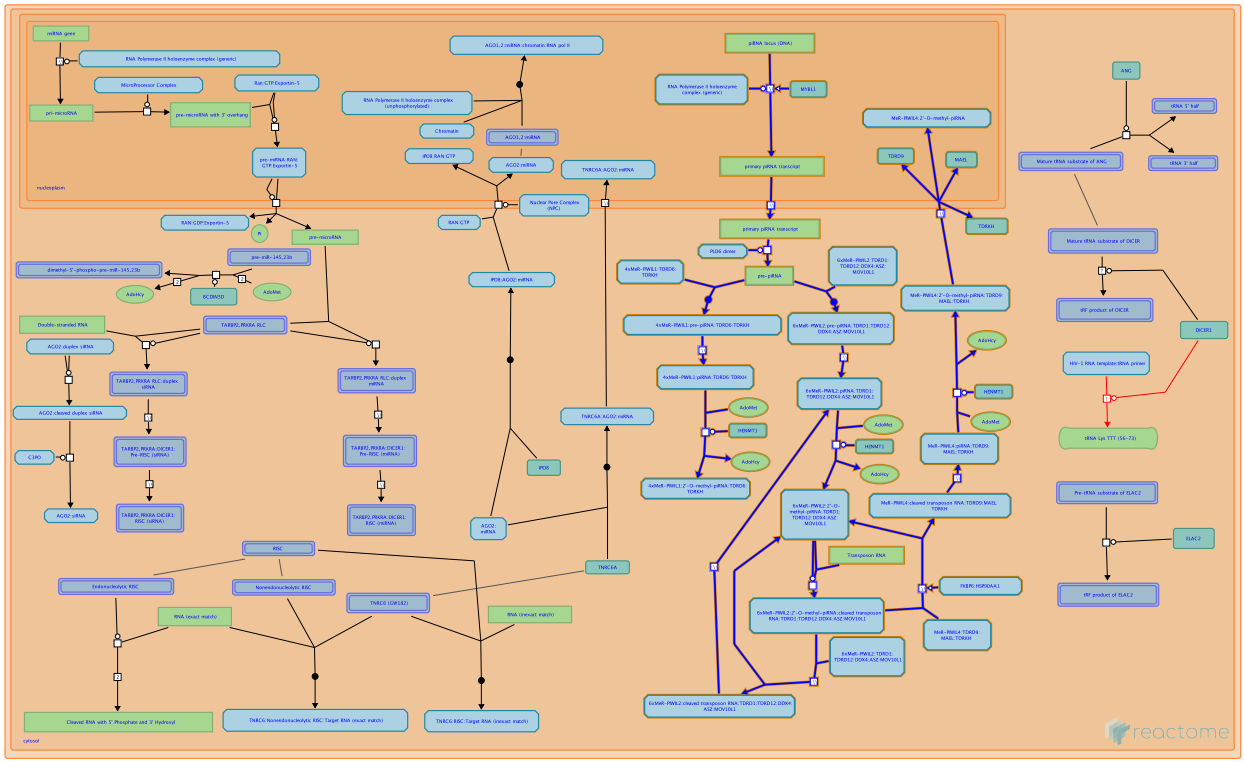
PIWI-interacting RNA (piRNA) biogenesis



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12/09/2021

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.

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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. ↗

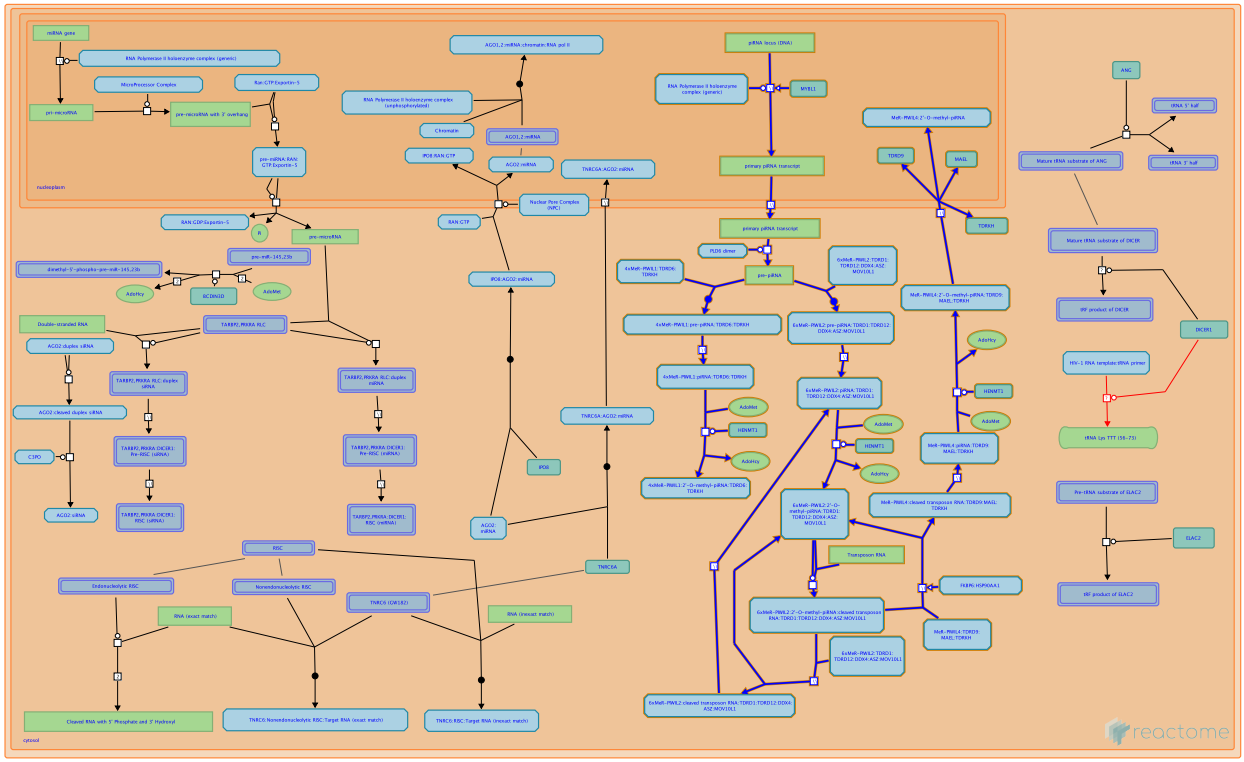
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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 database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

