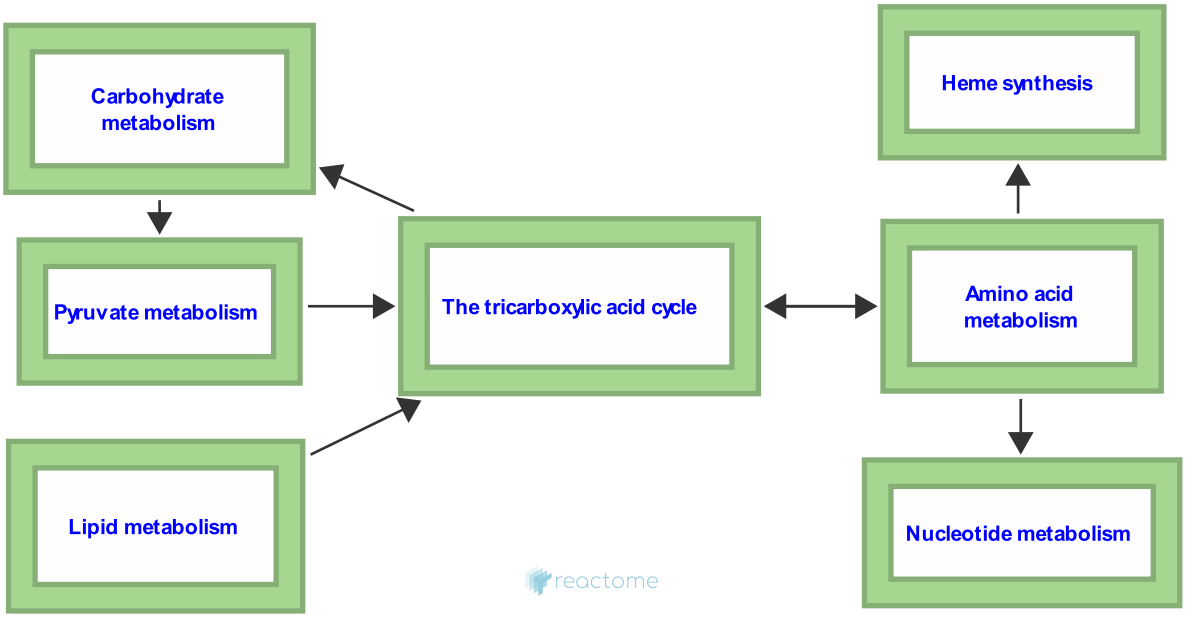
Metabolism



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12/10/2024

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. ↗

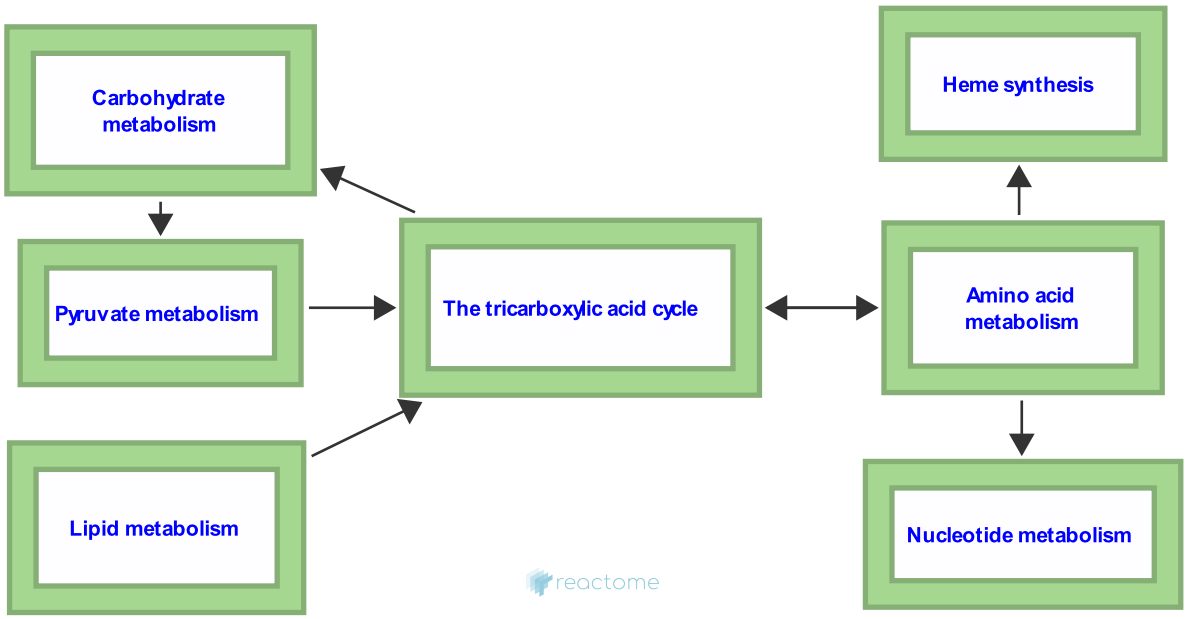
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Reactome database release: 90

