

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

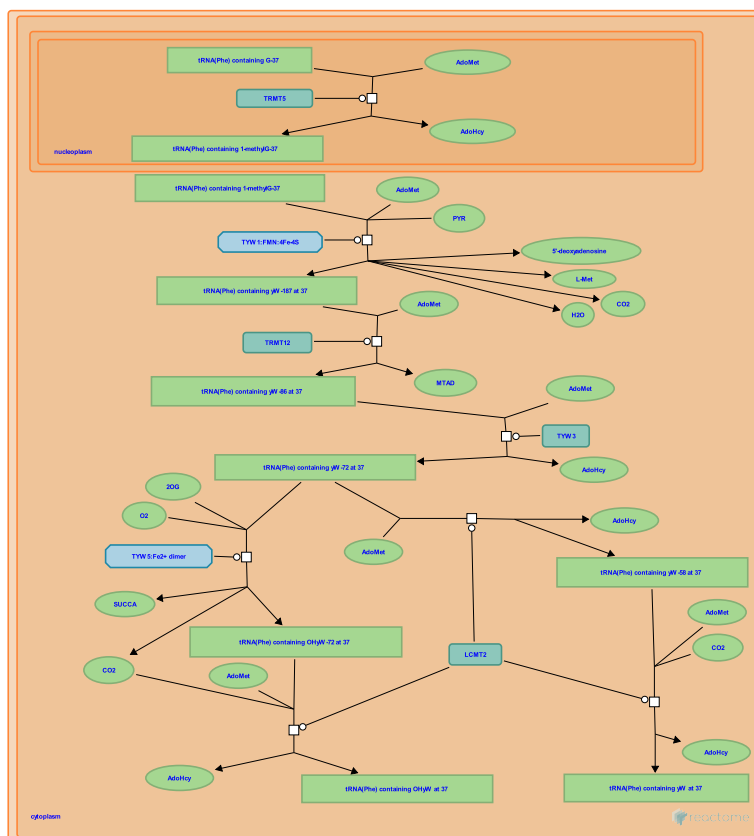
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Reactome database release: 88

This document contains 1 pathway and 8 reactions ([see Table of Contents](#))

Synthesis of wybutosine at G37 of tRNA(Phe) ↗

Stable identifier: R-HSA-6782861



Derivatives of wyosine are tricyclic bases found at nucleotide 37 of tRNA(Phe) in eukaryotes. The pathway of wybutosine synthesis begins with a templated guanosine residue and proceeds through 6 steps catalyzed by 5 enzymes: N1 methylation of guanosine, condensation of 1-methylguanosine with pyruvate to yield 4-demethylwyosine, addition of an aminocarboxypentyl group to yield yW-86, methylation of yW-86 to yield yW-72, methylation of yW-72 to yield yW-58, and methoxycarbonylation of yW-58 to yield wybutosine (reviewed in Young and Bandarian 2013, Perche-Letuvée et al. 2014). Wybutosine may further be modified by hydroxylation and methylation. Wyosine derivatives at position 37 of tRNAs participate in translational fidelity by stabilizing codon-anticodon pairing (Konevega et al. 2004) and preventing frameshifting (Waas et al. 2007).

Literature references

- Perche-Letuvée, P., Molle, T., Atta, M., Mulliez, E., Forouhar, F. (2014). Wybutosine biosynthesis: structural and mechanistic overview. *RNA Biol*, 11, 1508-18. ↗
- Rodnina, MV., Semenov, YP., Wintermeyer, W., Konevega, AL., Makhno, VI., Katunin, VI. et al. (2004). Purine bases at position 37 of tRNA stabilize codon-anticodon interaction in the ribosomal A site by stacking and Mg²⁺-dependent interactions. *RNA*, 10, 90-101. ↗
- Schimmel, P., Hanan, M., Waas, WF., Druzina, Z. (2007). Role of a tRNA base modification and its precursors in frameshifting in eukaryotes. *J. Biol. Chem.*, 282, 26026-34. ↗
- Bandarian, V., Young, AP. (2013). Radical mediated ring formation in the biosynthesis of the hypermodified tRNA base wybutosine. *Curr Opin Chem Biol*, 17, 613-8. ↗

Editions

2015-06-08	Authored, Edited	May, B.
2015-08-11	Reviewed	Levinger, L.
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TRMT5 methylates guanosine yielding 1-methylguanosine at nucleotide 37 of tRNA(Phe) ↗

