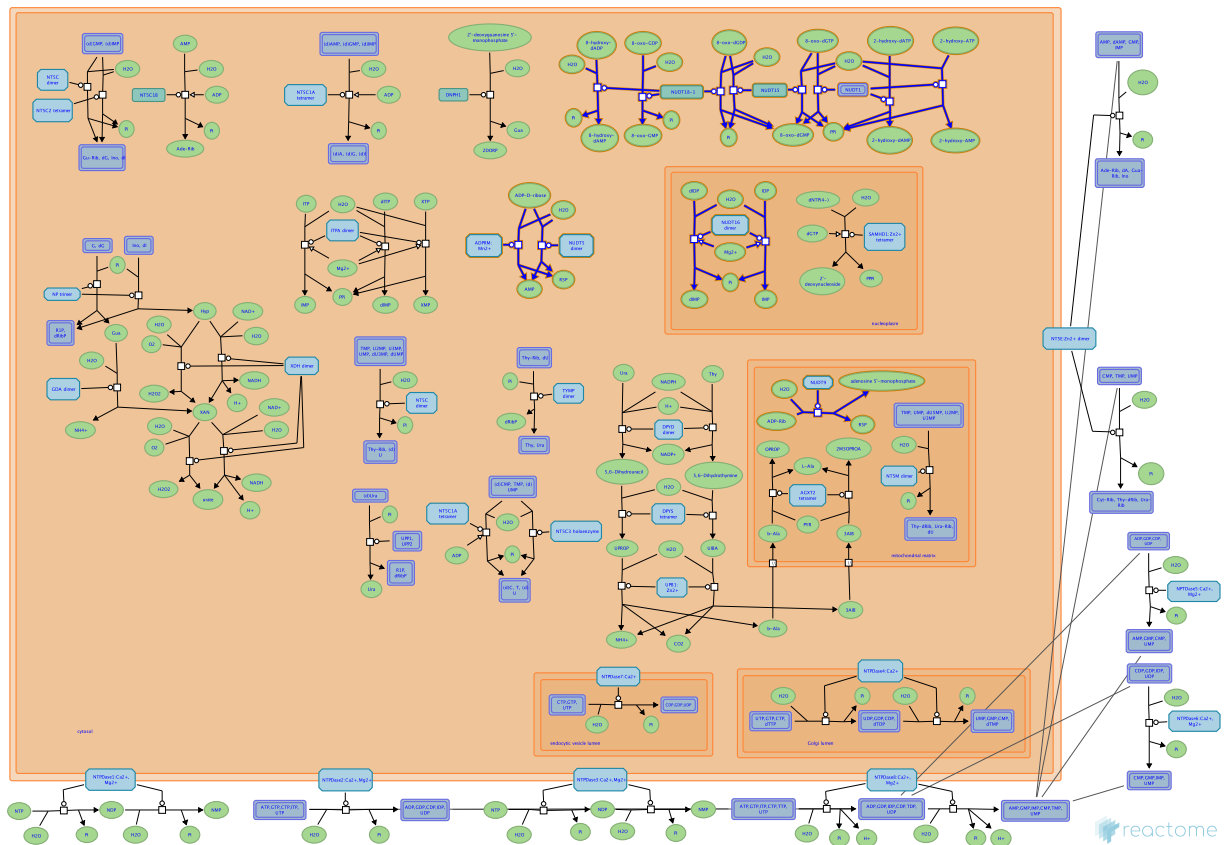


# Phosphate bond hydrolysis by NUDT proteins



D'Eustachio, P., Ito, R., Jassal, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://creativecommons.org/licenses/by/4.0/).

## 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

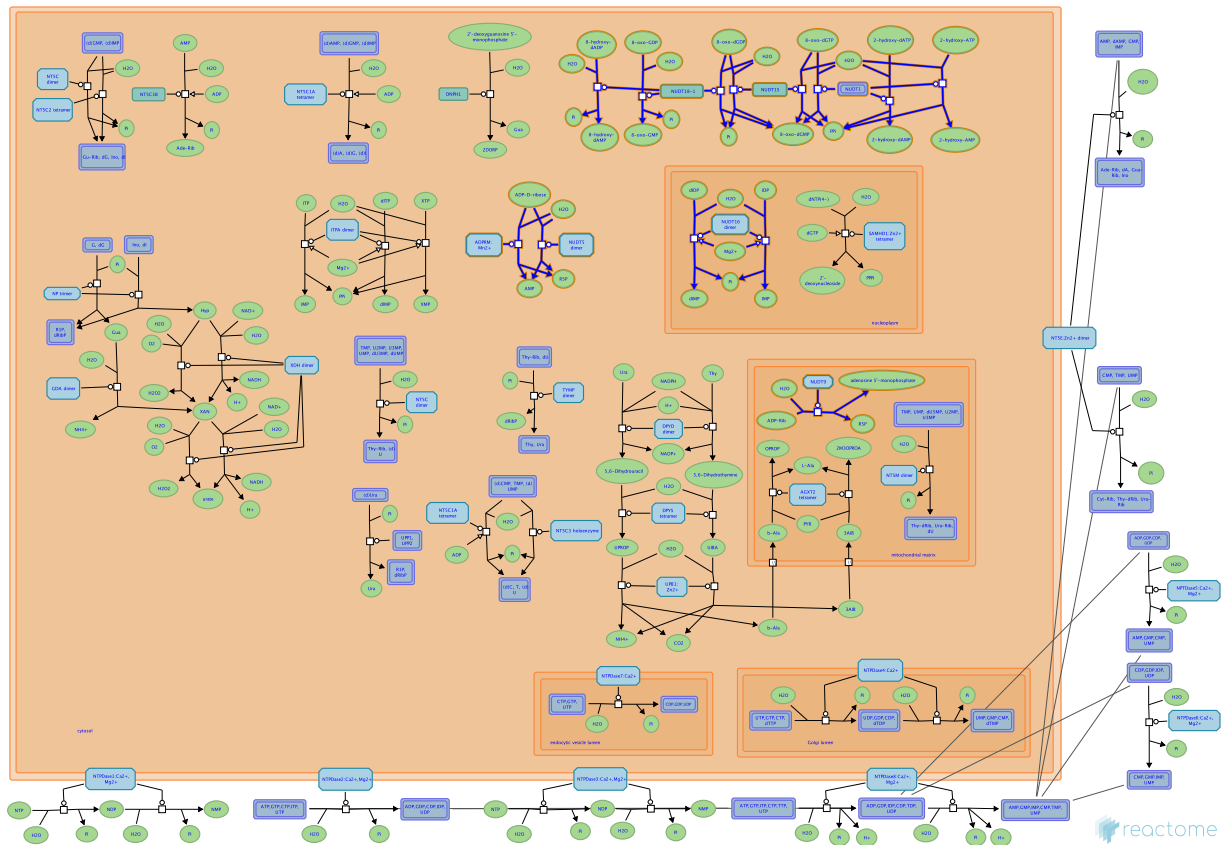
- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). 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: 77

This document contains 1 pathway and 13 reactions ([see Table of Contents](#))

# Phosphate bond hydrolysis by NUDT proteins ↗

Stable identifier: R-HSA-2393930



Enzymes that belong to the NUDT (Nudix) superfamily catalyze the hydrolysis of phosphodiester bonds in molecules including nucleoside triphosphates and diphosphates and nucleotide sugars. Family members are defined by the presence of an amino acid sequence motif shared with the *E. coli* MutT gene product, and are involved in diverse physiological processes (Mildvan et al. 2005; McLennan 2006).