This document contains 8 pathways (see Table of Contents)

Metabolism ↗

Stable identifier: R-GGA-1660598



Cellular metabolic processes generate energy through the oxidation of molecules consumed in the diet and mediate the synthesis of diverse essential molecules not taken in the diet as well as the inactivation and elimination of toxic ones generated endogenously or present in the extracellular environment. The processes of energy metabolism can be classified into two groups according to whether they involve carbohydrate-derived or lipid-derived molecules, and within each group it is useful to distinguish processes that mediate the breakdown and oxidation of these molecules to yield energy from ones that mediate their synthesis and storage as internal energy reserves. Synthetic reactions are conveniently grouped by the chemical nature of the end products, such as nucleotides, amino acids and related molecules, and porphyrins. Detoxification reactions (biological oxidations) are likewise conveniently classified by the chemical nature of the toxin.

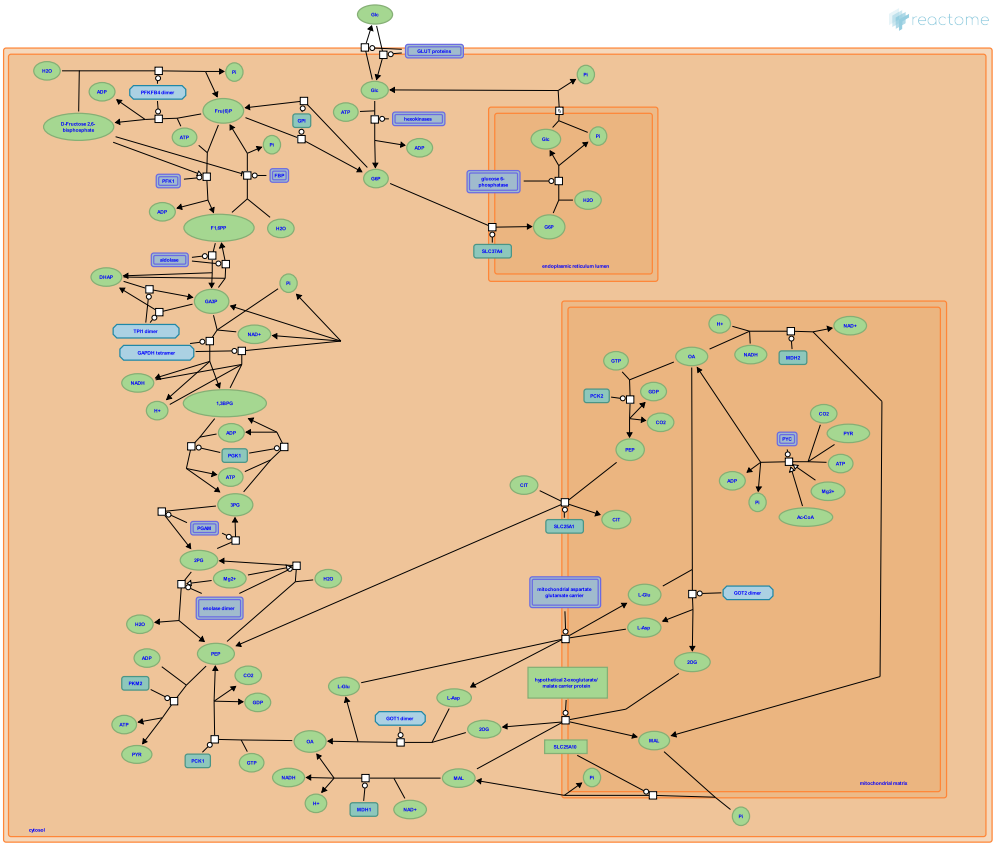
At the same time, all of these processes are tightly integrated. Intermediates in reactions of energy generation are starting materials for biosyntheses of amino acids and other compounds, broad-specificity oxidoreductase enzymes can be involved in both detoxification reactions and biosyntheses, and hormone-mediated signaling processes function to coordinate the operation of energy-generating and energy-storing reactions and to couple these to other biosynthetic processes.