PIWI-interacting RNA (piRNA) biogenesis ↗

Stable identifier: R-HSA-5601884



In germ cells of humans and mice, precursors of PIWI-interacting RNAs (piRNAs) are transcribed from a few hundred sequence clusters, as well as individual transposons, intergenic regions, and genes in the genome. These longer transcripts are processed to yield piRNAs of 26-30 nucleotides independently of DICER, the enzyme responsible for microRNAs (miRNAs) and small interfering RNAs (siRNAs) (reviewed in Girard and Hannon 2008, Siomi et al. 2011, Ishizu et al. 2012, Pillai and Chuma 2012, Bortvin 2013, Chuma and Nakano 2013, Sato and Siomi 2013). The initial step in processing long transcripts to piRNAs is cleavage by PLD6 (MitoPLD), which generates the mature 5' end. The cleavage products of PLD6 are bound by either PIWIL1 (HIWI, MIWI) or PIWIL2 (HILI, MILI) in complexes with several other proteins. The 3' end is trimmed by an unknown exonuclease to generate the mature piRNA. PIWIL1:piRNA complexes appear to be involved in post-transcriptional silencing in the cytosol while PIWIL2:piRNA complexes generate further piRNAs from transposon transcripts and other transcripts in the cytosol. Cleavage products from PIWIL2:piRNA may be loaded into either PIWIL2 or PIWIL4 (HIWI2, MIWI2). Loading into PIWIL2 forms a step in a cytosolic amplification loop called the "ping-pong cycle" which yields further PIWIL2:piRNA complexes from cleaved precursor RNAs. Loading into PIWIL4 yields a complex also containing TDRD9 that translocates to the nucleus and directs DNA methylation of cognate loci, causing transcriptional silencing during spermatogenesis. Transcriptional silencing by piRNAs is necessary to limit transposition of endogenous transposons such as L1 elements in the genome.

Literature references

Bortvin, A. (2013). PIWI-interacting RNAs (piRNAs) - a mouse testis perspective. *Biochemistry Mosc., 78*, 592-602. ↗

Chuma, S., Nakano, T. (2013). piRNA and spermatogenesis in mice. *Philos. Trans. R. Soc. Lond., B, Biol. Sci., 368*, 20110338. ↗

Sato, K., Siomi, MC. (2013). Piwi-interacting RNAs: biological functions and biogenesis. *Essays Biochem., 54*, 39-52. ↗

Girard, A., Hannon, GJ. (2008). Conserved themes in small-RNA-mediated transposon control. *Trends Cell Biol., 18*, 136-48. ↗

Ishizu, H., Siomi, H., Siomi, MC. (2012). Biology of PIWI-interacting RNAs: new insights into biogenesis and function inside and outside of germlines. *Genes Dev., 26*, 2361-73. ↗

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

RNA polymerase II polymerizes primary piRNA transcript ↗

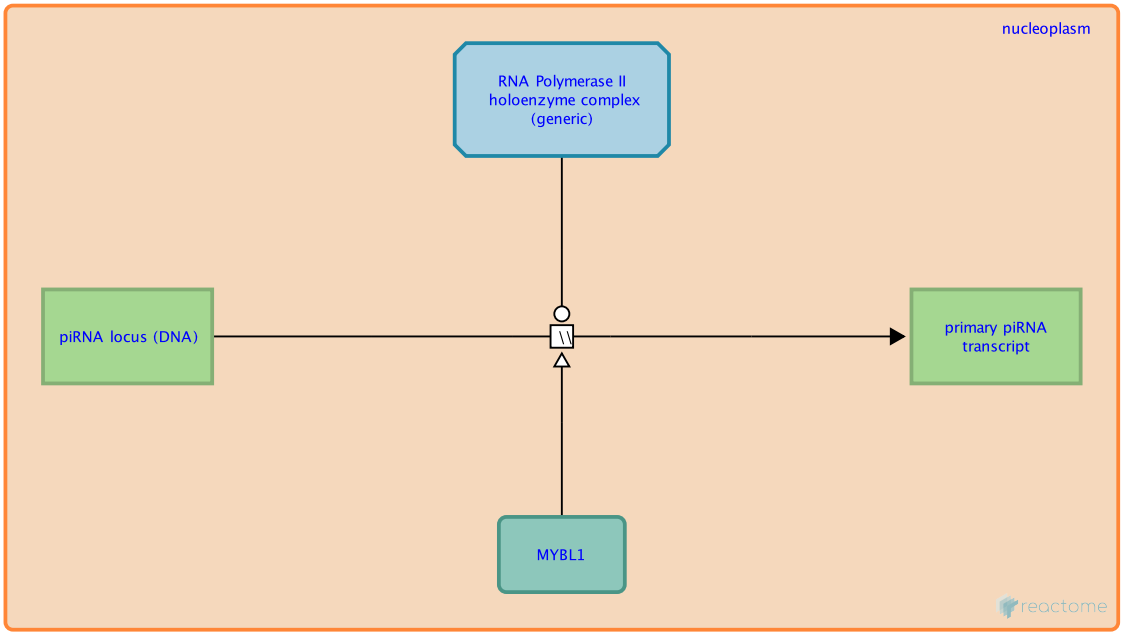
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601926

Type: omitted

Compartments: nucleoplasm

Inferred from: RNA polymerase II polymerizes primary piRNA transcript (Mus musculus)



As inferred from experiments with mouse homologs, primary piRNA transcripts originate from multiple copy transposable elements and unique copy non-coding RNAs and mRNAs. As male germ cells progress from fetus to adult, the composition of piRNAs shifts from transposons to unique copy sequences (reviewed in Bortvin 2013). Computational analyses have identified 161 to 242 piRNA clusters and many other smaller piRNA hotspots in the mouse genome (Aravin et al. 2008, Rosenkranz and Zischler 2012, Jung et al. 2014). About 18% of pre-pachytene piRNAs in mouse originate from mRNAs encoding proteins (Aravin et al. 2008). Likewise 235 to 368 piRNA clusters were identified in the human genome (Rosenkranz and Zischler 2012, Gould et al. 2012, Yang et al. 2013, Jung et al. 2014).

As inferred from the mouse homolog, the MYBL1 (A-MYB) transcription factor drives transcription of both piRNA precursors and mRNAs encoding PIWI family proteins.