The hydrolysis of nucleoside di and triphosphates whose purine bases have been oxidized or deaminated may protect the cell from the mutational damage that would occur if modified deoxyribonucleotides were incorporated into DNA and from the aberrant protein synthesis that would occur if modified ribonucleotides were incorporated into mRNA (Iyama et al. 2010; Takagi et al. 2012). The hydrolysis of ADP ribose may prevent the aberrant spontaneous ADP ribosylation of cellular proteins that could occur were this molecule to accumulate to high levels in the cell (Perraud et al. 2003; Shen et al. 2003). This hypothesis is further supported by the demonstration that mice lacking NUDT1 show an increased lifetime incidence of liver and other tumors compared to normal controls, and that rapidly metabolizing tumor cells in culture are killed under conditions where synthesis of NUDT1 protein is suppressed or its catalytic activity is inhibited (Gad et al. 2014; Huber et al. 2014).

## Literature references

- Iyama, T., Abolhassani, N., Tsuchimoto, D., Nonaka, M., Nakabeppu, Y. (2010). NUDT16 is a (deoxy)inosine diphosphatase, and its deficiency induces accumulation of single-strand breaks in nuclear DNA and growth arrest. *Nucleic Acids Res.*, 38, 4834-43. ↗
- Huber, KV., Salah, E., Radic, B., Gridling, M., Elkins, JM., Stukalov, A. et al. (2014). Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. *Nature*, 508, 222-7. ↗

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. [↗](#)

Mildvan, AS., Xia, Z., Azurmendi, HF., Saraswat, V., Legler, PM., Massiah, MA. et al. (2005). Structures and mechanisms of Nudix hydrolases. *Arch. Biochem. Biophys.*, 433, 129-43. [↗](#)

Gad, H., Koolmeister, T., Jemth, AS., Eshtad, S., Jacques, SA., Ström, CE. et al. (2014). MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. *Nature*, 508, 215-21. [↗](#)

## **Editions**

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.
2014-04-16	Revised	D'Eustachio, P.

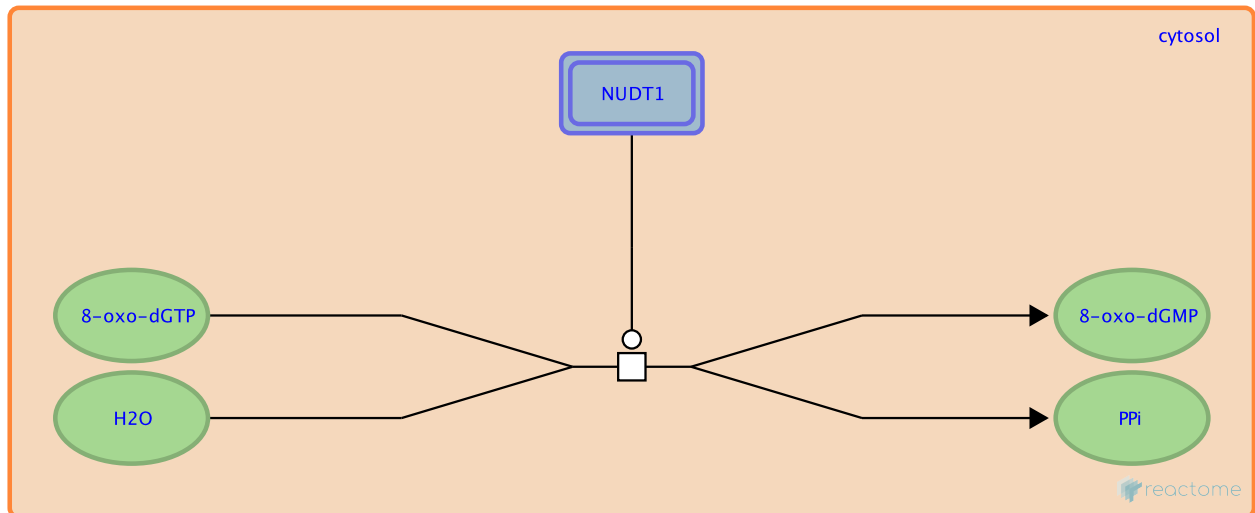
## NUDT1 hydrolyses 8-oxo-dGTP to 8-oxo-dGMP ↗

**Location:** Phosphate bond hydrolysis by NUDT proteins

**Stable identifier:** R-HSA-2395849

**Type:** transition

**Compartments:** cytosol



NUDT1 (MTH1) catalyzes the reaction of 8-oxo-dGTP and water to form 8-oxo-dGMP and PPi (pyrophosphate). Four NUDT1 proteins have been identified, encoded by a single gene with alternative start codons (Oda et al. 1999). The shortest of these, NUDT1 p18, has been biochemically (Sakumi et al. 1993; Takagi et al. 2012) and structurally (Mishima et al. 2004) characterized and shown to catalyze hydrolysis of 8-oxo-dGTP. The active enzyme is a monomer associated with a magnesium ion (Mishima et al. 2004). The longer isoforms all consist of the p18 polypeptide with aminoterminal extensions and are presumed to be active as well but have not been experimentally characterized. The p18 isoform is predominantly cytosolic (Kang et al. 1995). Its expression prevents the accumulation of oxo-guanine bases in DNA in mutant mouse cells lacking endogenous NUDT1 activity (Yoshimura et al. 2003).

Together, these data support the hypothesis that by cleaving 8-oxo-dGTP and thus preventing its incorporation into DNA NUDT1 provides a physiologically important defense against mutagenesis due to oxidative stress. This hypothesis is further supported by the demonstration that mice lacking NUDT1 show an increased lifetime incidence of liver and other tumors compared to normal controls, and that rapidly metabolizing tumor cells in culture are killed under conditions where synthesis of NUDT1 protein is suppressed or its catalytic activity is inhibited (Gad et al. 2014; Huber et al. 2014).