Annotations to date for *Gallus gallus* center on the steps of carbohydrate and pyruvate metabolism and the TCA cycle, specific aspects of amino acid and nucleotide metabolism, lipid biosynthesis (sphingolipid metabolism), and heme biosynthesis.

Carbohydrate metabolism ↗

Location: Metabolism

Stable identifier: R-GGA-353098



The pathways of carbohydrate metabolism are responsible for the extraction of energy and carbon skeletons for biosyntheses from dietary sugars and related molecules, and for the maintenance of blood glucose levels when dietary supplies are lacking. Here, the processes of glucose uptake, glycolysis, and gluconeogenesis are annotated.

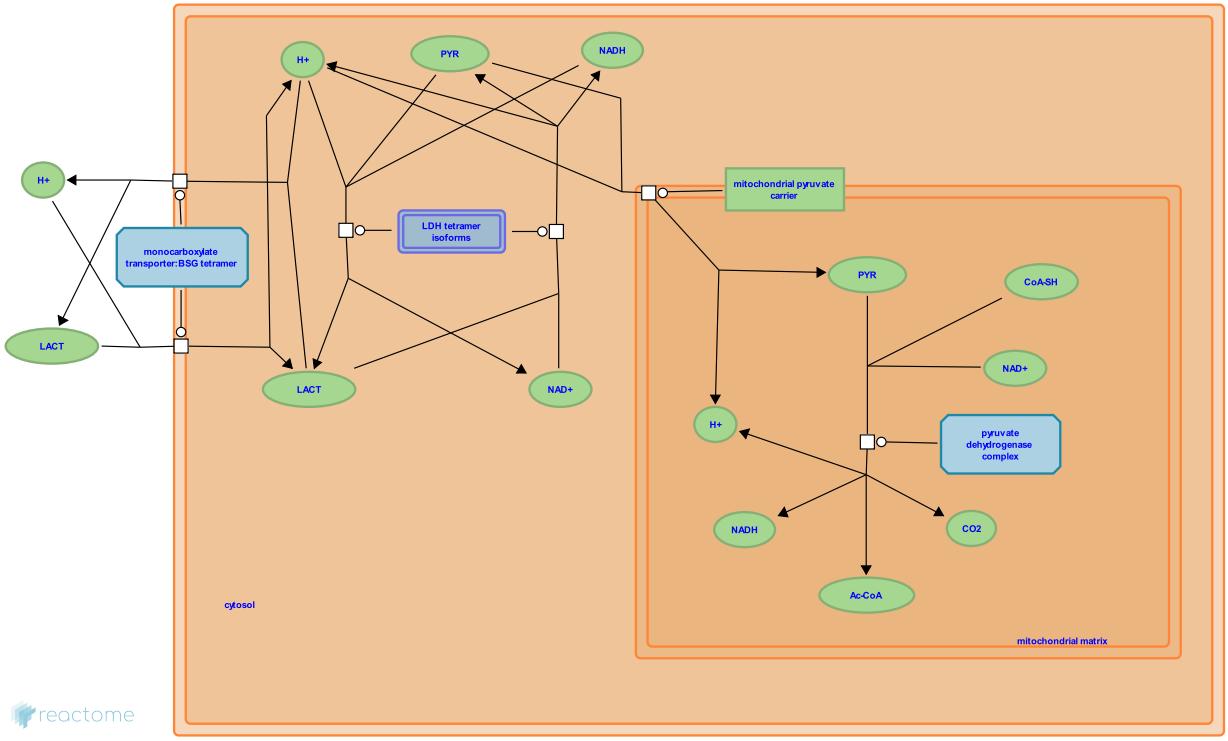
Editions

2008-09-10	Authored, Edited	D'Eustachio, P.
2008-09-10	Reviewed	Harris, RA.

