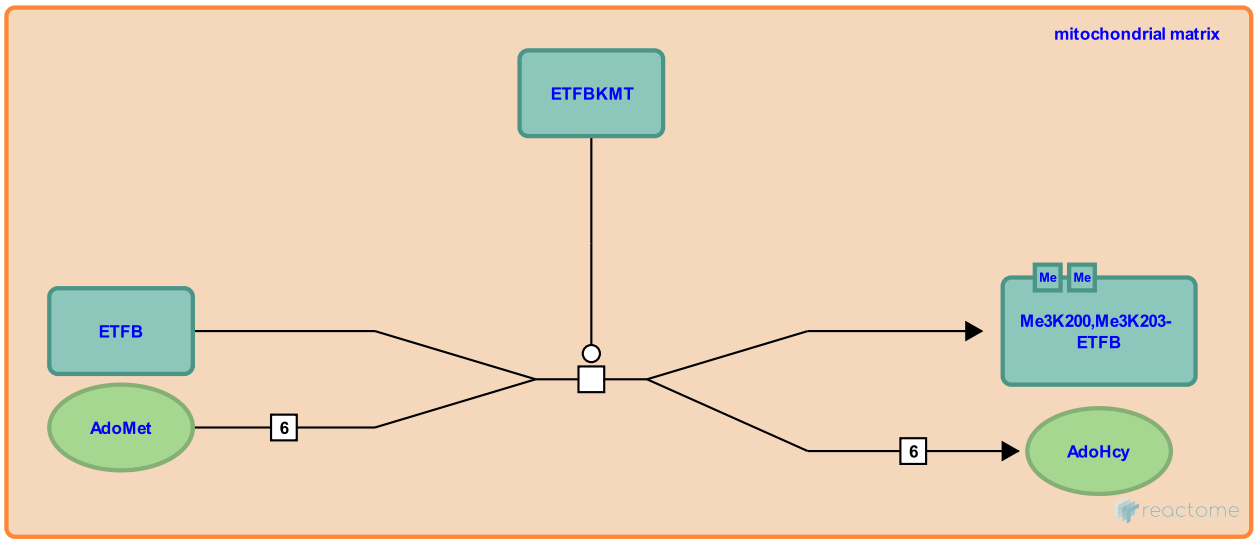
ETFBKMT transfers 3xCH3 from 3xAdoMet to ETFB ↗

Location: Protein methylation

Stable identifier: R-HSA-8931858

Type: transition

Compartments: mitochondrial matrix



Electron transfer flavoprotein beta subunit lysine methyltransferase (ETFBKMT, METTL20) specifically methylates Lys-200 and Lys-203 of Electron transfer flavoprotein beta (ETFB)) (Rhein et al 2014, Malecki et al. 2015). ETF shuttles electrons between several FAD-containing dehydrogenases present in the mitochondrial matrix and the membrane-bound ETF:quinone oxidoreductase (Ramsay et al. 1987). ETFB is proposed to contain 'recognition loop' at residues 191–200, responsible for interaction with the dehydrogenases (Toogood et al. 2004). Methylation of ETF impairs its ability to extract electrons from two acyl-CoA dehydrogenases, MCAD and GCDH, suggesting a functional role for ETFBKMT-mediated methylation of ETFB (Malecki et al. 2015).

Literature references

Falnes, PØ., Małecki, J., Moen, A., Dahl, HA., Ho, AY. (2015). Human METTL20 is a mitochondrial lysine methyltransferase that targets the β subunit of electron transfer flavoprotein (ETFβ) and modulates its activity. *J. Biol. Chem., 290*, 423-34. ↗