### Literature references

- Gad, H., Koolmeister, T., Jemth, AS., Eshtad, S., Jacques, SA., Ström, CE. et al. (2014). MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. *Nature*, 508, 215-21. ↗
- Huber, KV., Salah, E., Radic, B., Gridling, M., Elkins, JM., Stukalov, A. et al. (2014). Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. *Nature*, 508, 222-7. ↗
- Kang, D., Nishida, J., Iyama, A., Nakabeppu, Y., Furuichi, M., Fujiwara, T. et al. (1995). Intracellular localization of 8-oxo-dGTPase in human cells, with special reference to the role of the enzyme in mitochondria. *J. Biol. Chem.*, 270, 14659-65. ↗
- Mishima, M., Sakai, Y., Itoh, N., Kamiya, H., Furuichi, M., Takahashi, M. et al. (2004). Structure of human MTH1, a Nudix family hydrolase that selectively degrades oxidized purine nucleoside triphosphates. *J. Biol. Chem.*, 279, 33806-15. ↗

Oda, H., Taketomi, A., Maruyama, R., Itoh, R., Nishioka, K., Yakushiji, H. et al. (1999). Multi-forms of human MTH1 polypeptides produced by alternative translation initiation and single nucleotide polymorphism. *Nucleic Acids Res.*, 27, 4335-43. [↗](#)

## Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.
2014-04-16	Revised	D'Eustachio, P.

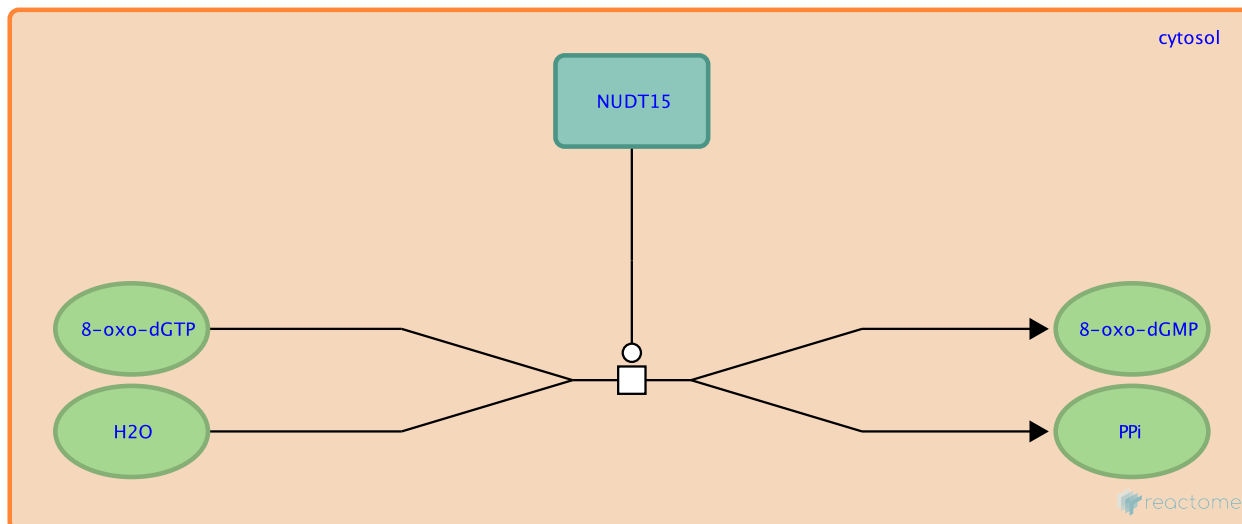
## NUDT15 hydrolyses 8-oxo-dGTP to 8-oxo-dGMP [↗](#)

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395869

**Type:** transition

**Compartments:** cytosol



NUDT15 (MTH2) catalyzes the reaction of 8-oxo-dGTP and water to form 8-oxo-dGMP and PPi (pyrophosphate). Cai et al. (2003) first identified this activity in studies of the homologous mouse protein; the activity of the human NUDT15 protein has since been confirmed experimentally (Takagi et al. 2012).

### Literature references

Cai, JP., Ishibashi, T., Takagi, Y., Hayakawa, H., Sekiguchi, M. (2003). Mouse MTH2 protein which prevents mutations caused by 8-oxoguanine nucleotides. *Biochem. Biophys. Res. Commun.*, 305, 1073-7. [↗](#)

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. [↗](#)

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

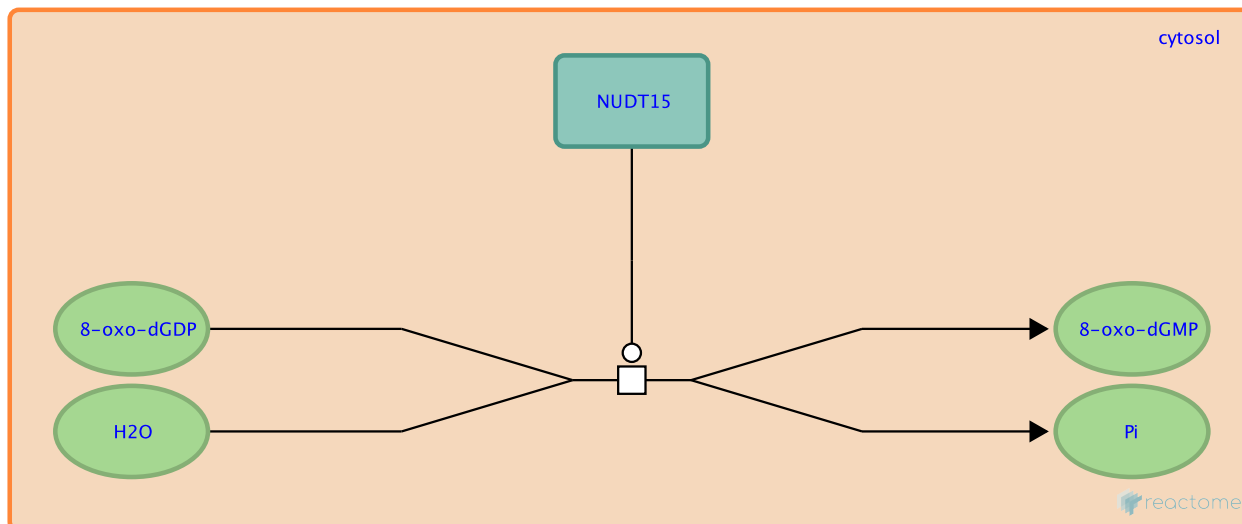
## NUDT15 hydrolyses 8-oxo-dGDP to 8-oxo-dGMP ↗

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395876

**Type:** transition

**Compartments:** cytosol



NUDT15 (MTH2) catalyzes the reaction of 8-oxo-dGDP and water to form 8-oxo-dGMP and Pi (orthophosphate) (Takagi et al. 2012). The subcellular location of NUDT15 has not been established but is assumed to be cytosolic like NUDT1.

### Literature references

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. ↗

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.