Pyruvate metabolism ↗

Location: Metabolism

Stable identifier: R-GGA-373920



Pyruvate sits at an intersection of key pathways of energy metabolism. It is the end product of glycolysis and the starting point for gluconeogenesis IWatford 1985). It can be converted by the pyruvate dehydrogenase complex to acetyl CoA which can enter the TCA cycle or serve as the starting point for the syntheses of long chain fatty acids, steroids, and ketone bodies. It also plays a central role in balancing the energy needs of various tissues in the body: under anaerobic conditions (e.g., rapidly exercising white muscle), pyruvate is reduced to lactate which is exported from the cell and taken up by tissues that can re-oxidize it to pyruvate for futher oxidative metabolism via acetyl CoA (e.g., red muscle) or for gluconeogenesis (e.g., kidney cortex) (Wilson et al. 1998; Yorita et al. 1987).

Literature references

Jackson, VN., Bonen, A., Halestrap, AP., Wilson, MC., Pilegaard, H., Juel, C. et al. (1998). Lactic acid efflux from white skeletal muscle is catalyzed by the monocarboxylate transporter isoform MCT3. *J Biol Chem, 273*, 15920-6. ↗

Yamano, T., Ikeda, K., Shiota, M., Yorita, K., Kobayashi, T., Sugano, T. (1987). Distribution of glycolysis and gluconeogenesis in perfused chicken kidney. *Am J Physiol, 253*, R679-86. ↗

Watford, M. (1985). Gluconeogenesis in the chicken: regulation of phosphoenolpyruvate carboxykinase gene expression. *Fed Proc, 44*, 2469-74. ↗

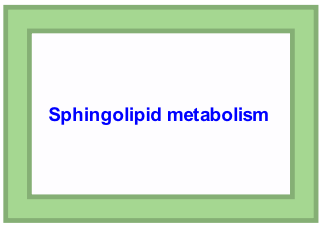
Editions

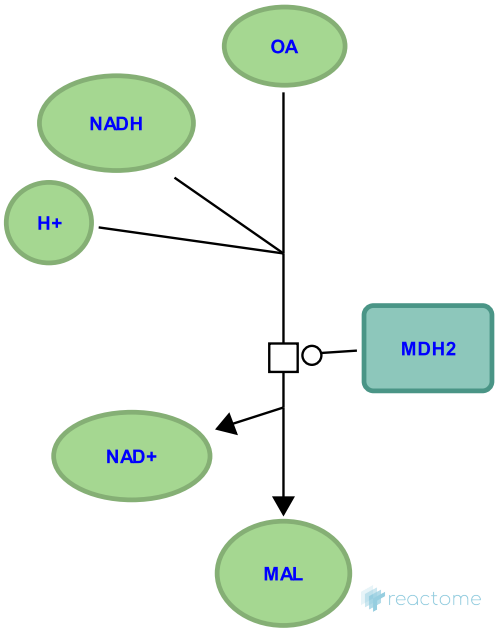
2008-09-10	Authored, Edited	D'Eustachio, P.

Lipid metabolism ↗

Location: Metabolism

Stable identifier: R-GGA-372442





The reduction of oxaloacetate to malate is a reaction in common between pathways of lipid and carbohydrate metabolism. Aspects of reactions involved in sphingolipid synthesis have been inferred from the known properties of the orthologous human enzymes.