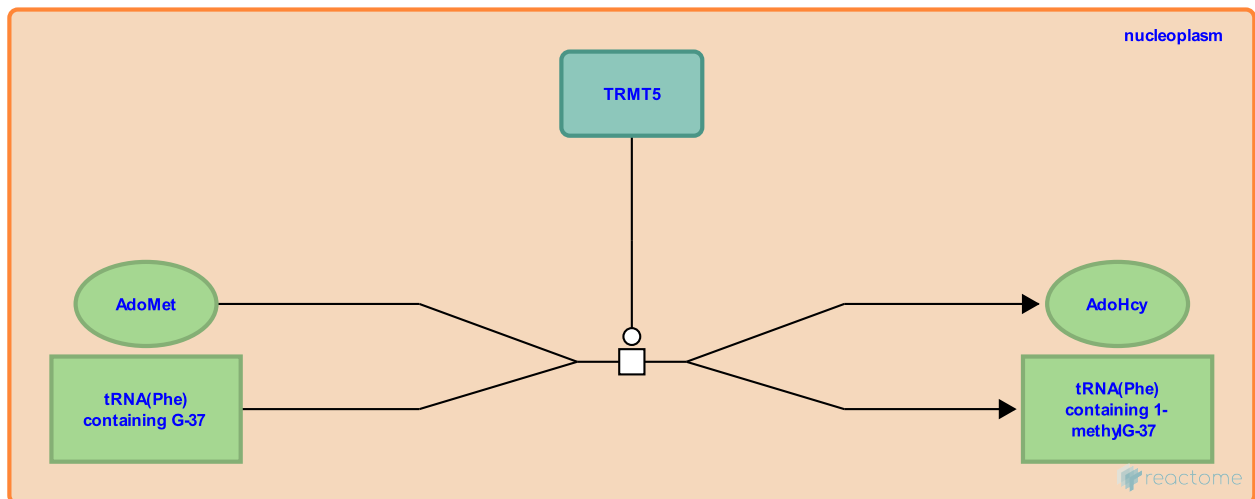
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782859

Type: transition

Compartments: nucleoplasm

Inferred from: [TRM5 methylates guanosine yielding 1-methylguanosine at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



TRMT5 transfers a methyl group from S-adenosylmethionine to the 1 position of guanosine-37 of tRNA(Phe) (Brulé et al. 2004, Christian et al. 2013). The yeast homolog, TRM5, catalyzes the same reaction.

Followed by: [TYW1:FMN:4Fe-4S transforms 1-methylguanosine yielding yW-187 \(4-demethylwyosine\) at nucleotide 37 of tRNA\(Phe\)](#)

Literature references

Gamper, H., Christian, T., Hou, YM. (2013). Conservation of structure and mechanism by Trm5 enzymes. *RNA*, 19, 1192-9. ↗

Elliott, M., Brulé, H., Holmes, WM., Redlak, M., Zehner, ZE. (2004). Isolation and characterization of the human tRNA-(N1G37) methyltransferase (TRM5) and comparison to the Escherichia coli TrmD protein. *Biochemistry*, 43, 9243-55. ↗

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2015-10-24	Reviewed	Jarrous, N.

TYW1:FMN:4Fe-4S transforms 1-methylguanosine yielding yW-187 (4-demethylwyosine) at nucleotide 37 of tRNA(Phe) ↗

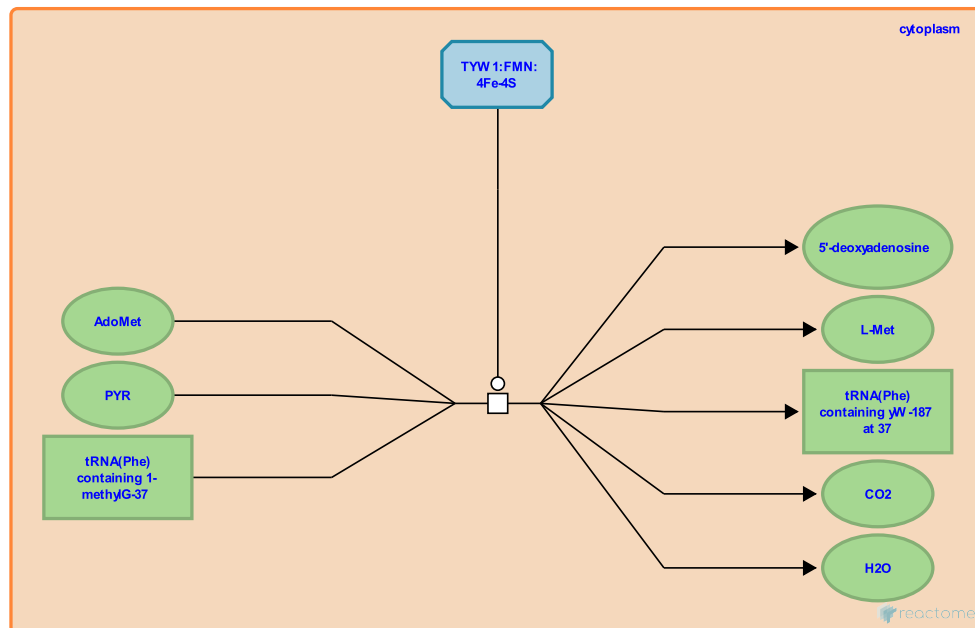
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782895

