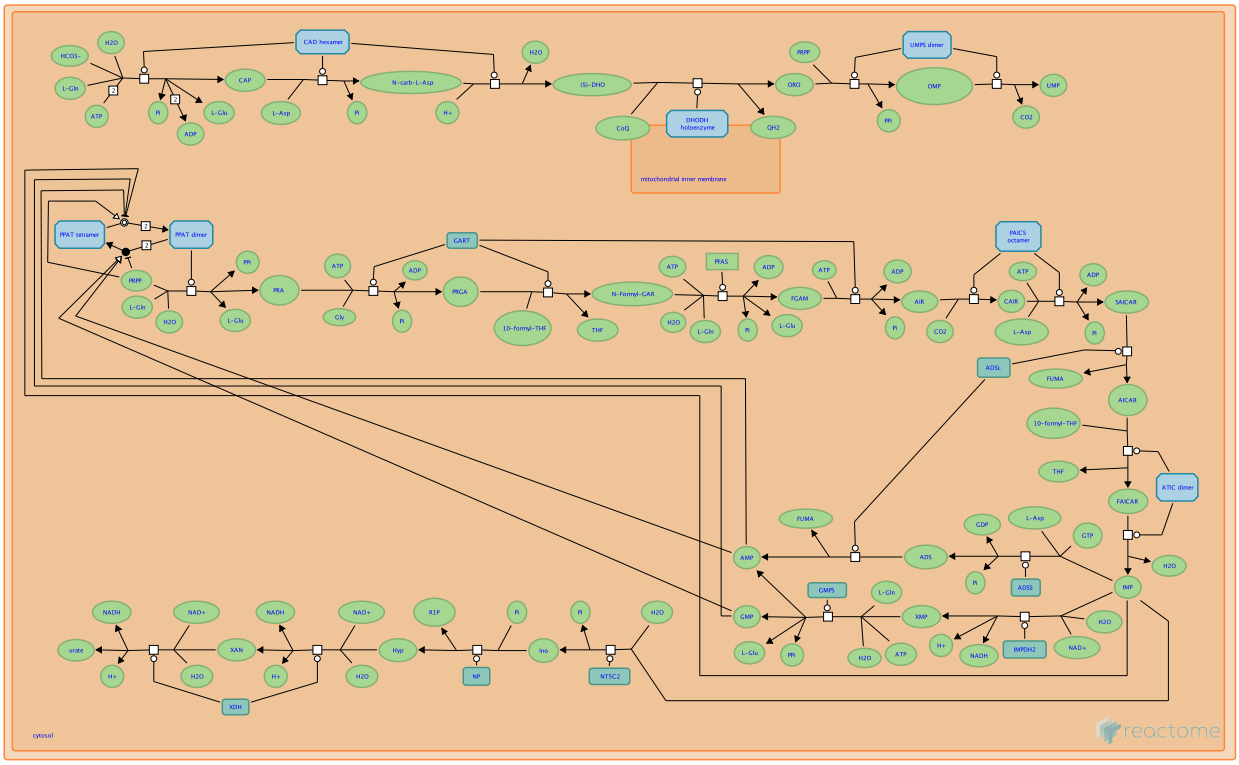
Nucleotide metabolism



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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. ↗

