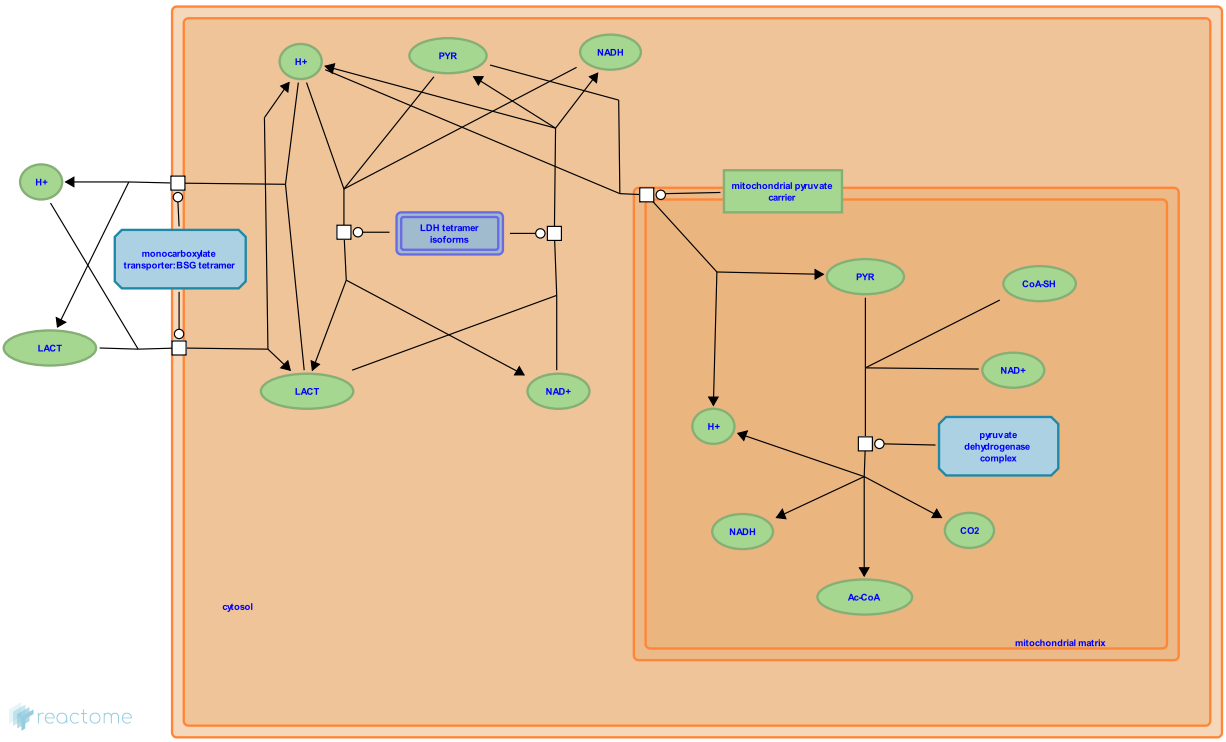
Pyruvate metabolism



D'Eustachio, P.