Followed by: Primary piRNA transcript translocates from nucleoplasm to cytosol

Literature references

Jung, I., Park, JC., Kim, S. (2014). piClust: A density based piRNA clustering algorithm. *Comput Biol Chem, 50*, 60-7. ↗

Rosenkranz, D., Zischler, H. (2012). proTRAC--a software for probabilistic piRNA cluster detection, visualization and analysis. *BMC Bioinformatics, 13*, 5. ↗

Yang, Q., Hua, J., Wang, L., Xu, B., Zhang, H., Ye, N. et al. (2013). MicroRNA and piRNA profiles in normal human testis detected by next generation sequencing. *PLoS ONE, 8*, e66809. ↗

Gould, DW., Lukic, S., Chen, KC. (2012). Selective constraint on copy number variation in human piwi-interacting RNA Loci. *PLoS ONE, 7*, e46611. ↗

Aravin, AA., Sachidanandam, R., Bourc'his, D., Schaefer, C., Pezic, D., Toth, KF. et al. (2008). A piRNA pathway primed by individual transposons is linked to de novo DNA methylation in mice. *Mol. Cell, 31*, 785-99. ↗

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

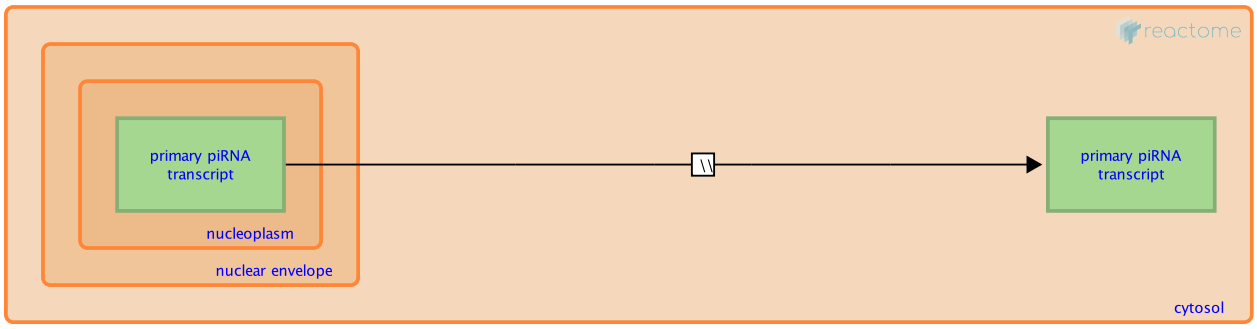
Primary piRNA transcript translocates from nucleoplasm to cytosol ↗

Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601924

Type: omitted

Compartments: cytosol, nuclear envelope, nucleoplasm



Primary (unprocessed) transcripts of piRNAs are transported from the nucleus to the cytosol by an unknown mechanism. Studies with Drosophila indicate that Uap56, Nxt1, Nxf2, Nup154, and Nup43 may be involved in exporting piRNA precursors from the nucleus (Zhang et al. 2012, Muerdter et al. 2013, Handler et al. 2013).

Preceded by: RNA polymerase II polymerizes primary piRNA transcript

Followed by: PLD6 dimer cleaves primary piRNA transcript to pre-piRNA

Literature references

Zhang, F., Wang, J., Xu, J., Zhang, Z., Koppetsch, BS., Schultz, N. et al. (2012). UAP56 couples piRNA clusters to the perinuclear transposon silencing machinery. *Cell, 151*, 871-84. ↗

Muerdter, F., Guzzardo, PM., Gillis, J., Luo, Y., Yu, Y., Chen, C. et al. (2013). A genome-wide RNAi screen draws a genetic framework for transposon control and primary piRNA biogenesis in Drosophila. *Mol. Cell, 50*, 736-48. ↗

Handler, D., Meixner, K., Pizka, M., Lauss, K., Schmied, C., Gruber, FS. et al. (2013). The genetic makeup of the Drosophila piRNA pathway. *Mol. Cell, 50*, 762-77. ↗

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

PLD6 dimer cleaves primary piRNA transcript to pre-piRNA ↗

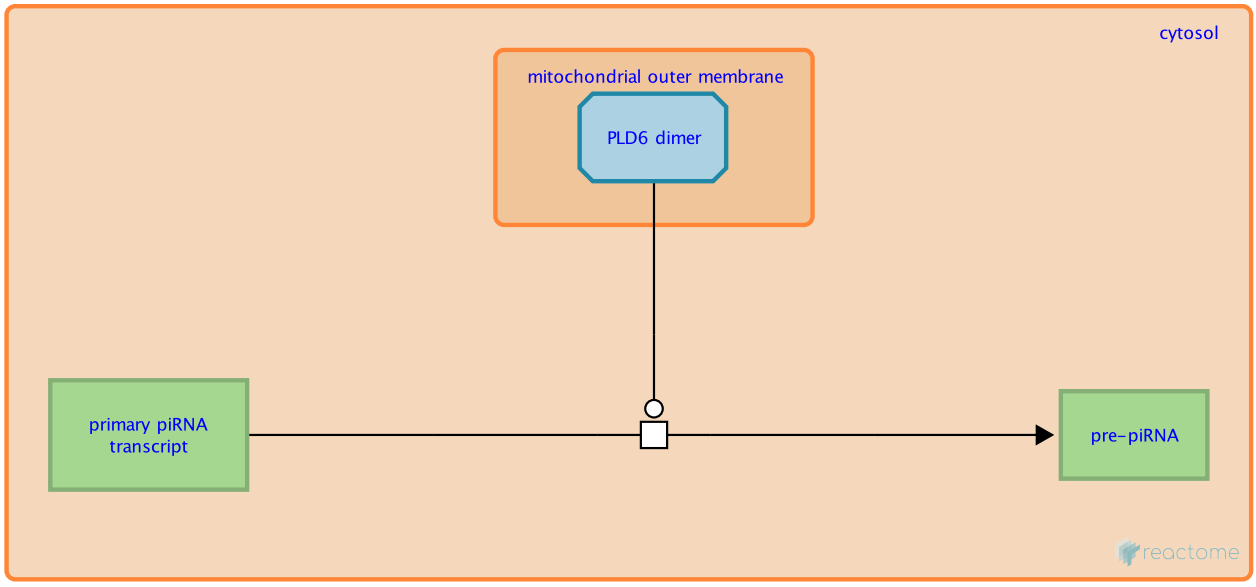
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601887

Type: transition

Compartments: cytosol, mitochondrial outer membrane

Inferred from: Pld6 dimer cleaves primary piRNA transcript to pre-piRNA (Mus musculus)



As inferred from homologs in Drosophila and mouse, PLD6 (MitoPLD) located on the cytoplasmic face of the mitochondrial outer membrane makes the first endonucleolytic cleavage of primary piRNA transcripts. The cleavage yields a 5' phosphate and a 3' hydroxyl. Cleavage is believed to precede loading into PIWIL1 (HIWI, MIWI) or PIWIL2 (HILI, MILI). Most mature piRNAs have uracil at the 5' end. This appears to be due to selective binding by PIWI proteins rather than selective cleavage (reviewed in Bortvin 2013).