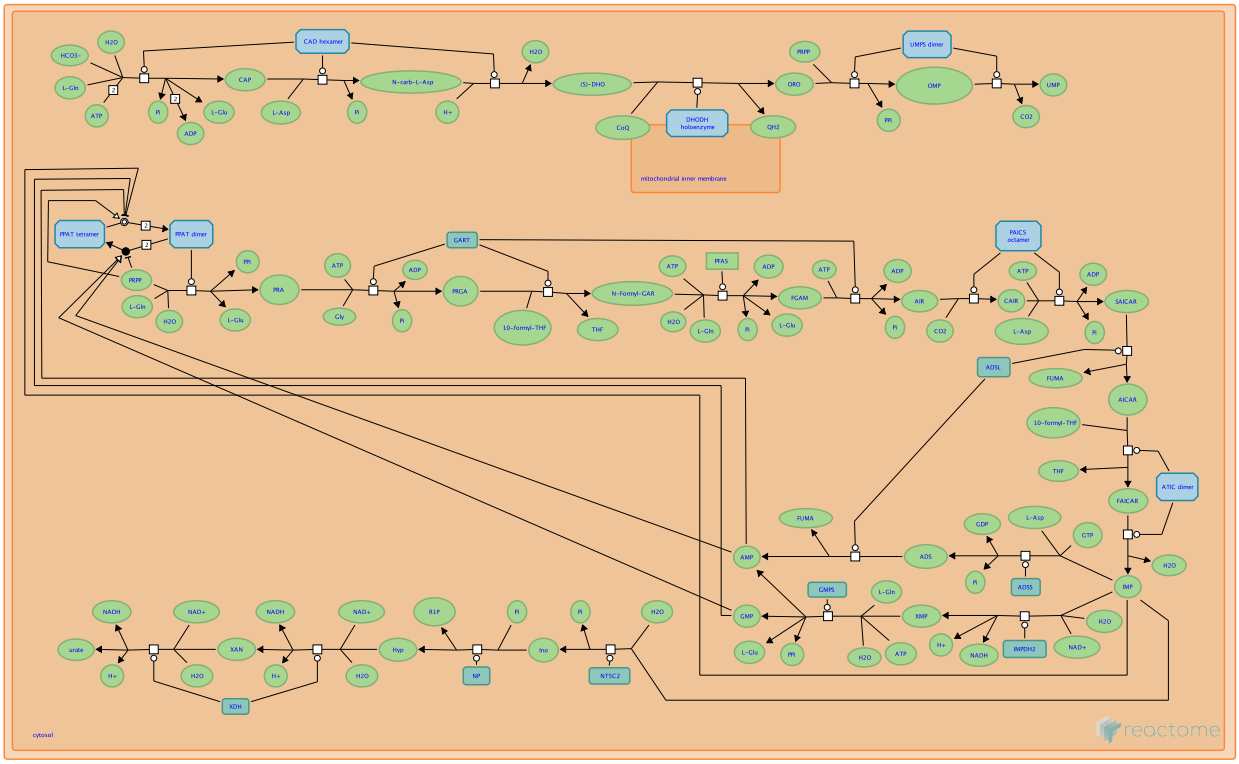
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 77

This document contains 3 pathways (see Table of Contents)

Nucleotide metabolism ↗

Stable identifier: R-GGA-419470



Nucleotides and their derivatives are used for short-term energy storage (ATP, GTP), for intra- and extracellular signaling (cAMP; adenosine), as enzyme cofactors (NAD, FAD), and for the synthesis of DNA and RNA. All of the nucleotides can be synthesized de novo. Additional metabolic pathways allow the interconversion of nucleotides, the salvage and reutilization of nucleotides released by degradation of DNA and RNA, and the catabolism of excess nucleotides. These pathways are regulated to control the total size of the intracellular nucleotide pool, to balance the relative amounts of individual nucleotides, and to couple the synthesis of deoxyribonucleotides to the onset of DNA replication (S phase of the cell cycle). The catabolism of purines via inosine monophosphate (IMP) to urate is the major route by which excess nitrogen is excreted from the body in chickens and other birds.