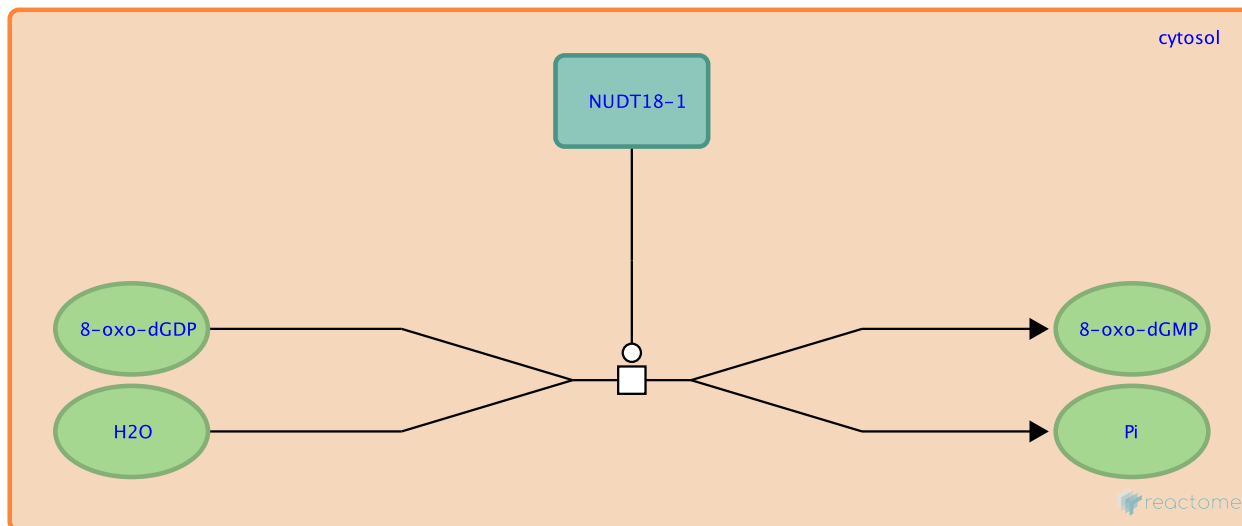
## NUDT18 hydrolyses 8-oxo-dGDP to 8-oxo-dGMP [↗](#)

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395879

**Type:** transition

**Compartments:** cytosol



NUDT18 (MTH3) catalyzes the reaction of 8-oxo-dGDP and water to form 8-oxo-dGMP and Pi (orthophosphate) (Takagi et al. 2012). The subcellular location of NUDT18 has not been established but is assumed to be cytosolic like NUDT1.

### Literature references

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. [↗](#)

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

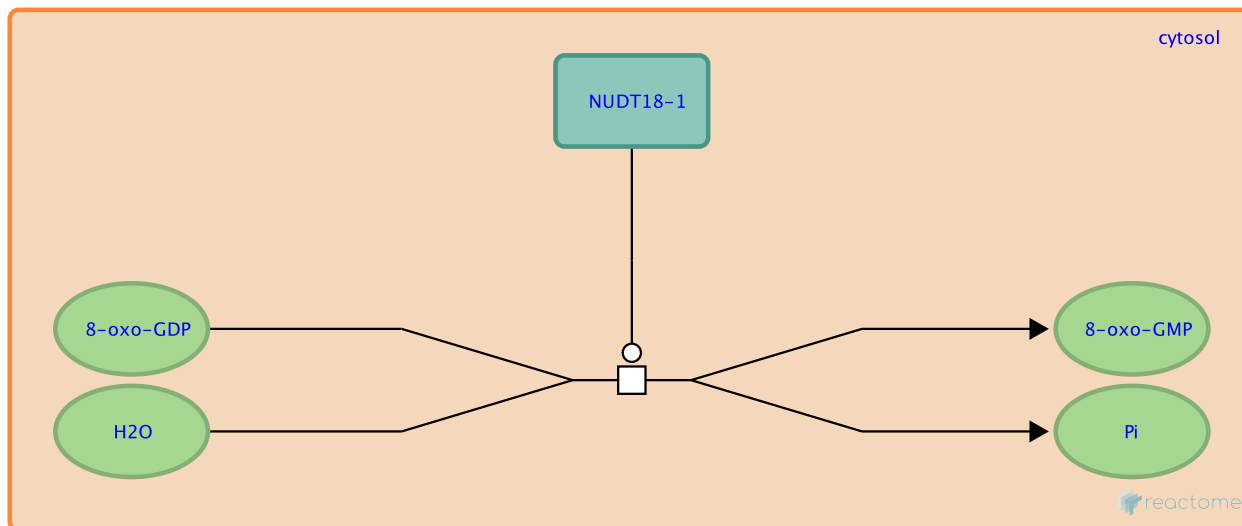
## NUDT18 hydrolyses 8-oxo-GDP to 8-oxo-GMP [↗](#)

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395873

**Type:** transition

**Compartments:** cytosol



NUDT18 (MTH3) catalyzes the reaction of 8-oxo-GDP and water to form 8-oxo-GMP and Pi (orthophosphate) (Takagi et al. 2012). The subcellular location of NUDT18 has not been established but is assumed to be cytosolic like NUDT1.

### Literature references

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. [↗](#)

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

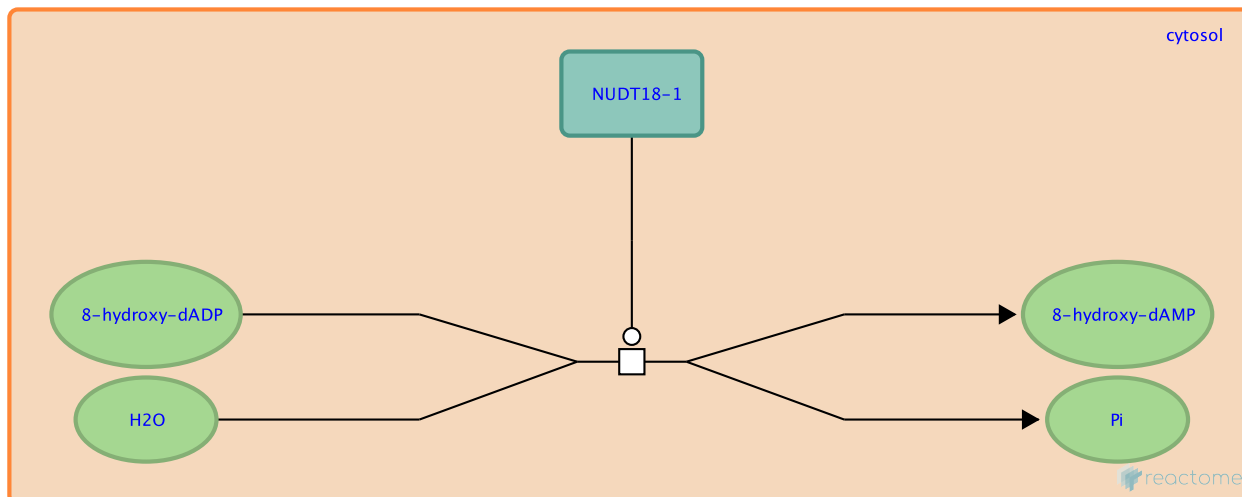
## NUDT18 hydrolyses 8-OH-dADP to 8-OH-dAMP ↗

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395965

**Type:** transition

**Compartments:** cytosol



NUDT18 (MTH3) catalyzes the reaction of 8-hydroxy-dADP and water to form 8-hydroxy-dAMP and Pi (orthophosphate) (Takagi et al. 2012). The subcellular location of NUDT18 has not been established but is assumed to be cytosolic like NUDT1.