Preceded by: Primary piRNA transcript translocates from nucleoplasm to cytosol

Followed by: Complexed PIWIL1 binds pre-piRNA, Complexed PIWIL2 binds pre-piRNA

Literature references

Bortvin, A. (2013). PIWI-interacting RNAs (piRNAs) - a mouse testis perspective. *Biochemistry Mosc., 78*, 592-602. ↗

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Complexed PIWIL1 binds pre-piRNA ↗

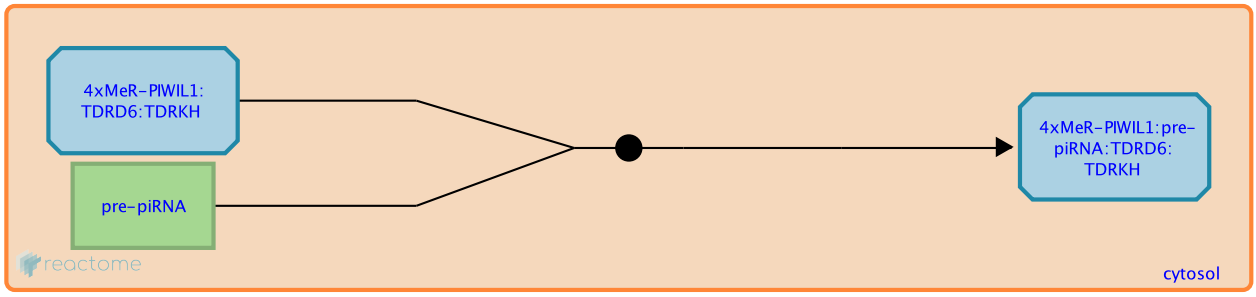
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5615682

Type: binding

Compartments: cytosol

Inferred from: Complexed Piwil1 binds pre-piRNA (Mus musculus)



After cleavage by PLD6 at the 5' end, the pre-piRNA is bound by PIWIL1 (HIWI, homolog of MIWI in mouse), likely in a complex with other proteins such as TDRD6 and TDRKH, which interact with methylated arginine residues on PIWIL1 and are required for piRNA biogenesis. Binding by PIWIL1 is believed to be selective for pre-piRNAs that have uracil residues at their 5' ends.

Preceded by: PLD6 dimer cleaves primary piRNA transcript to pre-piRNA

Followed by: Unknown nuclease cleaves pre-piRNA in 4xMeR-PIWIL1:pre-piRNA:TDRD6:TDRKH

Literature references

Zeng, L., Zhang, Q., Yan, K., Zhou, MM. (2011). Structural insights into piRNA recognition by the human PIWI-like 1 PAZ domain. *Proteins, 79*, 2004-9. ↗

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Complexed PIWIL2 binds pre-piRNA ↗

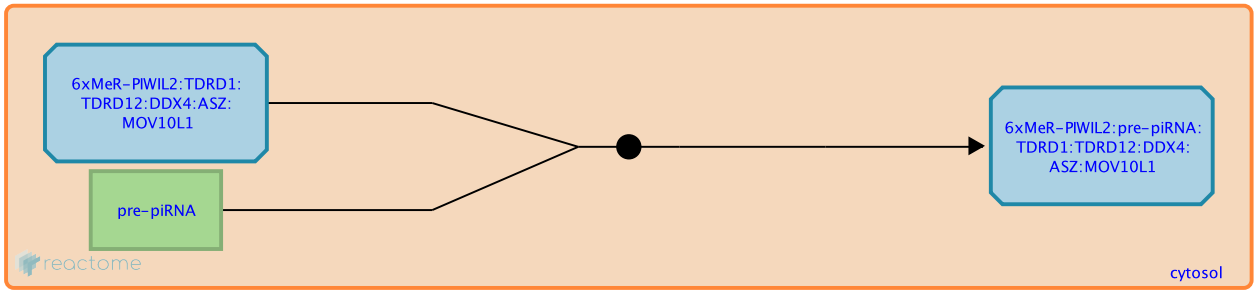
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5603062

Type: binding

Compartments: cytosol

Inferred from: Complexed Piwil2 binds pre-piRNA (Mus musculus)



After cleavage by PLD6 at the 5' end, the pre-piRNA is bound by PIWIL2 (HILI, homolog of MILI in mouse), likely in a complex with TDRD1, TDRD12, DDX4 (MVH), ASZ (GASZ), and MOV10L, all of which are required for wild-type levels of piRNA biogenesis. Binding by PIWIL2 is believed to be selective for pre-piRNAs that have uracil residues at their 5' ends.

Preceded by: PLD6 dimer cleaves primary piRNA transcript to pre-piRNA

Followed by: Unknown nuclease cleaves pre-piRNA in ASZ1:DDX4:MOV10L1:6xMeR-PIWIL2:pre-piRNA:TDRD1:TDRD12

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Unknown nuclease cleaves pre-piRNA in 4xMeR-PIWIL1:pre-piRNA:TDRD6:TDRKH

↗

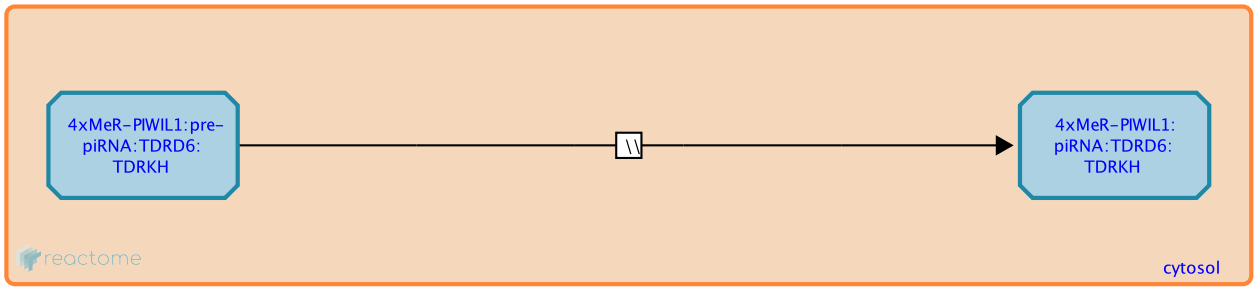
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601888

Type: omitted

Compartments: cytosol

Inferred from: Unknown nuclease cleaves pre-piRNA in 4xMeR-Piwil1:pre-piRNA:Tdrd6:Tdrkh (Mus musculus)



As inferred from mouse homologs, after binding PIWIL1 (HIWI in human, Miwi in mouse) the 3' end of the pre-piRNA is trimmed by an unknown nuclease. The final size of the piRNA appears to be determined by the particular PIWI protein with which it is associated. PIWIL1 and TDRD6 are located in the chromatoid body. Both TDRD6 and TDRKH are associated with PIWIL1 in adult testes but only TDRKH is present in embryonic prospermatogonia. TDRKH is required for spermatogenesis and appears to participate in trimming of the 3' end of pre-piRNAs.