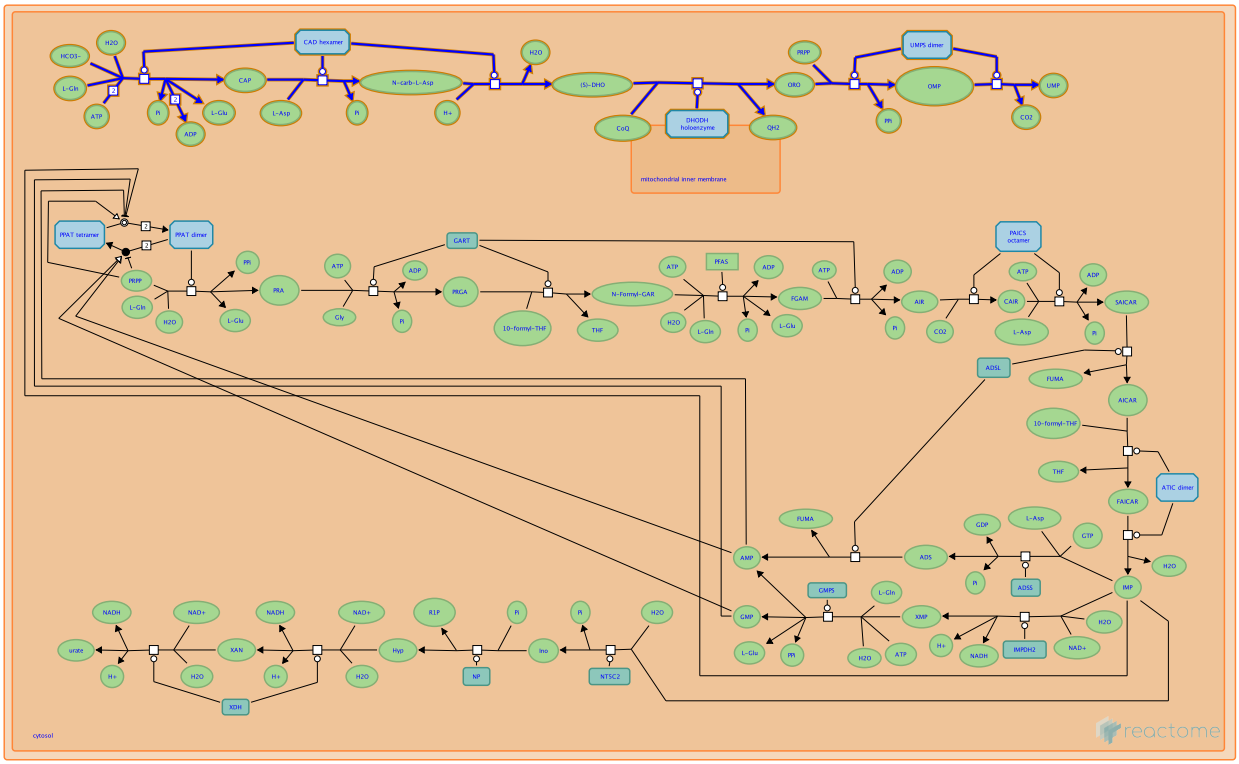
Editions

2009-05-01	Authored, Edited	D'Eustachio, P.

Pyrimidine metabolism: de novo synthesis of UMP ↗

Location: Nucleotide metabolism

Stable identifier: R-GGA-419469



The events of pyrimidine metabolism are conveniently if somewhat arbitrarily grouped into four pathways: de novo synthesis of uridine 5'-monophosphate (UMP), the biosynthesis of other pyrimidine ribo- and deoxyribonucleotides, pyrimidine salvage reactions, and pyrimidine catabolism. Here, the first of these pathways is annotated.

The pyrimidine orotate (orotic acid) is synthesized in a sequence of four reactions, deriving its atoms from glutamine, bicarbonate, and aspartate. A single multifunctional cytosolic enzyme catalyzes the first three of these reactions, while the last one is catalyzed by a mitochondrial enzyme. In two further reactions, catalyzed by a bifunctional cytosolic enzyme, orotate reacts with 1-phosphoribosyl 5-pyrophosphate (PRPP) to yield orotidine 5'-monophosphate, which is decarboxylated to yield uridine 5'-monophosphate (UMP). These reactions have been very well studied in mammals, including humans (Jones 1980). The chicken enzymes are known only as predicted gene products of open reading frames identified through sequencing of the chicken genome and high-throughput mRNA sequencing, and all molecular details of the chicken reactions described here are inferred from those of their human counterparts.