Type: transition

Compartments: cytoplasm

Inferred from: [TYW1:FMN:4Fe-4S transforms 1-methylguanosine yielding yW-187 at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



As inferred from homologs in *Saccharomyces cerevisiae*, TYW1 in a complex with FMN and an iron-sulfur cluster transfers 2 carbon atoms from pyruvate to 1-methylguanosine-37 of tRNA(Phe), yielding yW-187 (4-demethylwyosine) at nucleotide 37.

Preceded by: [TRMT5 methylates guanosine yielding 1-methylguanosine at nucleotide 37 of tRNA\(Phe\)](#)

Followed by: [TRMT12 transforms yW-187 yielding yW-86 at nucleotide 37 of tRNA\(Phe\)](#)

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TRMT12 transforms yW-187 yielding yW-86 at nucleotide 37 of tRNA(Phe) ↗

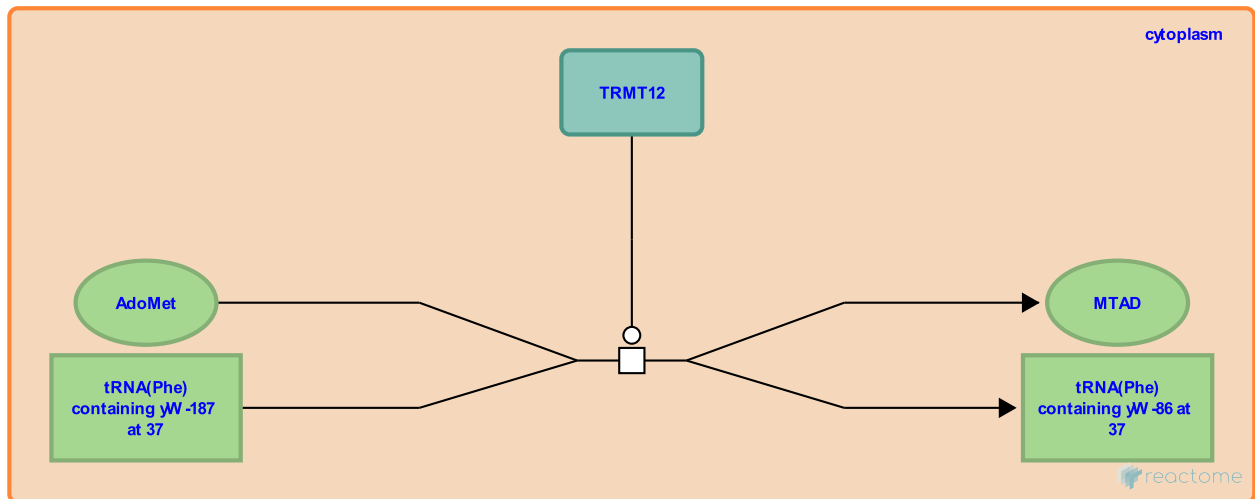
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782893

Type: transition

Compartments: cytoplasm

Inferred from: [TRM12 transforms yW-187 yielding yW-86 at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



As inferred from homologs in *Saccharomyces cerevisiae*, TRM12 transfers an aminocarboxypropyl group from S-adenosylmethionine to yW-187 (4-demethylwyosine) at nucleotide 37 of tRNA(Phe), yielding yW-86 (7-((3S)-3-amino-3-carboxypropyl)-4-demethylwyosine) and S-methyl-5'-thioadenosine.