Preceded by: Complexed PIWIL1 binds pre-piRNA

Followed by: HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 4xMeR-PIWIL1:piRNA:TDRD6:TDRKH

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 4xMeR-PIWIL1:piRNA:TDRD6:TDRKH ↗

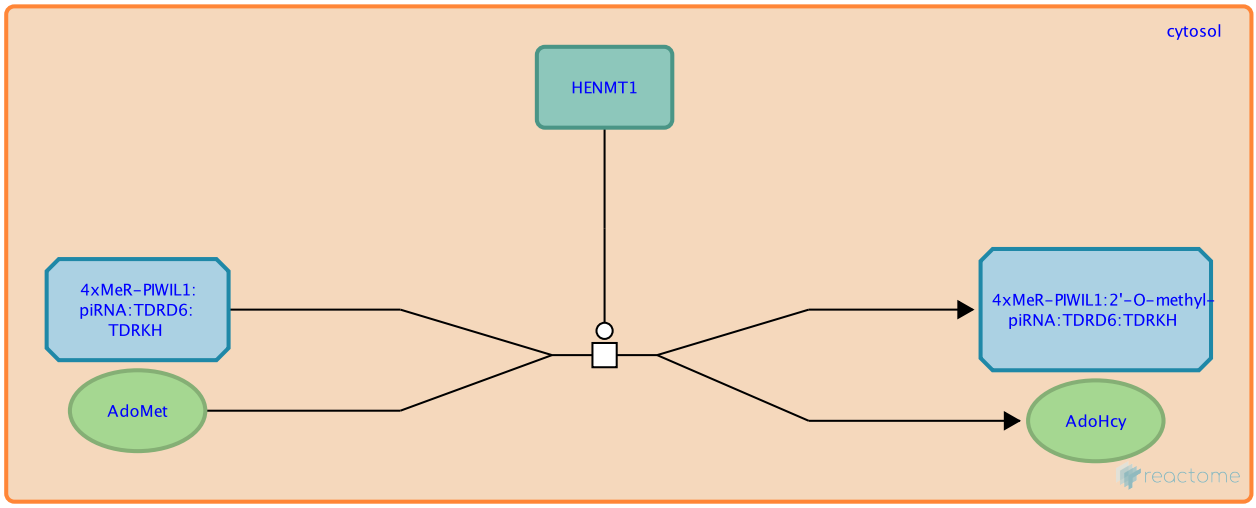
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5629203

Type: transition

Compartments: cytosol

Inferred from: Henmt1 methylates 2' hydroxyl at 3' end of piRNA in 4xMeR-Piwil1:piRNA:Tdrd6:Tdrkh (Mus musculus)



As inferred from mouse homologs, HENMT1 transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl group of a trimmed piRNA bound by the PIWIL1 complex in the cytosol.

Preceded by: Unknown nuclease cleaves pre-piRNA in 4xMeR-PIWIL1:pre-piRNA:TDRD6:TDRKH

Editions

2014-10-25	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Unknown nuclease cleaves pre-piRNA in ASZ1:DDX4:MOV10L1:6xMeR-PIWIL2:pre-piRNA:TDRD1:TDRD12 ↗

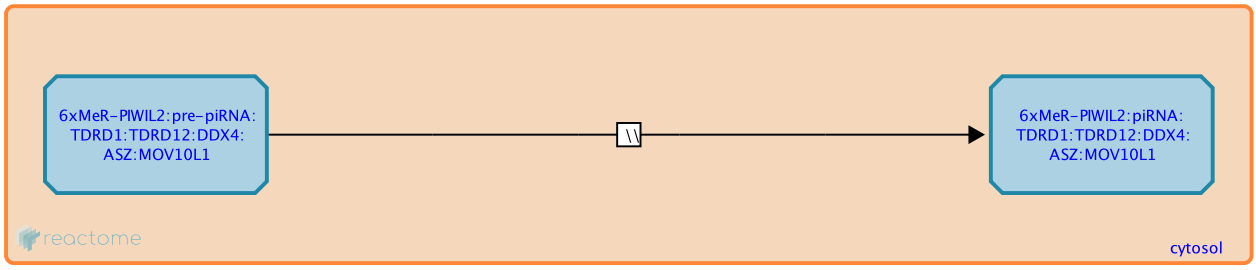
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5603067

Type: omitted

Compartments: cytosol

Inferred from: Unknown nuclease cleaves pre-piRNA in Asz1:Ddx4:Mov10l1:6xMeR-Piwil2:pre-piRNA:Tdrd1:Tdrd12 (Mus musculus)



As inferred from mouse homologs, after binding PIWIL2 (HILI in human, MILI in mouse) the 3' end of the pre-piRNA is trimmed by an unknown nuclease. The final size of the piRNA appears to be determined by the particular PIWI protein with which it is associated. MOV10L1, which has a helicase domain, associates with PIWIL2 and is required for loading PIWIL2 with piRNA. PIWIL2, TDRD1, MVH, and ASZ are located in the intermitochondrial cement, the chromatoid body, and the pi-body, a type of nuage (reviewed in Pillai and Chuma 2012). (Nuage is electron-dense perinuclear material also known as germinal granules.)

Preceded by: Complexed PIWIL2 binds pre-piRNA

Followed by: HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 6xMeR-PIWIL2:piRNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 6xMeR-PIWIL2:piRNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1 ↗

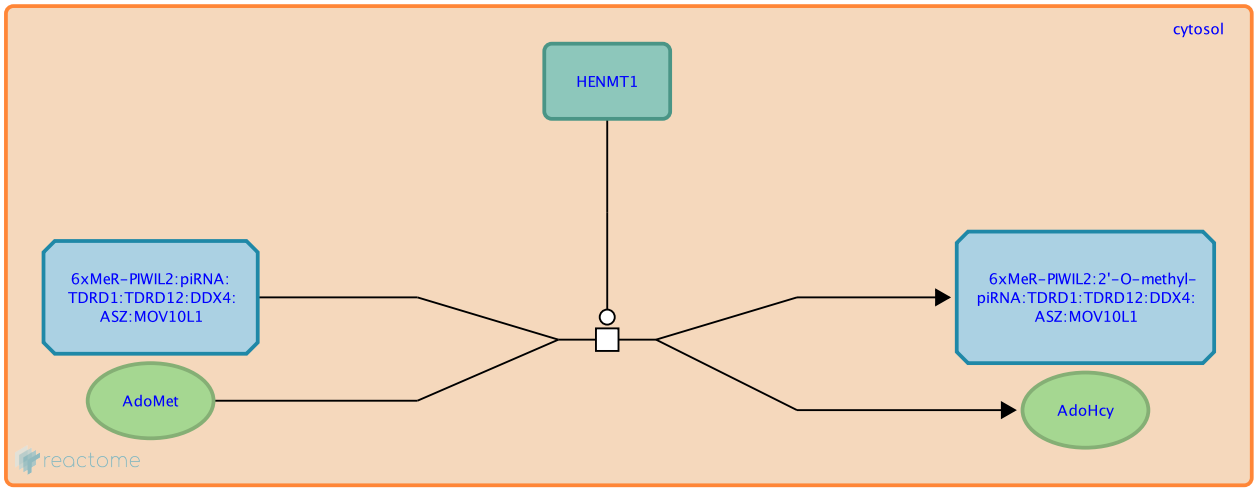
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5629218