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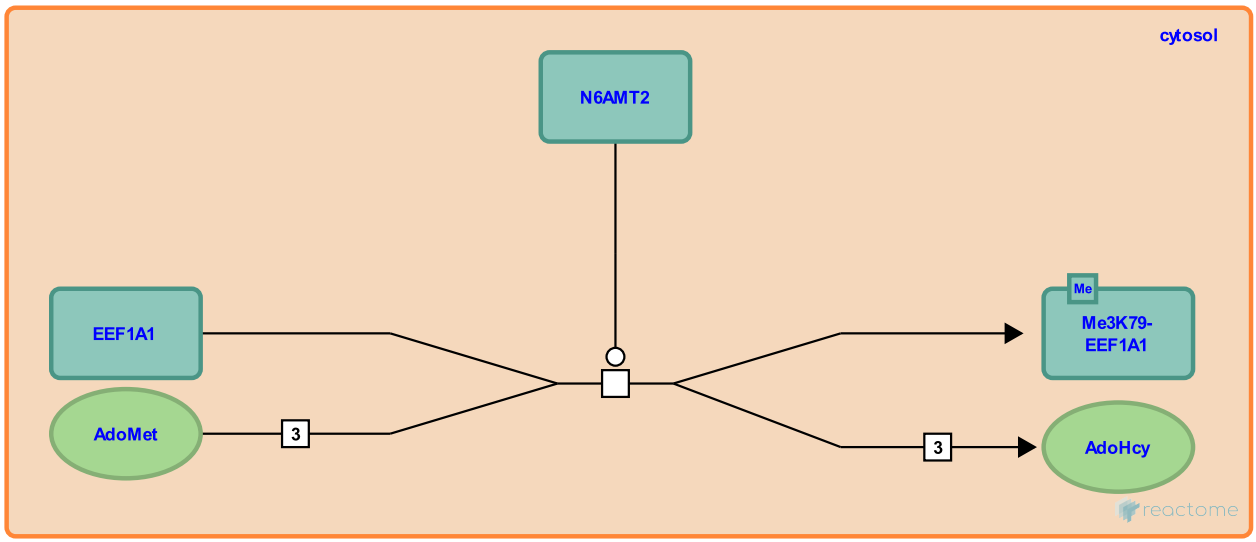
N6AMT2 transfers 3xCH3 from 3xAdoMet to EEF1A ↗

Location: Protein methylation

Stable identifier: R-HSA-8931974

Type: transition

Compartments: cytosol



Eukaryotic elongation factor 1A (EEF1A) is an essential, highly methylated protein that facilitates translational elongation by delivering aminoacyl-tRNAs to ribosomes. EEF1AKMT1 (N6AMT2) trimethylates EEF1A at Lys-79, a high-stoichiometry N-terminal site that is conserved from yeast to humans (Hamey et al. 2016).

Literature references

Wilkins, MR., Hart-Smith, G., Yagoub, D., Hamey, JJ., Winter, DL., Overall, CM. (2016). Novel N-terminal and Lysine Methyltransferases That Target Translation Elongation Factor 1A in Yeast and Human. *Mol. Cell Proteomics, 15*, 164-76. ↗

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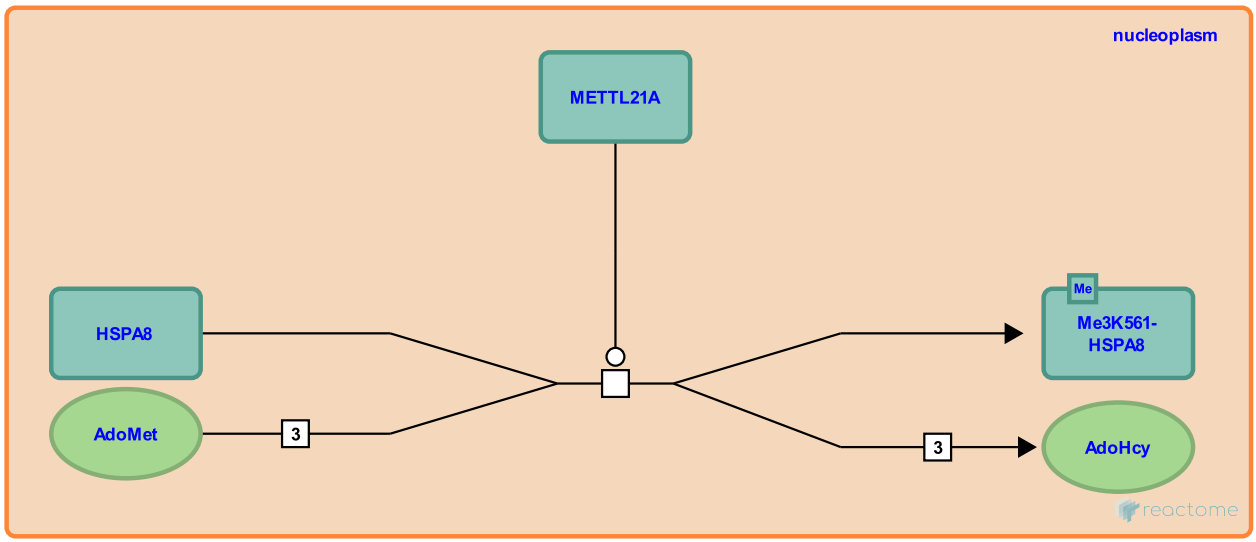
METTL21A transfers 3xCH3 from 3xAdoMet to HSPA8 ↗