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

15/12/2024

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. ↗

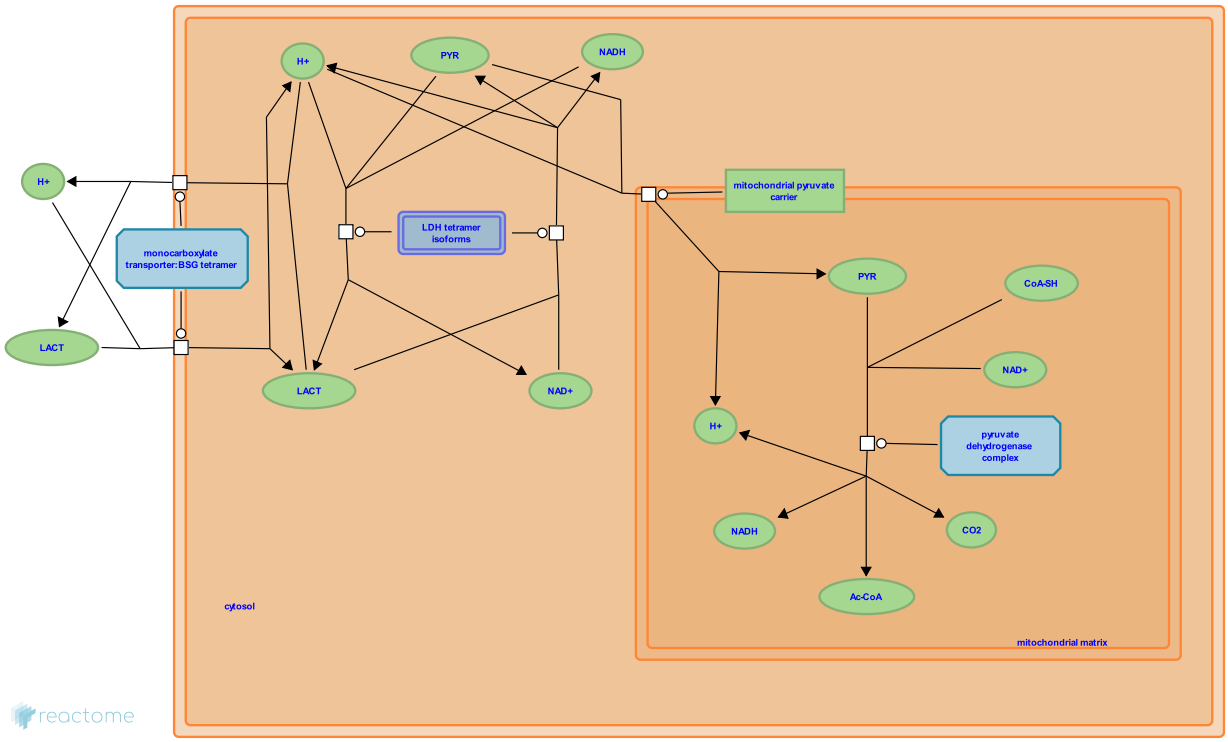
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Pyruvate 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.

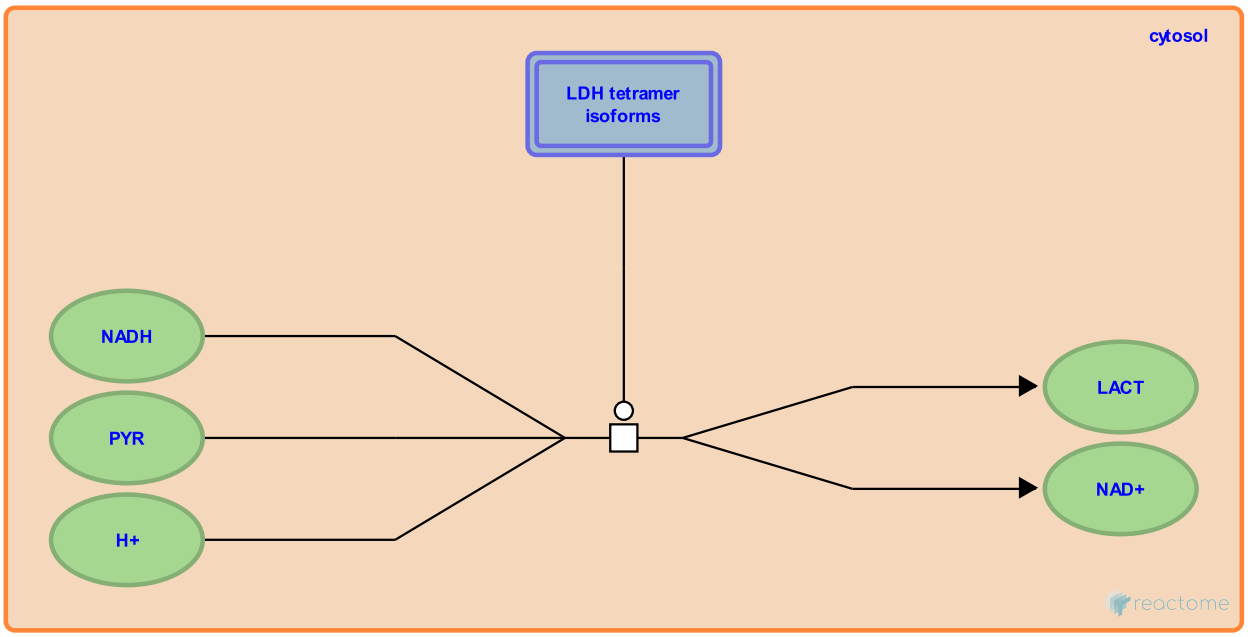
pyruvate + NADH + H+ <=> lactate + NAD+ ↗