Editions

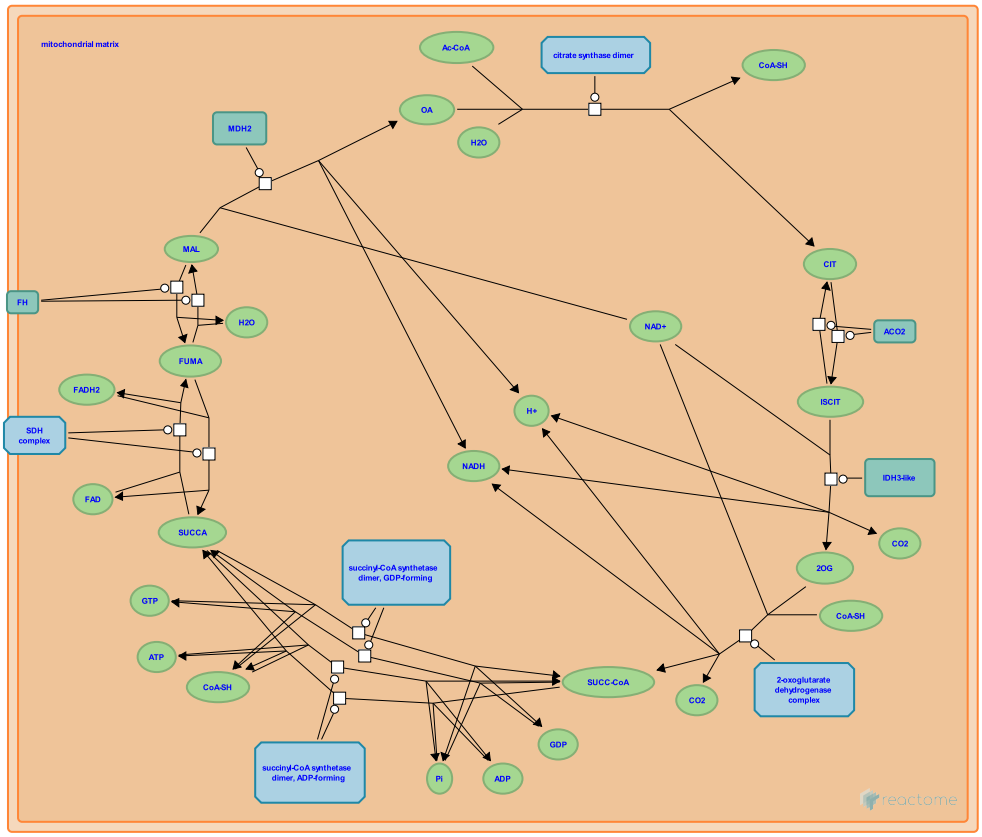
2008-09-10	Authored	D'Eustachio, P.

The tricarboxylic acid cycle ↗

Location: Metabolism

Stable identifier: R-GGA-372987

Compartments: mitochondrial matrix



The reactions of the tricarboxylic acid (TCA cycle) mediate the complete oxidation of two carbon atoms from acetyl CoA, derived from catabolism of glucose and long chain fatty acids, to CO2, and the generation of NADH + H+ and FADH2. Carbon skeletons derived from catabolism of amino acids enter the TCA cycle as oxaloacetate, 2-oxoglutarate, and succinyl CoA. The TCA cycle thus plays a central role in the generation of energy by catabolism of energy-rich molecules from the diet, but also plays a critical role in the interconversions of metabolic intermediates needed to maintain pools of amino acids and other metabolites at physiological levels.