Location: Protein methylation

Stable identifier: R-HSA-8932221

Type: transition

Compartments: nucleoplasm



Protein N-lysine methyltransferase METTL21A trimethylates lysine-561 of Heat shock cognate 71 kDa protein (HSPA8) and corresponding lysine residues in other Hsp70 isoforms (Jakobsson et al. 2013, Cloutier et al. 2013).

Literature references

Blanchette, M., Faubert, D., Cloutier, P., Coulombe, B., Lavallée-Adam, M. (2013). A newly uncovered group of distantly related lysine methyltransferases preferentially interact with molecular chaperones to regulate their activity. *PLoS Genet., 9*, e1003210. ↗

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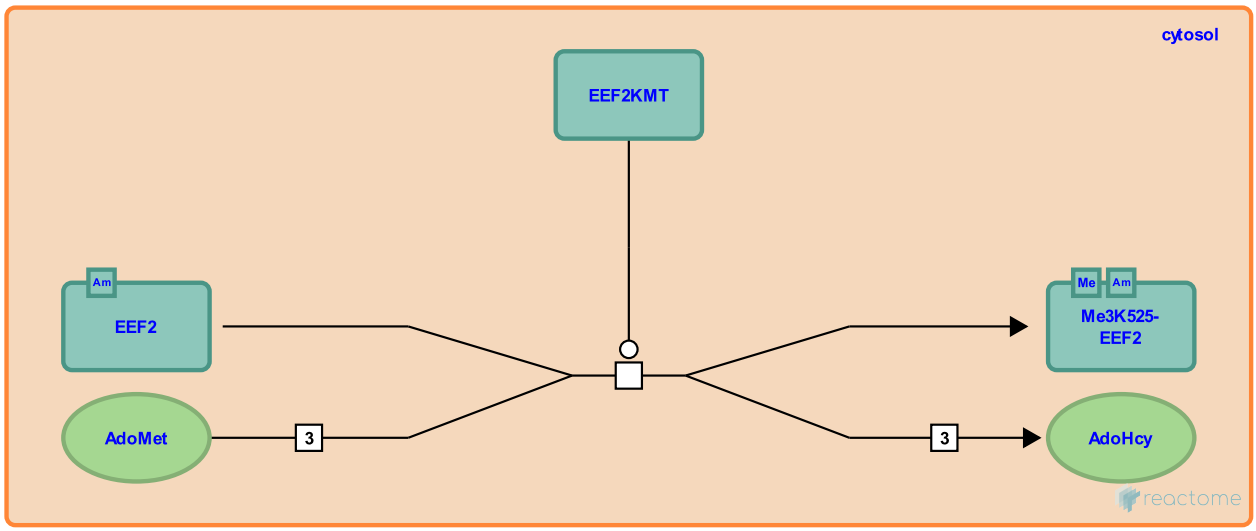
EEF2KMT transfers 3xCH3 from 3xAdoMet to EEF2 ↗

Location: Protein methylation

Stable identifier: R-HSA-8932243

Type: transition

Compartments: cytosol



Protein-lysine N-methyltransferase EEF2KMT (EEF2KMT) catalyzes the trimethylation of eukaryotic elongation factor 2 (EEF2) on Lys-525.

Literature references

Jakobsson, ME., Falnes, PØ., Davydova, E., Moen, A., Enserink, JM., Malecki, J. et al. (2014). Identification and characterization of a novel evolutionarily conserved lysine-specific methyltransferase targeting eukaryotic translation elongation factor 2 (eEF2). *J. Biol. Chem., 289*, 30499-510. ↗

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2016-10-10	Edited	Jupe, S.