Type: transition

Compartments: cytosol

Inferred from: Henmt1 methylates 2' hydroxyl at 3' end of piRNA in Asz1:Ddx4:Mov10l1:6xMeR-Piwil2:piRNA:Tdrd1:Tdrd12 (Mus musculus)



As inferred from mouse homologs, HENMT1 transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl group at the 3' end of piRNA bound to the PIWIL2 complex in the cytosol.

Preceded by: Unknown nuclease cleaves pre-piRNA in ASZ1:DDX4:MOV10L1:6xMeR-PIWIL2:pre-piRNA:TDRD1:TDRD12, Unknown nuclease cleaves cleaved transposon RNA bound in MeR-PIWIL4:cleaved transposon RNA:TDRD9:MAEL:TDRKH

Followed by: Complexed PIWIL2:2'-O-methyl-piRNA cleaves transposon RNA

Editions

2014-10-25	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Complexed PIWIL2:2'-O-methyl-piRNA cleaves transposon RNA ↗

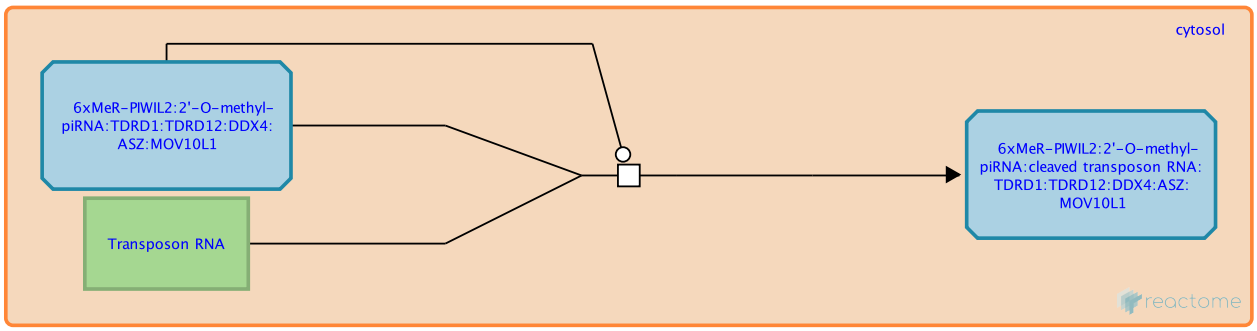
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601910

Type: transition

Compartments: cytosol

Inferred from: Complexed Piwil2:2'-O-methyl-piRNA cleaves transposon RNA (Mus musculus)



As inferred from homologs in mouse, PIWIL2 (HILI in human, homolog of MILI in mouse) bound to a piRNA cleaves target RNAs complementary to the piRNA. The cleaved RNA can either be transferred to another PIWIL2 as part of the "ping pong cycle" that generates secondary piRNAs or the cleaved RNA can be transferred to PIWIL4, which then transits to the nucleus to transcriptionally silence loci complementary to the piRNA.

Preceded by: HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 6xMeR-PIWIL2:piRNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1

Followed by: Complexed PIWIL2 binds cleaved transposon RNA, Complexed PIWIL4 binds cleaved transposon RNA

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Complexed PIWIL2 binds cleaved transposon RNA ↗

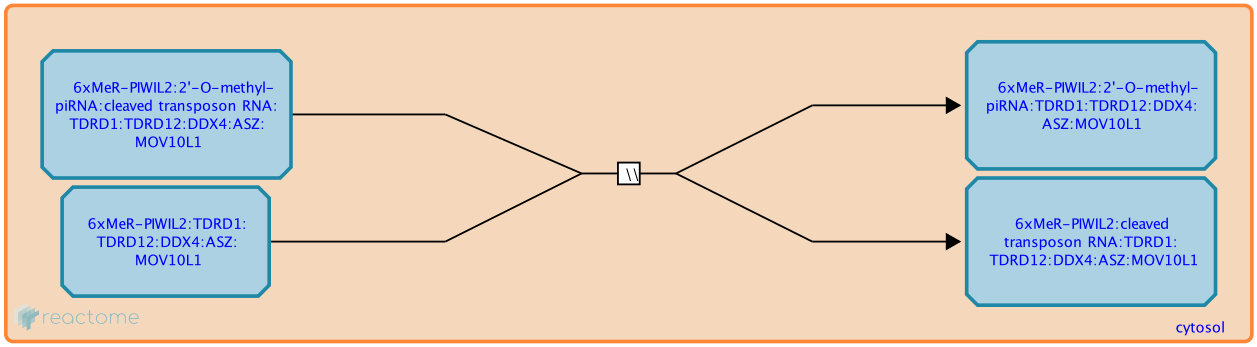
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601922

Type: omitted

Compartments: cytosol

Inferred from: Complexed Piwil2 binds cleaved transposon RNA (Mus musculus)



RNA cleaved by PIWIL2 (HILI in human, homolog of MILI in mouse) can be transferred to another molecule of PIWIL2. This is part of the "ping pong cycle" that generates further secondary piRNAs from a longer precursor.

Preceded by: Complexed PIWIL2:2'-O-methyl-piRNA cleaves transposon RNA

Followed by: Unknown nuclease cleaves cleaved transposon RNA in 6xMeR-PIWIL2:cleaved transposon RNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Unknown nuclease cleaves cleaved transposon RNA in 6xMeR-PIWIL2:cleaved transposon RNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1 ↗

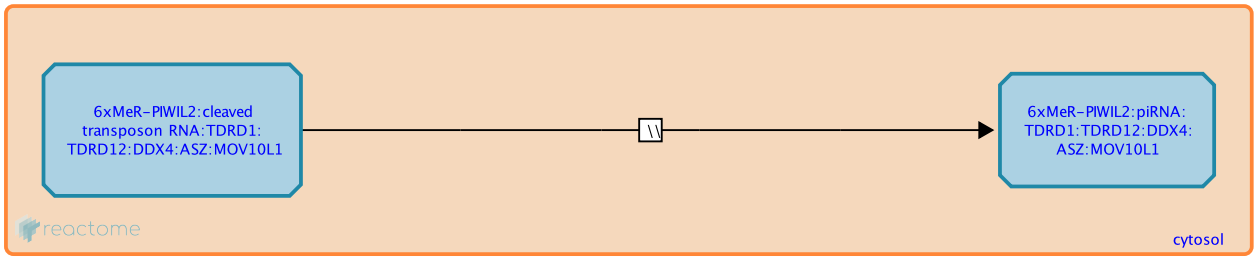
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601929

Type: omitted

Compartments: cytosol

Inferred from: Unknown nuclease cleaves cleaved transposon RNA in Asz1:Ddx4:Mov10l1:6xMeR-Piwil2:piRNA:Tdrd1:Tdrd12 (Mus musculus)



After the cleaved RNA binds PIWIL2 (HILI in human, homolog of Mili in mouse) the 3' end is trimmed by an unknown nuclease to generate a mature piRNA. The resulting PIWIL2:piRNA complex can then participate in further amplification by the "ping-pong" cycle.