Location: Pyruvate metabolism

Stable identifier: R-GGA-372910

Type: transition

Compartments: cytosol



Cytosolic lactate dehydrogenase catalyzes the reversible reaction of pyruvate and NADH + H+ to form lactate and NAD+. There are two isoforms of lactate dehydrogenase encoded by two different genes whose expression levels vary from tissue to tissue and as a function of developmental stage. The active form of the enzyme is a tetramer, whose composition in a tissue appears to be determined by the relative abundances of the two monomer isoforms. All five possible lactate dehydrogenase isoforms have been described; no functional differences among them have been found (Lindsay 1963; Hirota et al. 1990).

Followed by: lactate + H+ [cytosol] <=> lactate + H+ [extracellular]

Literature references

Hirota, Y., Katsumata, A., Takeya, T. (1990). Nucleotide and deduced amino acid sequences of chicken lactate dehydrogenase-A. *Nucl Acids Res, 18*, 6432. ↗

Lindsay, DT. (1963). Isozymic patterns and properties of lactate dehydrogenase from developing tissues of the chicken. *J Exp Zool, 152*, 75-89. ↗

Editions

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

lactate + H+ [cytosol] <=> lactate + H+ [extracellular] ↗

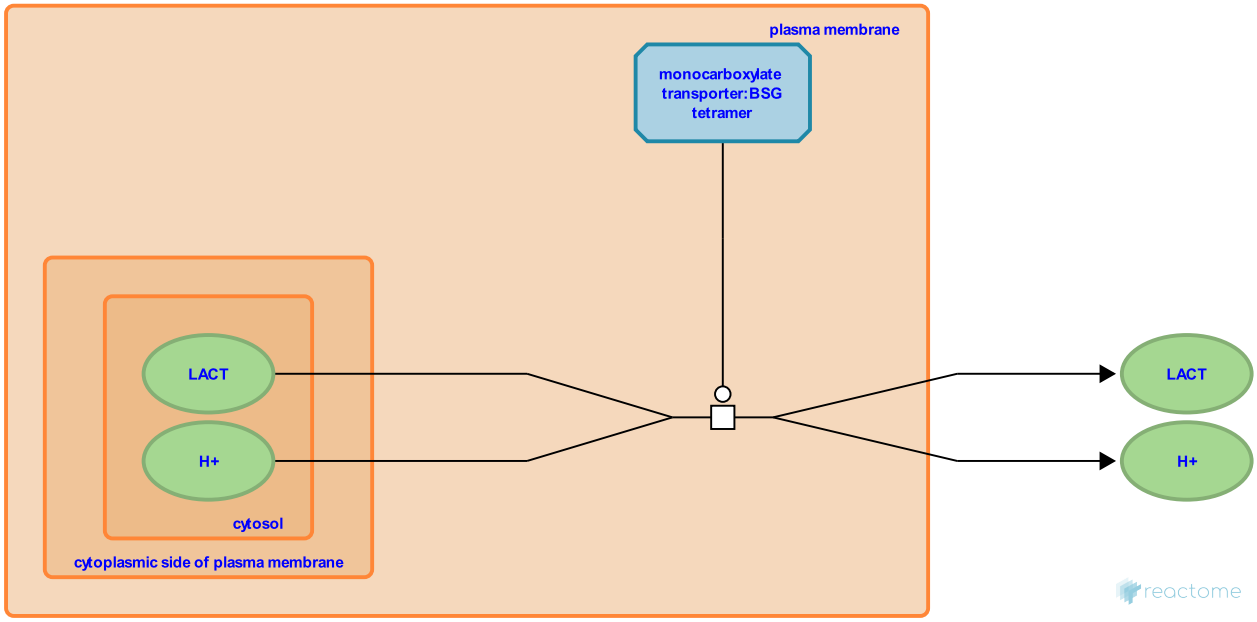
Location: Pyruvate metabolism

Stable identifier: R-GGA-373889

Type: transition

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: BSG:MCTs cotransport LACT, H+ from cytosol to extracellular region (Homo sapiens)