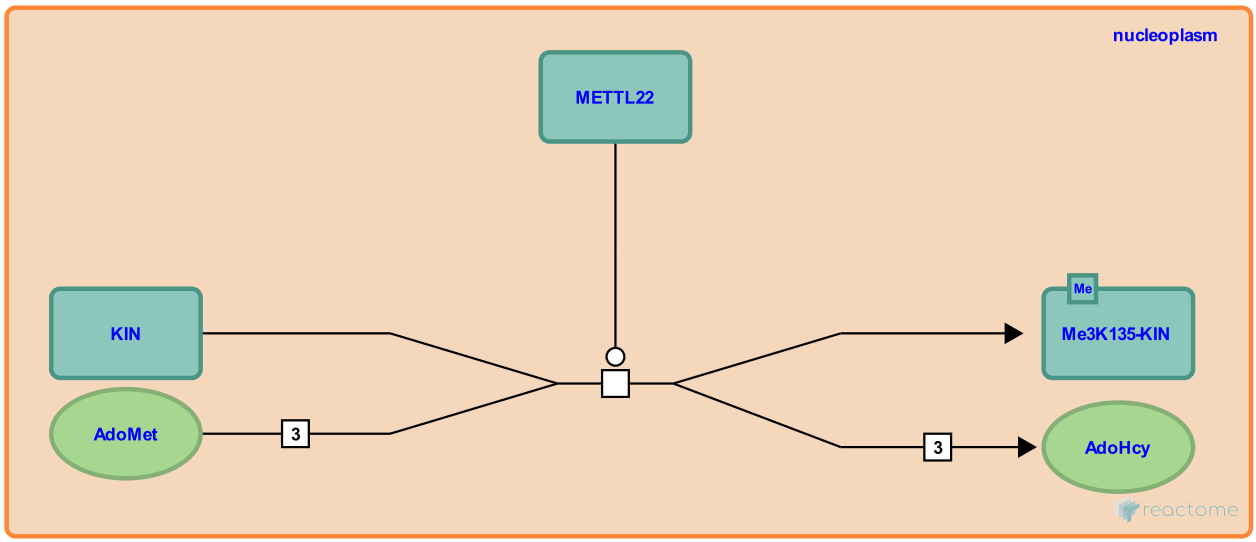
METTL22 transfers 3xCH3 from 3xAdoMet to KIN ↗

Location: Protein methylation

Stable identifier: R-HSA-8932275

Type: transition

Compartments: nucleoplasm



METTL22 trimethylates lysine-135 of DNA/RNA-binding protein KIN17 (KIN) (Cloutier et al. 2013)

Literature references

Blanchette, M., Faubert, D., Cloutier, P., Coulombe, B., Lavallée-Adam, M. (2013). A newly uncovered group of distantly related lysine methyltransferases preferentially interact with molecular chaperones to regulate their activity. *PLoS Genet., 9*, e1003210. ↗