Preceded by: Complexed PIWIL2 binds cleaved transposon RNA

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Complexed PIWIL4 binds cleaved transposon RNA ↗

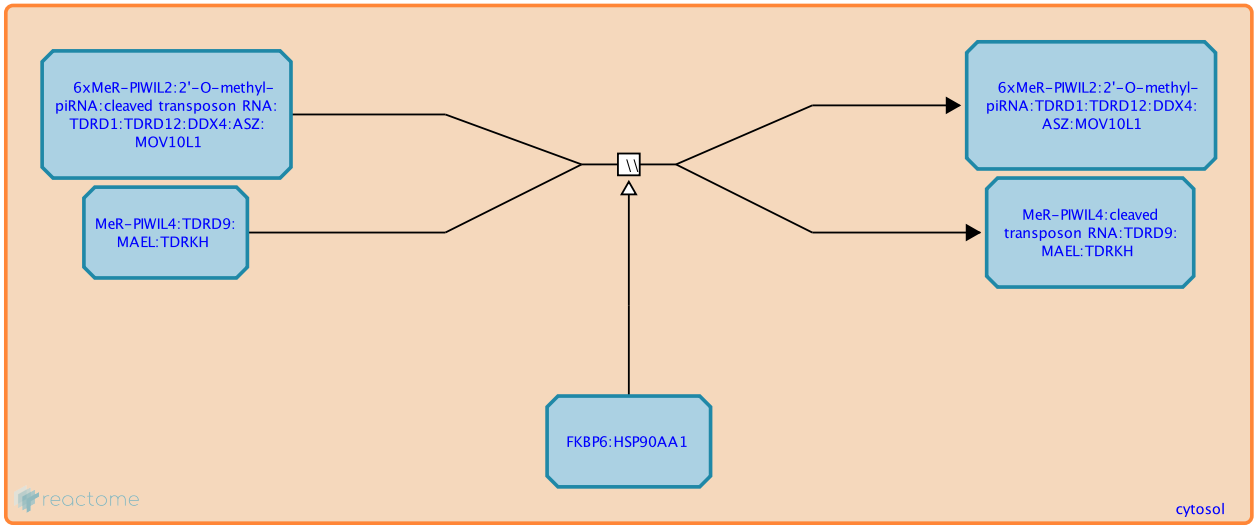
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601883

Type: omitted

Compartments: cytosol

Inferred from: Complexed Piwil4 binds cleaved transposon RNA (Mus musculus)



RNA cleaved by PIWIL2:piRNA is transferred to PIWIL4 (HIWI2 in human, MIWI2 in mouse). The reaction requires MAEL and is enhanced by the chaperone activity of FKBP6:HSP90. PIWIL4, TDRD9, and MAEL are located in piP bodies, a type of nuage (electron-dense perinuclear material). PIWIL4 and PIWIL2 are in separate nuages.

Preceded by: Complexed PIWIL2:2'-O-methyl-piRNA cleaves transposon RNA

Followed by: Unknown nuclease cleaves cleaved transposon RNA bound in MeR-PIWIL4:cleaved transposon RNA:TDRD9:MAEL:TDRKH

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

Unknown nuclease cleaves cleaved transposon RNA bound in MeR-PIWIL4:cleaved transposon RNA:TDRD9:MAEL:TDRKH ↗

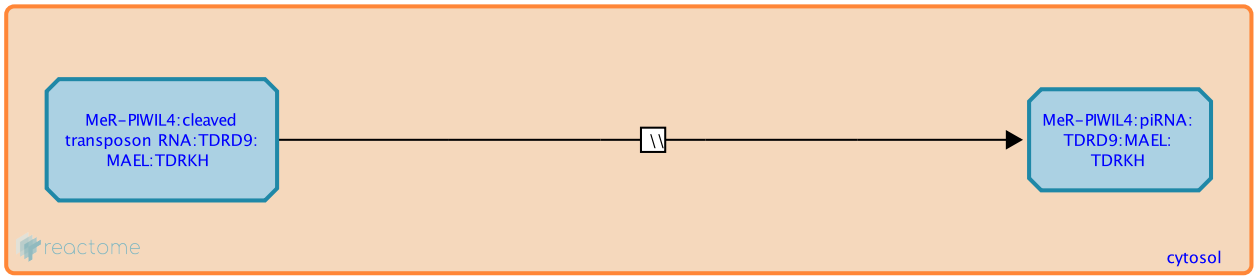
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601919

Type: omitted

Compartments: cytosol

Inferred from: Unknown nuclease cleaves cleaved transposon RNA in MeR-Piwil4:cleaved transposon RNA:Tdrd9:Mael:Tdrkh (Mus musculus)



After the cleaved RNA binds PIWIL4 the 3' end is trimmed by an unknown nuclease to generate a mature piRNA.

Preceded by: Complexed PIWIL4 binds cleaved transposon RNA

Followed by: HENMT1 methylates 2' hydroxyl at 3' end of piRNA in MeR-PIWIL4:piRNA:TDRD9:MAEL:TDRKH, HENMT1 methylates 2' hydroxyl at 3' end of piRNA in 6xMeR-PIWIL2:piRNA:TDRD1:TDRD12:DDX4:ASZ:MOV10L1

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

HENMT1 methylates 2' hydroxyl at 3' end of piRNA in MeR-PIWIL4:piRNA:TDRD9:MAEL:TDRKH ↗