### Literature references

Takagi, Y., Setoyama, D., Ito, R., Kamiya, H., Yamagata, Y., Sekiguchi, M. (2012). Human MTH3 (NUDT18) Protein Hydrolyzes Oxidized Forms of Guanosine and Deoxyguanosine Diphosphates: COMPARISON WITH MTH1 AND MTH2. *J. Biol. Chem.*, 287, 21541-9. ↗

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

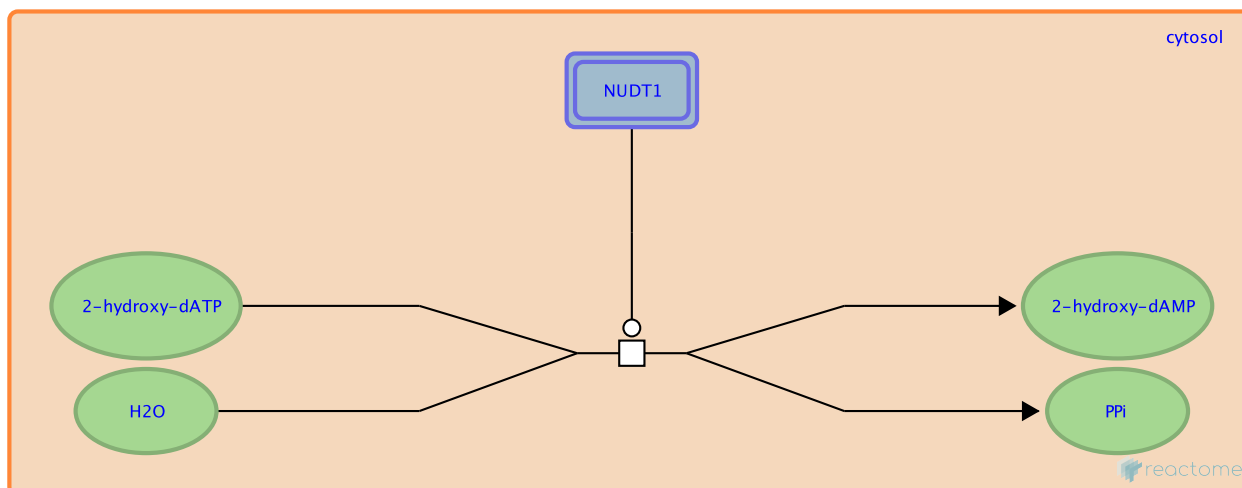
## NUDT1 hydrolyses 2-OH-dATP to 2-OH-dAMP ↗

**Location:** Phosphate bond hydrolysis by NUDT proteins

**Stable identifier:** R-HSA-2395818

**Type:** transition

**Compartments:** cytosol



NUDT1 (MTH1) catalyzes the reaction of 2-hydroxy-dATP and water to form 2-hydroxy-dAMP and PPi (pyrophosphate). Four NUDT1 proteins have been identified, encoded by a single gene with alternative start codons (Oda et al. 1999). The shortest of these, NUDT1 p18, has been shown to catalyze hydrolysis of 2-hydroxy-dATP (Fujikawa et al. 1993; Sakai et al. 2002). The active enzyme is a monomer associated with a magnesium ion (Mishima et al. 2004). The longer isoforms all consist of the p18 polypeptide with aminoterminal extensions and are presumed to be active as well but have not been experimentally characterized. The p18 isoform is predominantly cytosolic (Kang et al. 1995). Its expression prevents the accumulation of modified adenosine bases in DNA in mutant mouse cells lacking endogenous NUDT1 activity (Yoshimura et al. 2003).

Together, these data support the hypothesis that by cleaving 2-hydroxy-dATP and thus preventing its incorporation into DNA, NUDT1 provides a physiologically important defense against mutagenesis due to oxidative stress. This hypothesis is further supported by the demonstration that mice lacking NUDT1 show an increased lifetime incidence of liver and other tumors compared to normal controls, and that rapidly metabolizing tumor cells in culture are killed under conditions where synthesis of NUDT1 protein is suppressed or its catalytic activity is inhibited (Gad et al. 2014; Huber et al. 2014).

### Literature references

- Fujikawa, K., Kamiya, H., Yakushiji, H., Fujii, Y., Nakabeppu, Y., Kasai, H. (1999). The oxidized forms of dATP are substrates for the human MutT homologue, the hMTH1 protein. *J. Biol. Chem.*, 274, 18201-5. ↗
- Gad, H., Koolmeister, T., Jemth, AS., Eshtad, S., Jacques, SA., Ström, CE. et al. (2014). MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. *Nature*, 508, 215-21. ↗
- Huber, KV., Salah, E., Radic, B., Gridling, M., Elkins, JM., Stukalov, A. et al. (2014). Stereospecific targeting of MTH1 by (S)-crizotinib as an anticancer strategy. *Nature*, 508, 222-7. ↗
- Kang, D., Nishida, J., Iyama, A., Nakabeppu, Y., Furuichi, M., Fujiwara, T. et al. (1995). Intracellular localization of 8-oxo-dGTPase in human cells, with special reference to the role of the enzyme in mitochondria. *J. Biol. Chem.*, 270, 14659-65. ↗

Mishima, M., Sakai, Y., Itoh, N., Kamiya, H., Furuichi, M., Takahashi, M. et al. (2004). Structure of human MTH1, a Nudix family hydrolase that selectively degrades oxidized purine nucleoside triphosphates. *J. Biol. Chem.*, 279, 33806-15. [↗](#)

## Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.
2014-04-16	Revised	D'Eustachio, P.

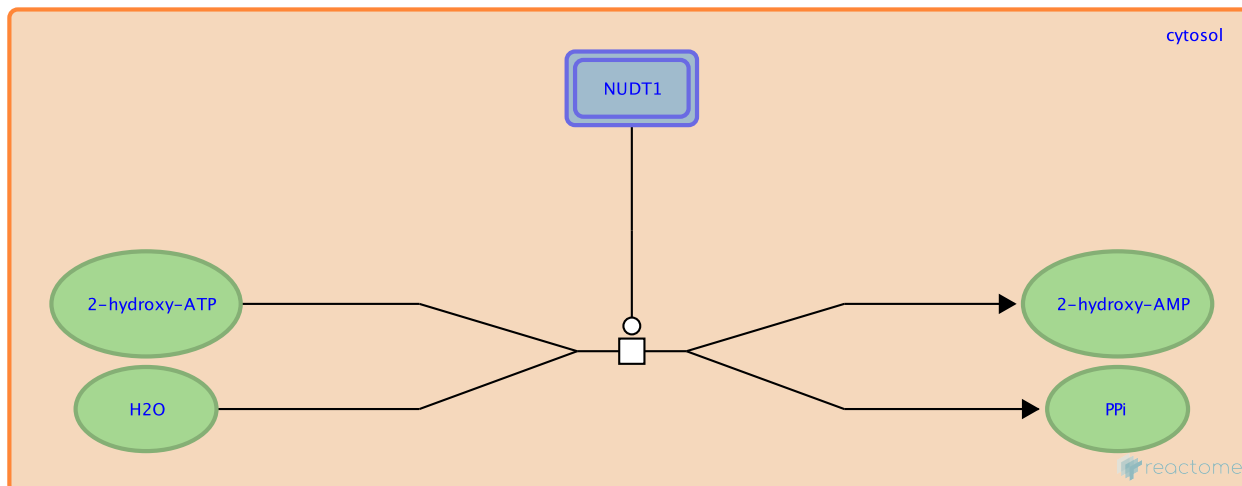
## NUDT1 hydrolyses 2-OH-ATP to 2-OH-AMP ↗