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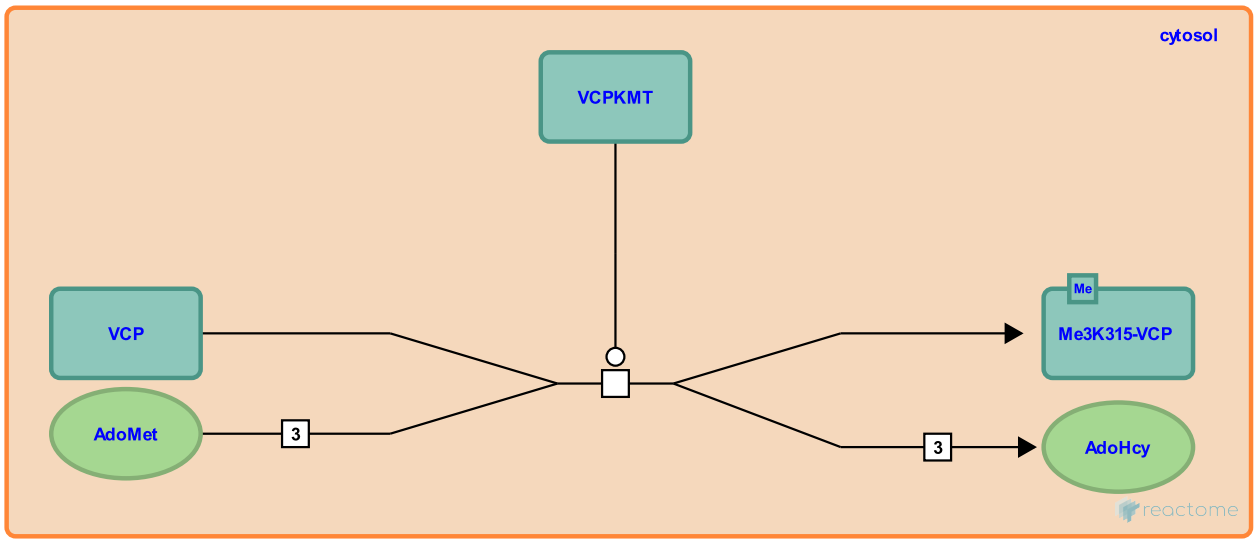
VCPKMT (METTL21D) transfers 3xCH3 from 3xAdoMet to VCP ↗

Location: Protein methylation

Stable identifier: R-HSA-8932276

Type: transition

Compartments: cytosol



Protein N-lysine methyltransferase METTL21D (VCPKMT) trimethylates lysine-315 of VCP (Kernstock et al. 2012, Cloutier et al. 2013).

Literature references

Wang, L., Chen, Z., Wang, HH., Wei, J., Huang, QH., Wu, XY. et al. (2005). Identification and characterization of a novel human histone H3 lysine 36-specific methyltransferase. *J. Biol. Chem., 280*, 35261-71. ↗

Editions

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2016-10-10	Reviewed	Falnes, PØ.
2016-10-10	Edited	Jupe, S.

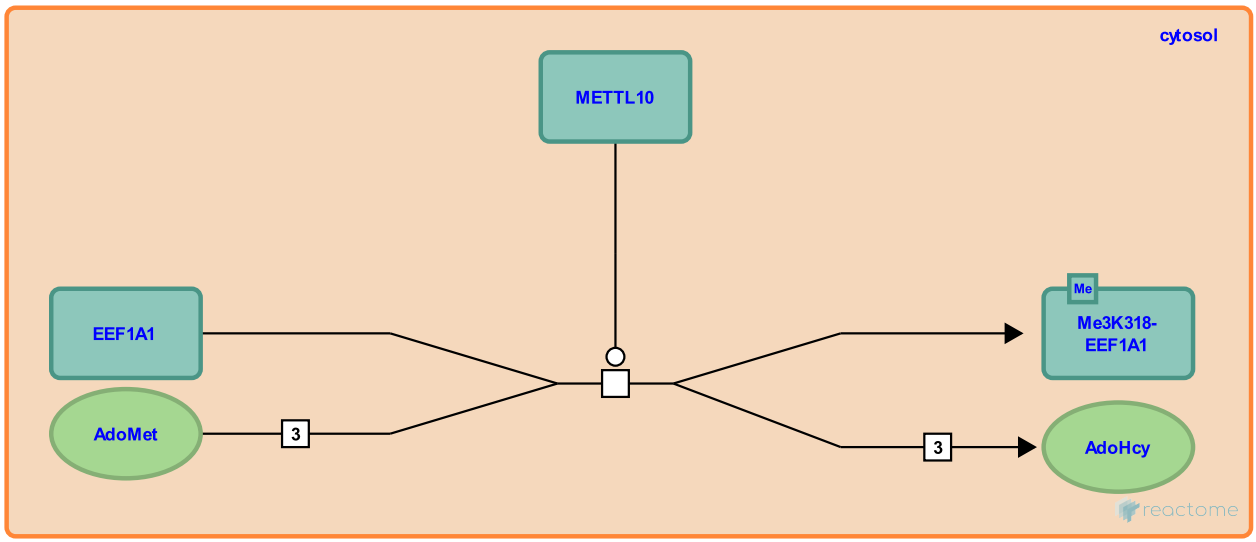
METTL10 transfers 3xCH3 from 3xAdoMet to EEF1A1 ↗

Location: Protein methylation

Stable identifier: R-HSA-8932413

Type: transition

Compartments: cytosol



Protein-lysine N-methyltransferase METTL10 trimethylates Elongation factor 1-alpha 1 (EF1A1) at lysine-318 (Shimazu et al. 2014).