Preceded by: [TYW1:FMN:4Fe-4S transforms 1-methylguanosine yielding yW-187 \(4-demethylwyosine\) at nucleotide 37 of tRNA\(Phe\)](#)

Followed by: [TYW3 methylates yW-86 yielding yW-72 at nucleotide 37 of tRNA\(Phe\)](#)

Literature references

Suzuki, T., Chandrasekharappa, SC., Rodriguez, V., Noma, A., Carlson, BA., Vasudevan, S. et al. (2012). Structure-function analysis of human TYW2 enzyme required for the biosynthesis of a highly modified Wybutosine (yW) base in phenylalanine-tRNA. *PLoS ONE*, 7, e39297. ↗

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TYW3 methylates yW-86 yielding yW-72 at nucleotide 37 of tRNA(Phe) ↗

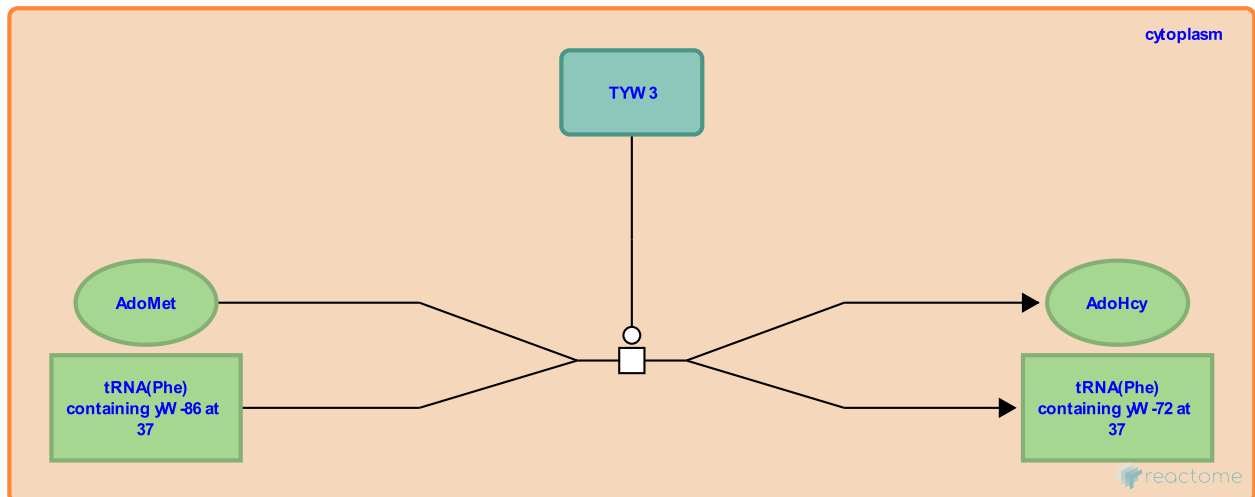
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782879

Type: transition

Compartments: cytoplasm

Inferred from: [TYW3 methylates yW-86 yielding yW-72 at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



As inferred from homologs in *Saccharomyces cerevisiae*, TYW3 transfers a methyl group from S-adenosylmethionine to yW-86 (7-((3S)-(3-amino-3-carboxypropyl))-4-demethylwyosine) at nucleotide 37 of tRNA(Phe), yielding yW-72 (7-((3S)-(3-amino-3-carboxypropyl))wyosine) and S-adenosylhomocysteine.

Preceded by: [TRMT12 transforms yW-187 yielding yW-86 at nucleotide 37 of tRNA\(Phe\)](#)

Followed by: [TYW5 hydroxylates yW-72 yielding OHyW-72 at nucleotide 37 of tRNA\(Phe\)](#), [LCMT2 methylates yW-72 yielding yW-58 at nucleotide 37 of tRNA\(Phe\)](#)

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LCMT2 methylates yW-72 yielding yW-58 at nucleotide 37 of tRNA(Phe) ↗