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2395872

**Type:** transition

**Compartments:** cytosol



NUDT1 (MTH1) catalyzes the reaction of 2-hydroxy-ATP and water to form 2-hydroxy-AMP and PPi (pyrophosphate). Four NUDT1 proteins have been identified, encoded by a single gene with alternative start codons (Oda et al. 1999). The shortest of these, NUDT1 p18, has been shown to catalyze hydrolysis of 2-hydroxy-ATP (Fujikawa et al. 2001). The active enzyme is a monomer associated with a magnesium ion (Mishima et al. 2004). The longer isoforms all consist of the p18 polypeptide with aminoterminal extensions and are presumed to be active as well, but have not been experimentally characterized. The p18 isoform is predominantly cytosolic (Kang et al. 1995).

### Literature references

- Fujikawa, K., Kamiya, H., Yakushiji, H., Nakabeppu, Y., Kasai, H. (2001). Human MTH1 protein hydrolyzes the oxidized ribonucleotide, 2-hydroxy-ATP. *Nucleic Acids Res.*, 29, 449-54. ↗
- Kang, D., Nishida, J., Iyama, A., Nakabeppu, Y., Furuichi, M., Fujiwara, T. et al. (1995). Intracellular localization of 8-oxo-dGTPase in human cells, with special reference to the role of the enzyme in mitochondria. *J. Biol. Chem.*, 270, 14659-65. ↗
- Mishima, M., Sakai, Y., Itoh, N., Kamiya, H., Furuichi, M., Takahashi, M. et al. (2004). Structure of human MTH1, a Nudix family hydrolase that selectively degrades oxidized purine nucleoside triphosphates. *J. Biol. Chem.*, 279, 33806-15. ↗

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

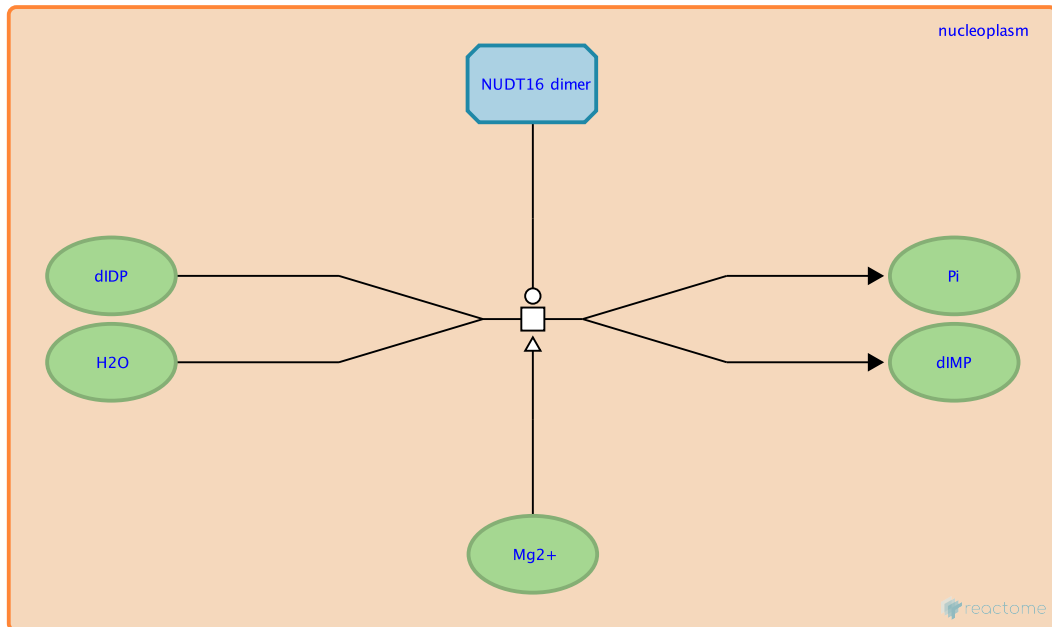
## NUDT16 hydrolyses dIDP to dIMP [↗](#)

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2509793

**Type:** transition

**Compartments:** nucleoplasm



NUDT16 dimer catalyzes the reaction of dIDP and water to form dIMP and Pi (orthophosphate). Mg<sup>++</sup> is required for enzymatic activity. The protein is mostly located in the nucleus and concentrated in the nucleolus, where it can also mediate the decapping of U8 small nucleolar RNA (Iyama et al. 2010; Peculis et al. 2007).

### Literature references

Iyama, T., Abolhassani, N., Tsuchimoto, D., Nonaka, M., Nakabeppu, Y. (2010). NUDT16 is a (deoxy)inosine diphosphatase, and its deficiency induces accumulation of single-strand breaks in nuclear DNA and growth arrest. *Nucleic Acids Res.*, 38, 4834-43. [↗](#)

Peculis, BA., Reynolds, K., Cleland, M. (2007). Metal determines efficiency and substrate specificity of the nuclear NUDIX decapping proteins X29 and H29K (Nudt16). *J. Biol. Chem.*, 282, 24792-805. [↗](#)