Literature references

Shinkai, Y., Sodeoka, M., Sohtome, Y., Barjau, J., Shimazu, T. (2014). Selenium-based S-adenosylmethionine analog reveals the mammalian seven-beta-strand methyltransferase METTL10 to be an EF1A1 lysine methyltransferase. *PLoS ONE, 9*, e105394. ↗

Editions

2016-06-16	Authored	Jupe, S.
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2016-10-10	Edited	Jupe, S.

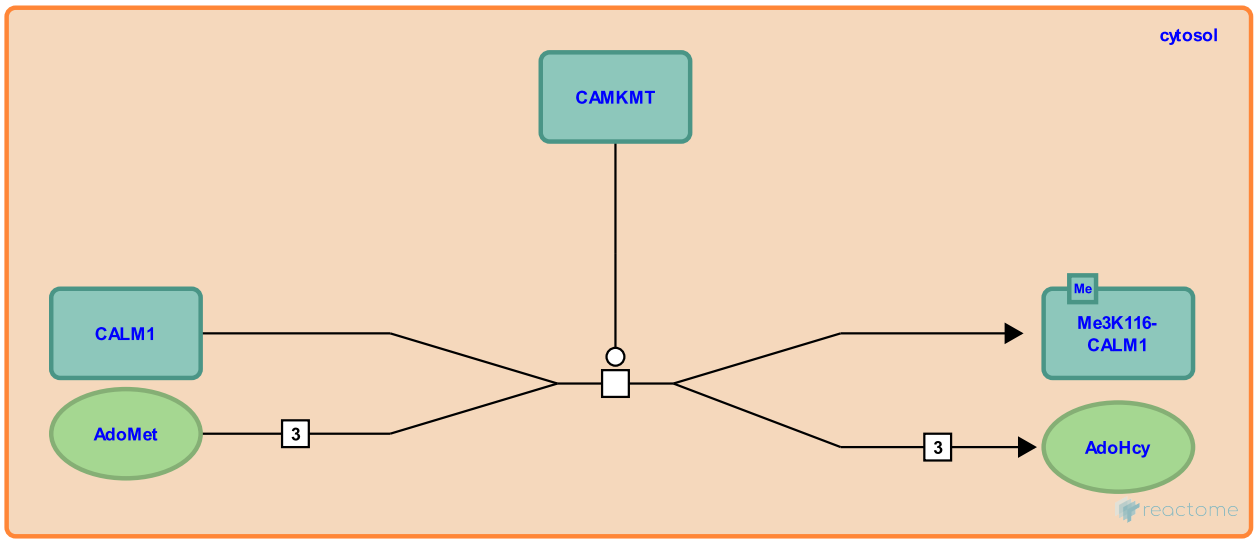
KAMKMT transfers 3xCH3 groups from 3xAdoMet to CALM1 ↗

Location: Protein methylation

Stable identifier: R-HSA-6786205

Type: transition

Compartments: cytosol



Calmodulin (CALM1) is a ubiquitous key mediator of Ca2+-dependent signalling and is subject to regulatory post-translational modifications which can affect protein-protein interactions. CALM1 is frequently trimethylated at Lys-116 which can influence changes in growth and development and its activator properties with target enzymes. The cytosolic enzyme calmodulin-lysine N-methyltransferase (CAMKMT) catalyses the transfer of 3 methyl groups from high energy donor S-adenosyl-L-methionine (AdoMet) to lysine residue 116 in CALM1, forming a trimethylated protein (triMe-K116-CALM1) (Magnani et al. 2010).

Literature references

Houtz, RL., Magnani, R., Trievel, RC., Dirk, LM. (2010). Calmodulin methyltransferase is an evolutionarily conserved enzyme that trimethylates Lys-115 in calmodulin. *Nat Commun, 1*, 43. ↗

Editions

2015-07-06	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

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