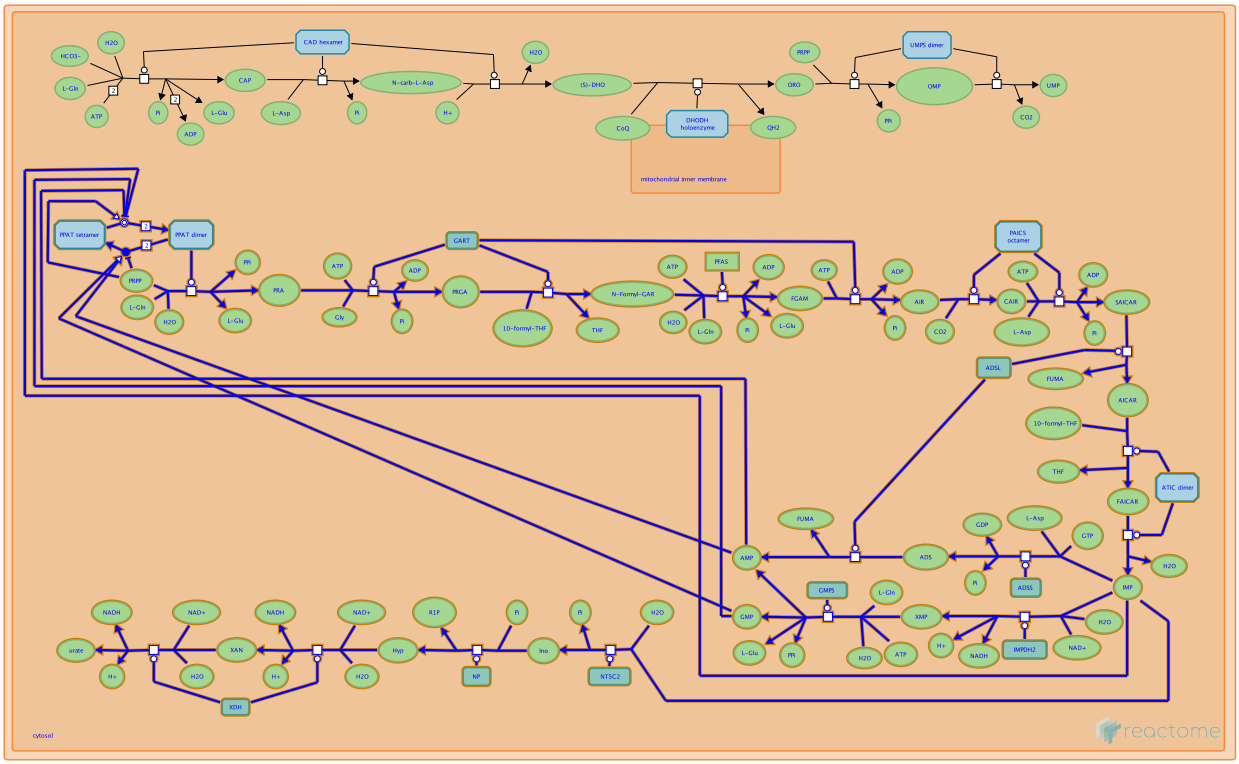
Editions

2009-05-01	Authored, Edited	D'Eustachio, P.

Purine metabolism ↗

Location: Nucleotide metabolism

Stable identifier: R-GGA-419474



The events of purine metabolism are conveniently if somewhat arbitrarily grouped into four pathways: de novo synthesis of inosine 5'-monophosphate (IMP), the biosynthesis of other purine ribo- and deoxyribonucleotides, purine salvage reactions, and purine catabolism. Here, the pathways of IMP, AMP, and GMP synthesis are annotated, as well as that for urate synthesis. Urate synthesis is notable as this molecule provides the major route for excretion of excess nitrogen in chickens and other birds (Krebs 1977).

Literature references

Krebs, HA. (1977). Regulatory mechanisms in purine biosynthesis. *Adv Enzyme Regul, 16*, 409-22. ↗

Editions

2009-05-01	Authored, Edited	D'Eustachio, P.

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