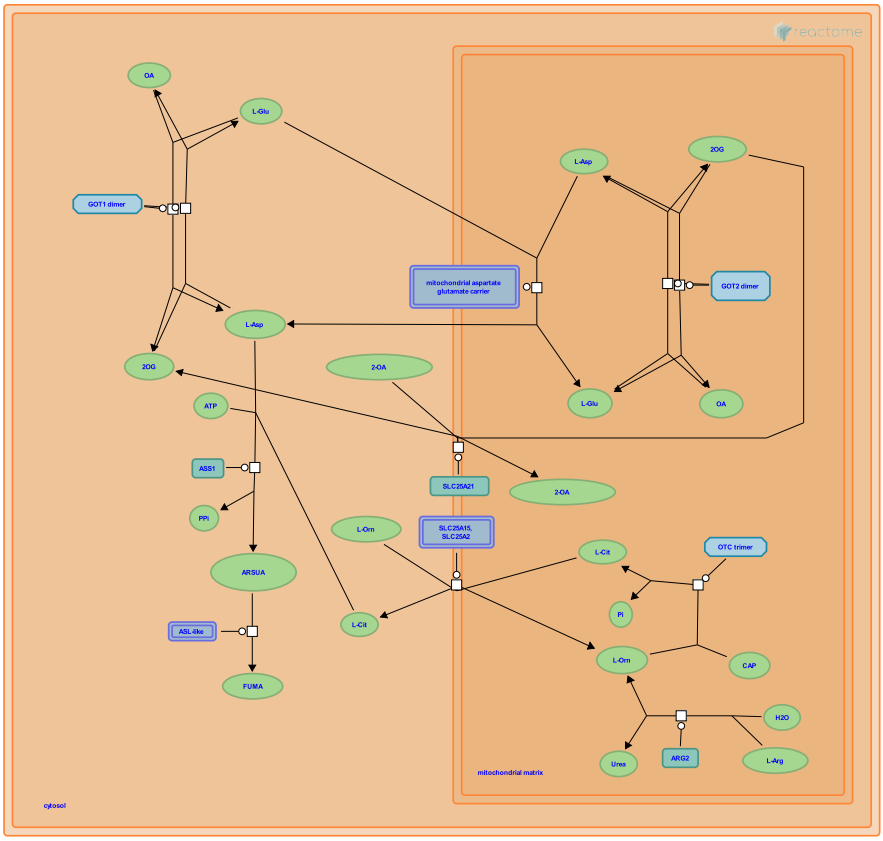
Editions

2008-09-10	Authored, Edited	D'Eustachio, P.

Amino acid metabolism ↗

Location: Metabolism

Stable identifier: R-GGA-372568



Several intracellular transport processes and transamination reactions that are components of amino acid metabolism are also needed for gluconeogenesis. These reactions are listed here together with four reactions associated with arginine metabolism.

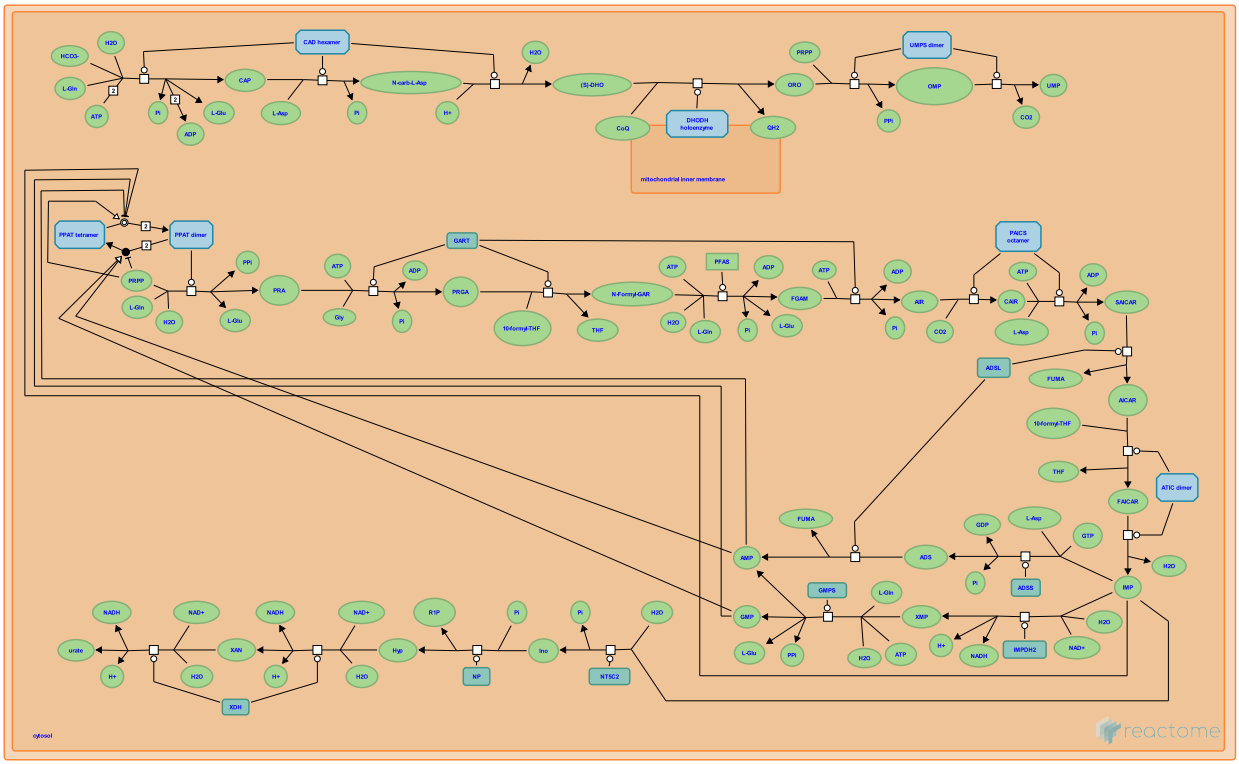
Editions

2008-09-10	Authored, Edited	D'Eustachio, P.