### Editions

2012-10-05	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

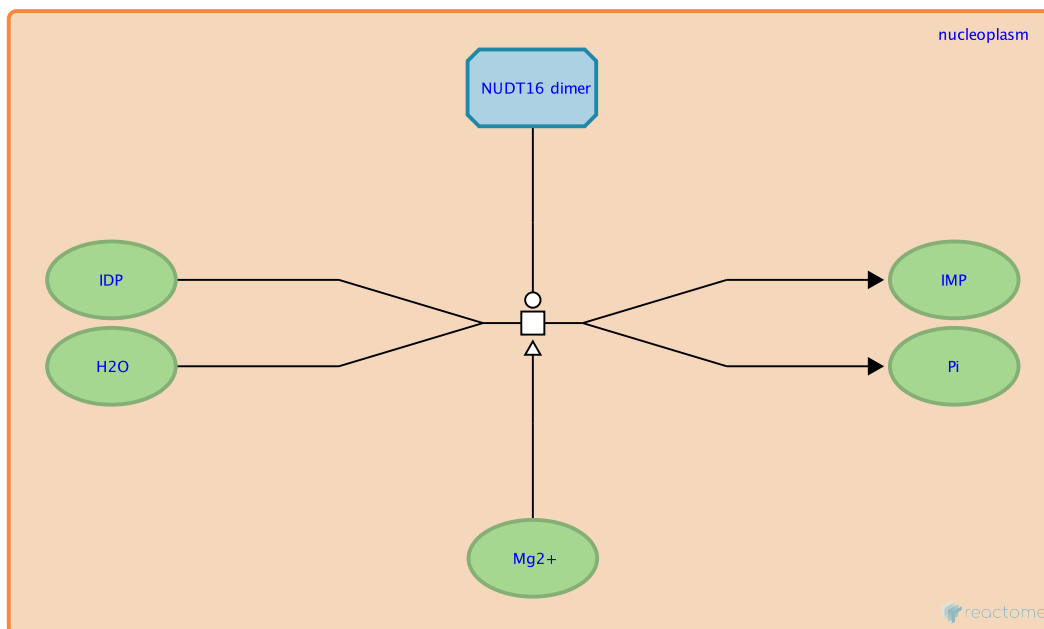
## NUDT16 hydrolyses IDP to IMP ↗

**Location:** Phosphate bond hydrolysis by NUDT proteins

**Stable identifier:** R-HSA-2509816

**Type:** transition

**Compartments:** nucleoplasm



NUDT16 dimer catalyzes the reaction of IDP and water to form IMP and Pi (orthophosphate). Mg<sup>++</sup> is required for enzymatic activity. The protein is mostly located in the nucleus and concentrated in the nucleolus, where it can also mediate the decapping of U8 small nucleolar RNA (Iyama et al. 2010; Peculis et al. 2007).

### Literature references

Iyama, T., Abolhassani, N., Tsuchimoto, D., Nonaka, M., Nakabeppu, Y. (2010). NUDT16 is a (deoxy)inosine diphosphatase, and its deficiency induces accumulation of single-strand breaks in nuclear DNA and growth arrest. *Nucleic Acids Res.*, 38, 4834-43. ↗

Peculis, BA., Reynolds, K., Cleland, M. (2007). Metal determines efficiency and substrate specificity of the nuclear NUDIX decapping proteins X29 and H29K (Nudt16). *J. Biol. Chem.*, 282, 24792-805. ↗

### Editions

2012-10-05	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.



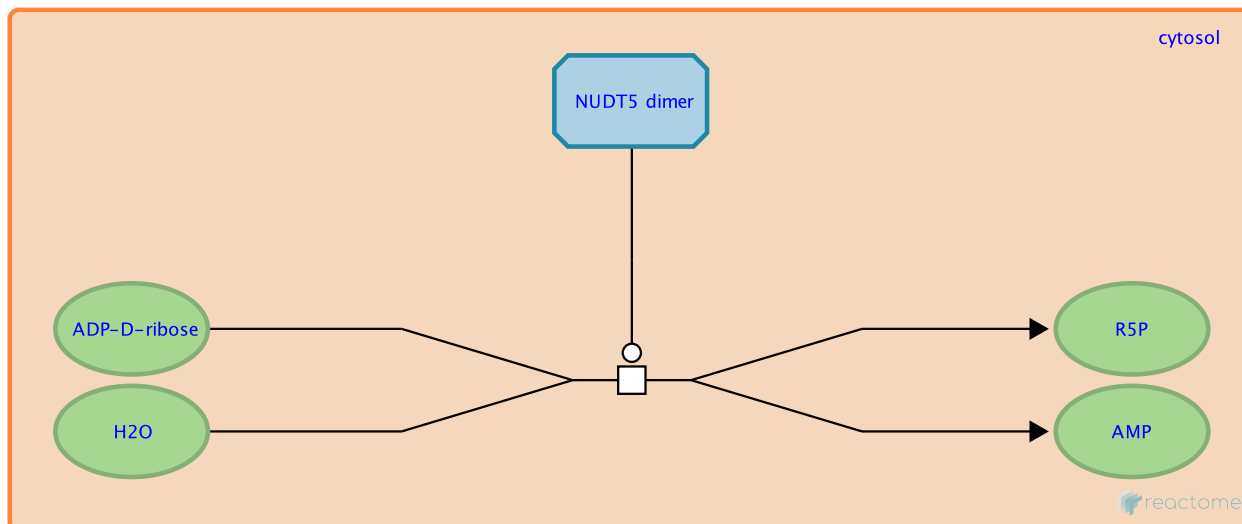
## Cytosolic NUDT5 hydrolyses ADP-ribose to R5P and AMP ↗

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2393939

**Type:** transition

**Compartments:** cytosol



Cytosolic NUDT5 dimer (ADP-ribose pyrophosphatase) catalyzes the hydrolysis of ADP-ribose to form AMP and D-ribose 5-phosphate. Each NUDT5 subunit is associated with three magnesium ions (Zha et al. 2006, 2008). NUDT5 also catalyzes the hydrolysis of 8-oxo-dGTP but with a strongly alkaline pH optimum (Ito et al. 2011) so the physiological relevance of this reaction is unclear and it is not annotated here.

### Literature references

Zha, M., Zhong, C., Peng, Y., Hu, H., Ding, J. (2006). Crystal structures of human NUDT5 reveal insights into the structural basis of the substrate specificity. *J. Mol. Biol.*, 364, 1021-33. ↗

Zha, M., Guo, Q., Zhang, Y., Yu, B., Ou, Y., Zhong, C. et al. (2008). Molecular mechanism of ADP-ribose hydrolysis by human NUDT5 from structural and kinetic studies. *J. Mol. Biol.*, 379, 568-78. ↗

Ito, R., Sekiguchi, M., Setoyama, D., Nakatsu, Y., Yamagata, Y., Hayakawa, H. (2011). Cleavage of oxidized guanine nucleotide and ADP sugar by human NUDT5 protein. *J. Biochem.*, 149, 731-8. ↗