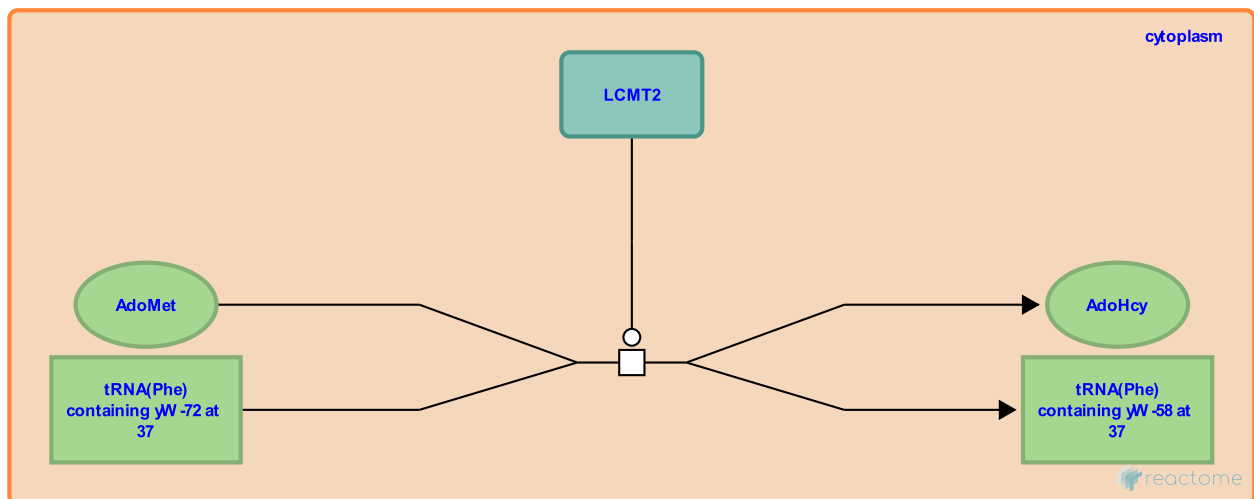
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782881

Type: transition

Compartments: cytoplasm

Inferred from: [PPM2 methylates yW-72 yielding yW-58 at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



As inferred from homologues in *Saccharomyces cerevisiae*, LCMT2 (TYW4) transfers a methyl group from S-adenosylmethionine to yW-72 (7-((3S)-3-amino-3-carboxypropyl)wyosine) at nucleotide 37 of tRNA(Phe), yielding yW-58 (7-((3S)-3-amino-3-(methoxycarbonyl)propyl)wyosine) and S-adenosylhomocysteine.

Preceded by: [TYW3 methylates yW-86 yielding yW-72 at nucleotide 37 of tRNA\(Phe\)](#)

Followed by: [LCMT2 methoxycarbonylates yW-58 yielding yW \(wybutosine\) at nucleotide 37 of tRNA\(Phe\)](#)

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LCMT2 methoxycarbonylates yW-58 yielding yW (wybutosine) at nucleotide 37 of tRNA(Phe) ↗

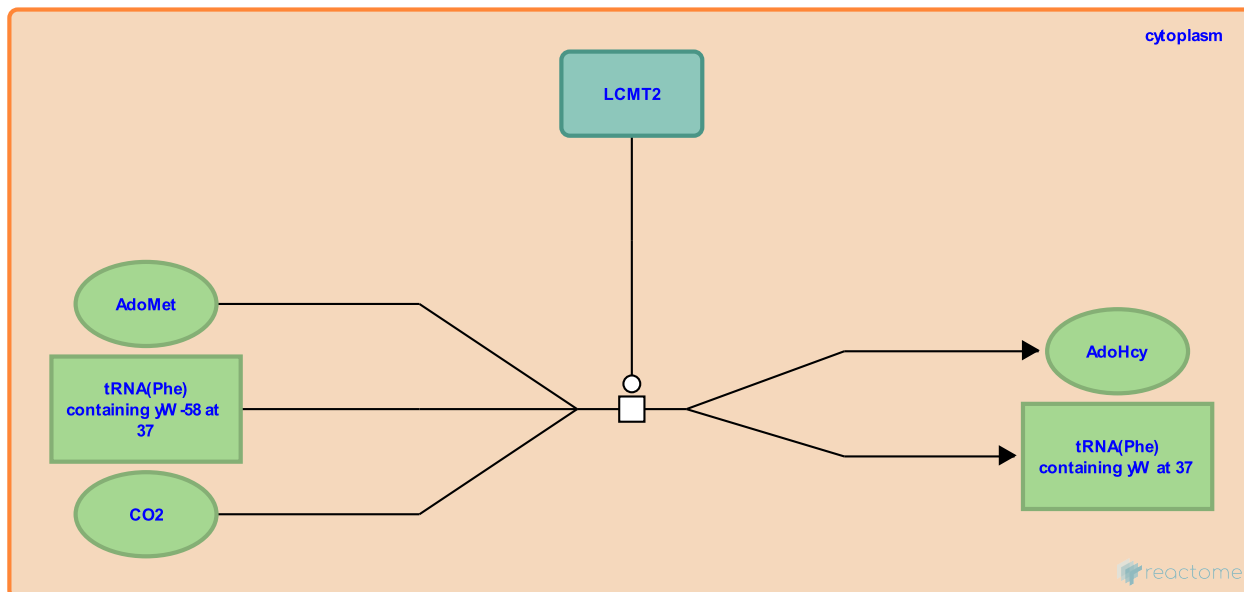
Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6782890