Nucleotide metabolism ↗

Location: Metabolism

Stable identifier: R-GGA-419470



Nucleotides and their derivatives are used for short-term energy storage (ATP, GTP), for intra- and extra-cellular 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.

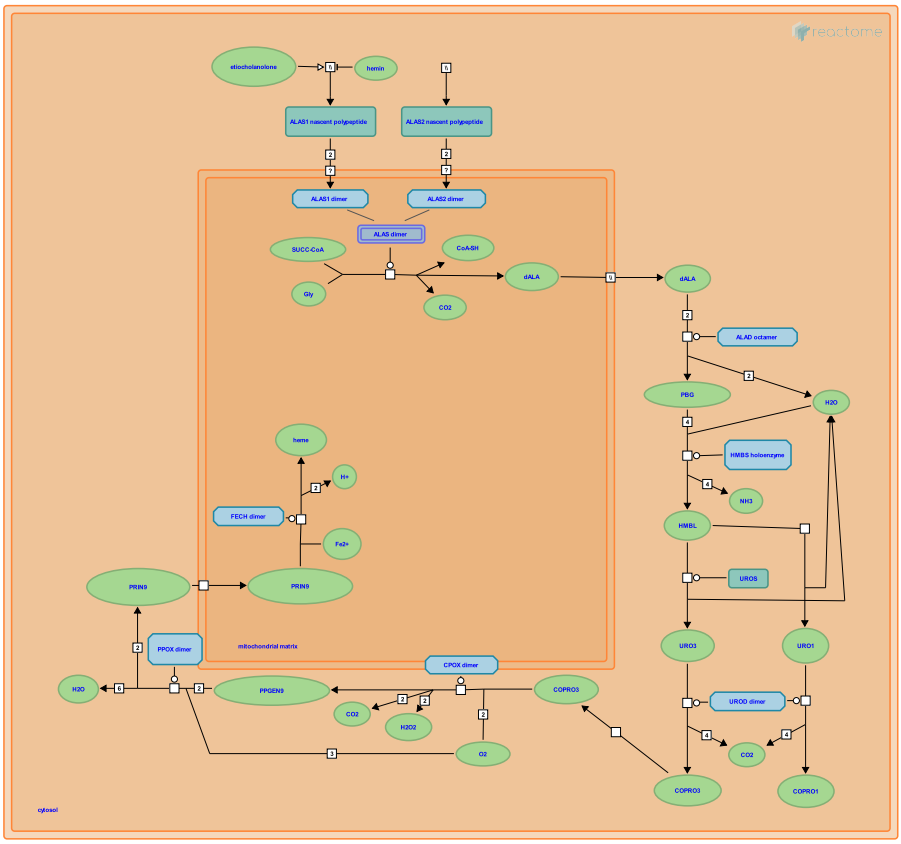
Editions

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

Heme synthesis ↗

Location: Metabolism

Stable identifier: R-GGA-421984



Eight enzymes are involved in heme biosynthesis, four each in the mitochondria and the cytosol. The process starts in the mitochondria with the condensation of succinyl CoA (from the TCA cycle) and glycine to form 5-aminolevulinate (ALA). The next four steps take place in the cytosol. Two molecules of ALA are condensed to form the monopyrrole porphobilinogen (PBG). The next two steps convert four molecules of PBG into the cyclic tetrapyrrole uroporphyringen III, which is then decarboxylated into coproporphyrinogen III. The last three steps occur in the mitochondria and involve modifications to the tetrapyrrole side chains and finally, insertion of iron. In addition to these synthetic steps, a spontaneous cytosolic reaction allows the formation of uroporphyringen I which is then enzymatically decarboxylated to coproporphyrinogen I, which cannot be metabolized further.

Two heme biosynthetic processes can be distinguished in vivo: one confined to immature erythroid cells that provides the large amount of heme needed for hemoglobin, and a ubiquitous one that provides the variable amounts of heme needed for cytochrome P450 enzymes (Riddle et al. 1989). The two processes differ most significantly at their first step, the condensation of succinyl CoA and glycine catalyzed by delta-aminolevulinate synthase, and its regulation.

Literature references

Severance, S., Hamza, I. (2009). Trafficking of heme and porphyrins in metazoa. *Chem Rev, 109,* 4596-616. ↗

Editions

2009-05-23	Authored, Edited, Reviewed	D'Eustachio, P.

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