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

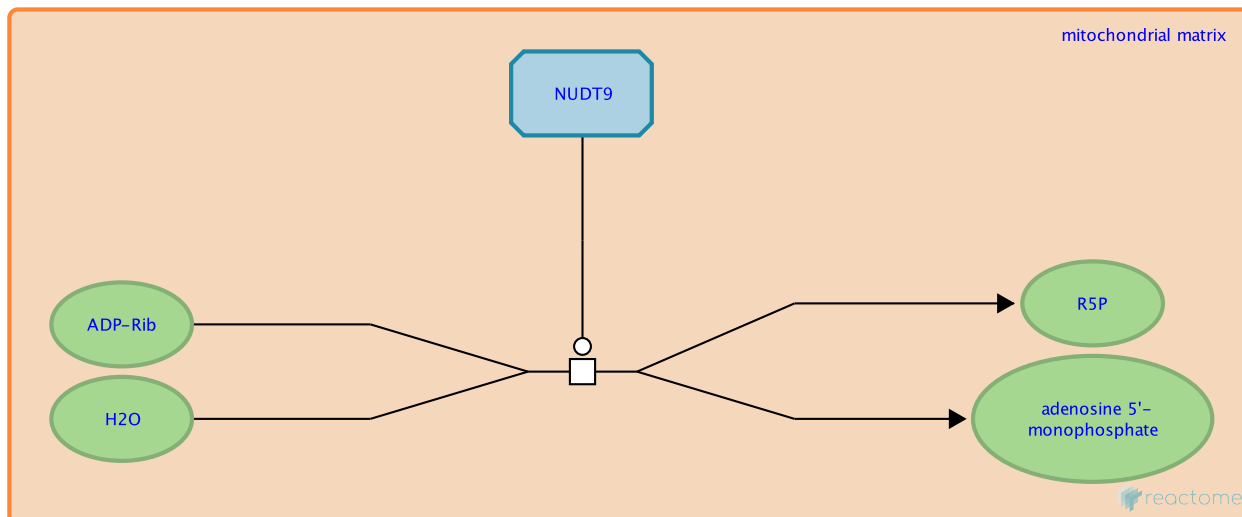
## Mitochondrial NUDT9 hydrolyses ADP-ribose to R5P and AMP ↗

**Location:** [Phosphate bond hydrolysis by NUDT proteins](#)

**Stable identifier:** R-HSA-2393954

**Type:** transition

**Compartments:** mitochondrial matrix



Mitochondrial NUDT9 (ADP-ribose pyrophosphatase) catalyzes the hydrolysis of ADP-ribose to form AMP and D-ribose 5-phosphate. The active enzyme is the longer of two isoforms generated by alternative splicing and is a monomer complexed with two magnesium ions (Perraud et al. 2003; Shen et al. 2003).

### Literature references

Perraud, AL., Shen, BW., Dunn, CA., Rippe, K., Smith, MK., Bessman, MJ. et al. (2003). NUDT9, a member of the Nudix hydrolase family, is an evolutionarily conserved mitochondrial ADP-ribose pyrophosphatase. *J. Biol. Chem.*, 278, 1794-801. ↗

Shen, BW., Perraud, AL., Scharenberg, AM., Stoddard, BL. (2003). The crystal structure and mutational analysis of human NUDT9. *J. Mol. Biol.*, 332, 385-98. ↗

### Editions

2012-07-06	Authored, Edited	D'Eustachio, P.
2012-10-05	Reviewed	Ito, R.

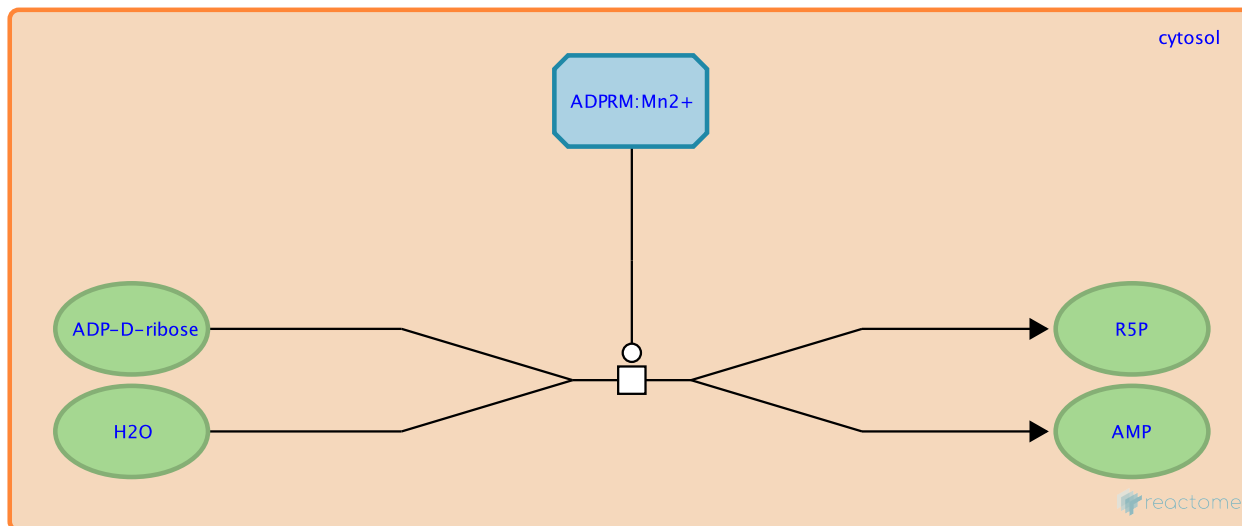
## ADPRM hydrolyses ADP-ribose to R5P and AMP ↗

**Location:** Phosphate bond hydrolysis by NUDT proteins

**Stable identifier:** R-HSA-5696049

**Type:** transition

**Compartments:** cytosol



Manganese-dependent ADP-ribose/CDP-alcohol diphosphatase (ADPRM:Mn<sup>2+</sup>) can mediate the hydrolysis of ADP-ribose and less efficiently, CDP-alcohols and 2',3'-cAMP (Cabezas et al. 2015).

### Literature references

Cabezas, A., Ribeiro, JM., Rodrigues, JR., López-Villamizar, I., Fernández, A., Canales, J. et al. (2015). Molecular bases of catalysis and ADP-ribose preference of human Mn<sup>2+</sup>-dependent ADP-ribose/CDP-alcohol diphosphatase and conversion by mutagenesis to a preferential cyclic ADP-ribose phosphohydrolase. *PLoS ONE*, 10, e0118680. ↗

### Editions

2015-05-27	Authored, Edited	Jassal, B.
2015-06-26	Reviewed	D'Eustachio, P.

# Table of Contents

Introduction	1
☞ Phosphate bond hydrolysis by NUDT proteins	2
☞ NUDT1 hydrolyses 8-oxo-dGTP to 8-oxo-dGMP	4
☞ NUDT15 hydrolyses 8-oxo-dGTP to 8-oxo-dGMP	6
☞ NUDT15 hydrolyses 8-oxo-dGDP to 8-oxo-dGMP	7
☞ NUDT18 hydrolyses 8-oxo-dGDP to 8-oxo-dGMP	8
☞ NUDT18 hydrolyses 8-oxo-GDP to 8-oxo-GMP	9
☞ NUDT18 hydrolyses 8-OH-dADP to 8-OH-dAMP	10
☞ NUDT1 hydrolyses 2-OH-dATP to 2-OH-dAMP	11
☞ NUDT1 hydrolyses 2-OH-ATP to 2-OH-AMP	13
☞ NUDT16 hydrolyses dIDP to dIMP	14
☞ NUDT16 hydrolyses IDP to IMP	15
☞ Cytosolic NUDT5 hydrolyses ADP-ribose to R5P and AMP	16
☞ Mitochondrial NUDT9 hydrolyses ADP-ribose to R5P and AMP	17
☞ ADPRM hydrolyses ADP-ribose to R5P and AMP	18
Table of Contents	19