Type: transition

Compartments: cytoplasm

Inferred from: [PPM2 methoxycarbonylates yW-58 yielding yW at nucleotide 37 of tRNA\(Phe\) \(Saccharomyces cerevisiae\)](#)



As inferred from homologues in *Saccharomyces cerevisiae*, LCMT2 (TYW4) methoxycarbonylates yW-58 (7-((3S)-3-amino-3-(methoxycarbonyl)propyl)wyosine) at nucleotide 37 of tRNA(Phe) yielding yW (wybutosine). A molecule of carbon dioxide is incorporated during the reaction.

Preceded by: [LCMT2 methylates yW-72 yielding yW-58 at nucleotide 37 of tRNA\(Phe\)](#)

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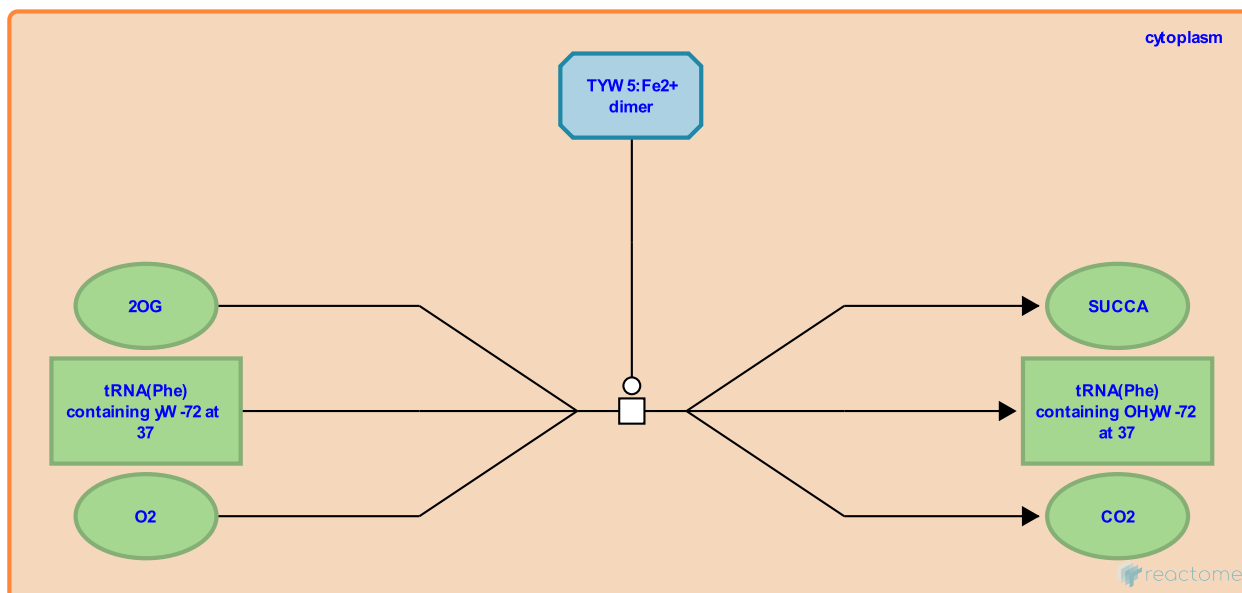
TYW5 hydroxylates yW-72 yielding OHyW-72 at nucleotide 37 of tRNA(Phe) ↗

Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6783455

Type: transition

Compartments: cytoplasm



TYW5 uses 2-oxoglutarate and molecular oxygen to hydroxylate yW-72 (7-(3-amino-3-carboxypropyl)wyosine) at nucleotide 37 of tRNA(Phe), yielding OHyW-72 (7-(2-hydroxy-3-amino-3-carboxypropyl)wyosine), carbon dioxide, and succinate (Noma et al. 2010, Kato et al. 2011).