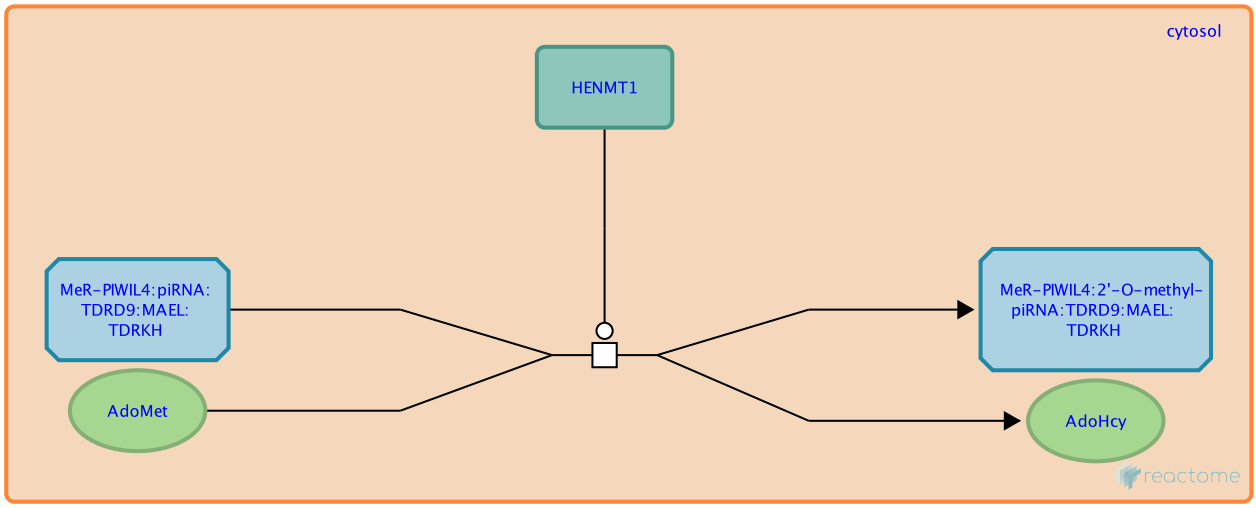
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5629237

Type: transition

Compartments: cytosol

Inferred from: Henmt1 methylates 2' hydroxyl at 3' end of piRNA in MeR-Piwil4:piRNA:Tdrd9:Mael:Tdrkh (Mus musculus)



As inferred from mouse homologs, HENMT1 transfers a methyl group from S-adenosylmethionine to the 2' hydroxyl group at the 3' end of a piRNA bound by PIWIL4.

Preceded by: Unknown nuclease cleaves cleaved transposon RNA bound in MeR-PIWIL4:cleaved transposon RNA:TDRD9:MAEL:TDRKH

Followed by: MeR-PIWIL4:2'-O-methyl-piRNA:TDRD9:MAEL:TDRKH dissociates and MeR-PIWIL4:2'-O-methylpiRNA, TDRD9, MAEL translocate from cytosol to nucleus in an unknown association and order of events

Editions

2014-10-25	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

MeR-PIWIL4:2'-O-methyl-piRNA:TDRD9:MAEL:TDRKH dissociates and MeR-PIWIL4:2'-O-methylpiRNA, TDRD9, MAEL translocate from cytosol to nucleus in an unknown association and order of events ↗

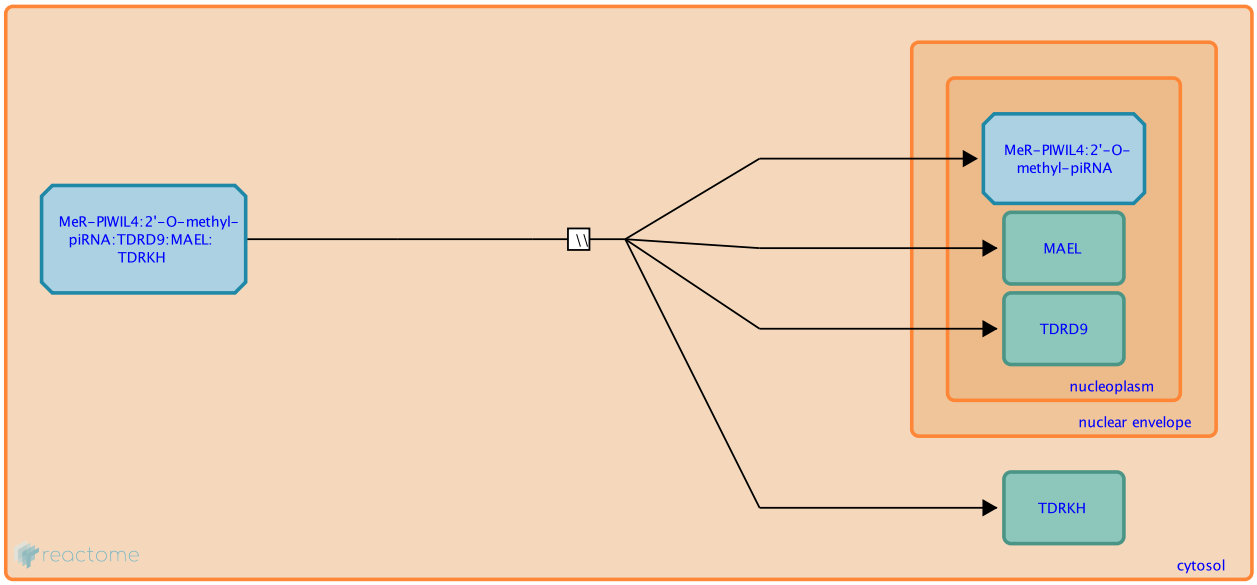
Location: PIWI-interacting RNA (piRNA) biogenesis

Stable identifier: R-HSA-5601897

Type: omitted

Compartments: cytosol, nuclear envelope, nucleoplasm

Inferred from: MeR-Piwil4:2'-O-methyl-piRNA:Tdrd9:Mael:Tdrkh dissociates and MeR-Piwil4:2'-O-methyl-piRNA, Tdrd9, Mael translocate from cytosol to nucleus in unknown association and unknown order of events (Mus musculus)



As inferred from homologs in mouse, PIWIL4 is loaded with piRNA in the cytosol and then translocates to the nucleus where it directs transcriptional silencing of cognate loci by an unknown mechanism. Most cellular PIWIL4 is translocated to the nucleus at E16.5 of mouse development and proper localization depends on PIWIL2 and TDRD1. TDRD9 and MAEL interact with PIWIL4, are observed in the nucleus, and may play a role in the translocation of PIWIL4. Knockout of TDRD9, however, does not affect nuclear localization of PIWIL4. Knockout of MAEL delays but does not prevent localization of PIWI4L to the nucleus. TDRKH is required for translocation of PIWIL4, however TDRKH is only observed in the cytosol.

Preceded by: HENMT1 methylates 2' hydroxyl at 3' end of piRNA in MeR-PIWIL4:piRNA:TDRD9:MAEL:TDRKH

Editions

2014-06-14	Authored, Edited	May, B.
2014-10-25	Reviewed	Saito, K.

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