Preceded by: [TYW3 methylates yW-86 yielding yW-72 at nucleotide 37 of tRNA\(Phe\)](#)

Followed by: [LCMT2 methoxycarbonylates OHyW-72 yielding OHyW \(hydroxywybutosine\) at nucleotide 37 of tRNA\(Phe\)](#)

Literature references

Suzuki, T., Noma, A., Kato, M., Nureki, O., Nagao, A., Ishitani, R. (2010). Expanding role of the jumonji C domain as an RNA hydroxylase. *J. Biol. Chem.*, 285, 34503-7. ↗

Suzuki, T., Noma, A., Araiso, Y., Kato, M., Nureki, O., Nagao, A. et al. (2011). Crystal structure of a novel JmjC-domain-containing protein, TYW5, involved in tRNA modification. *Nucleic Acids Res.*, 39, 1576-85. ↗

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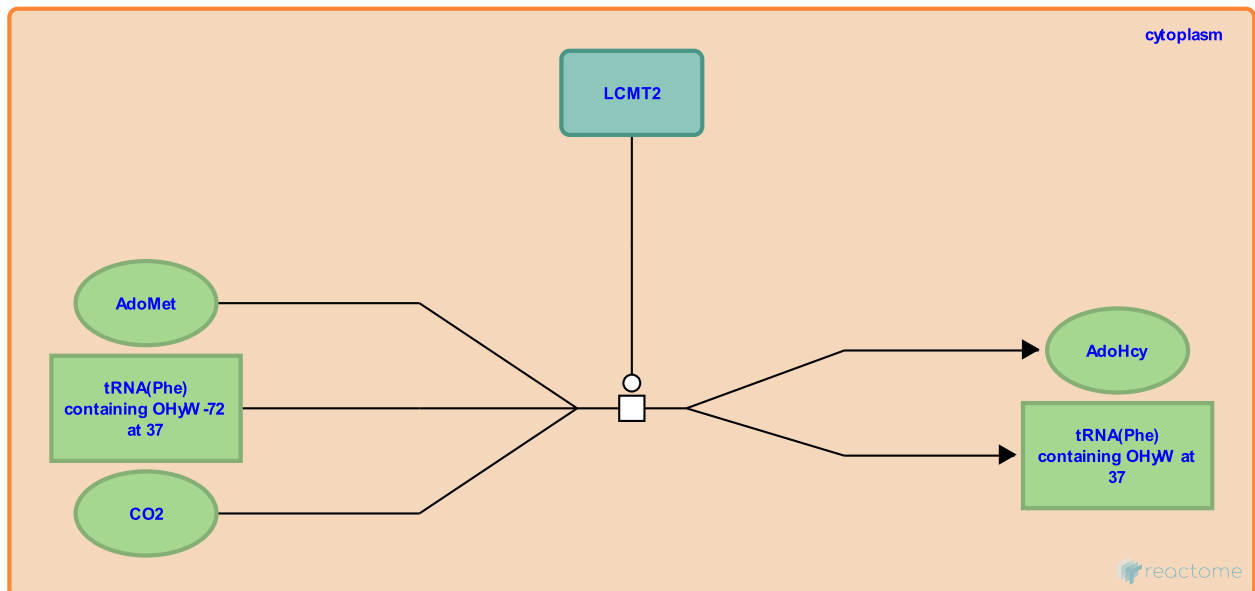
LCMT2 methoxycarbonylates OHyW-72 yielding OHyW (hydroxywybutosine) at nucleotide 37 of tRNA(Phe) ↗

Location: [Synthesis of wybutosine at G37 of tRNA\(Phe\)](#)

Stable identifier: R-HSA-6783473

Type: transition

Compartments: cytoplasm



LCMT2 (TYW4) methoxycarbonylates OHyW-72 (7-(2-hydroxy-3-amino-3-carboxypropyl)wyosine) at nucleotide 37 of tRNA(Phe), yielding OHyW (hydroxywybutosine) (Noma et al. 2010).

Preceded by: [TYW5 hydroxylates yW-72 yielding OHyW-72 at nucleotide 37 of tRNA\(Phe\)](#)

Literature references

Suzuki, T., Noma, A., Kato, M., Nureki, O., Nagao, A., Ishitani, R. (2010). Expanding role of the jumonji C domain as an RNA hydroxylase. *J. Biol. Chem.*, 285, 34503-7. ↗

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