The monocarboxylate transporter:basigin complex, associated with the plasma membrane, mediates the reversible export of cytosolic lactate and a hydrogen ion. No chicken transporter capable of mediating this reaction has been experimentally characterized, although open reading frames capable of encoding protein closely similar to components of the human MCT:basigin complex have been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Preceded by: pyruvate + NADH + H+ <=> lactate + NAD+

Editions

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

lactate + H+ [extracellular] <=> lactate + H+ [cytosol] ↗

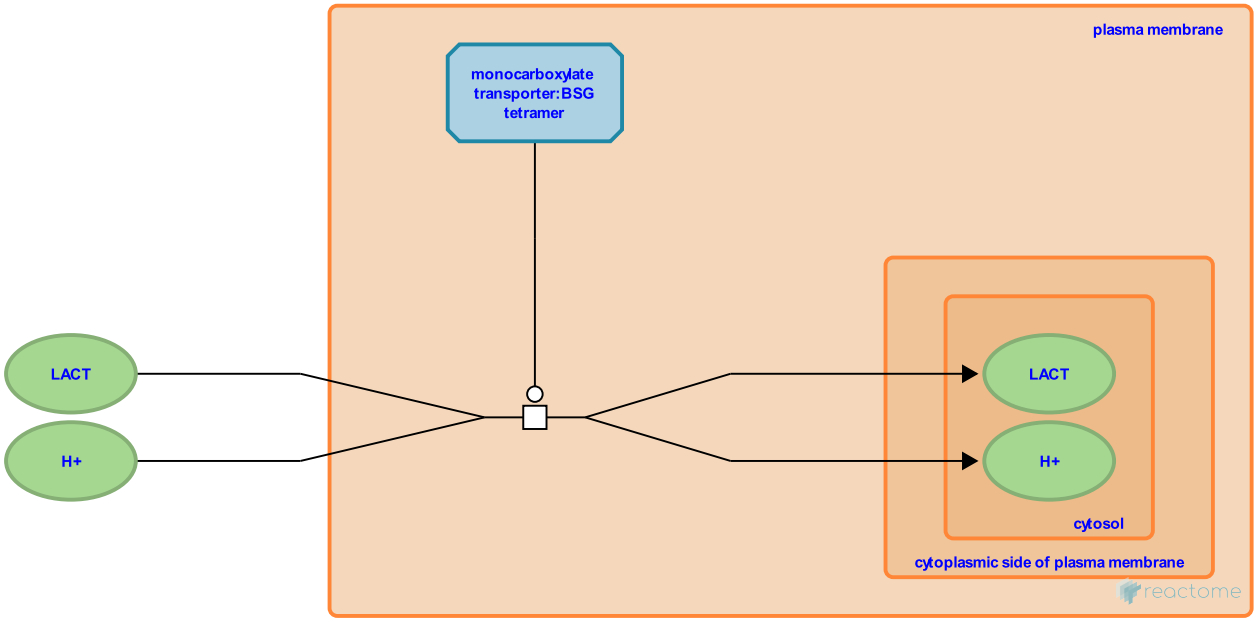
Location: Pyruvate metabolism

Stable identifier: R-GGA-373887

Type: transition

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: BSG:MCTs cotransport LACT, H+ from extracellular region to cytosol (Homo sapiens)



The monocarboxylate transporter:basigin complex, associated with the plasma membrane, mediates the reversible uptake of extracellular lactate and a hydrogen ion. No chicken transporter capable of mediating this reaction has been experimentally characterized, although open reading frames capable of encoding protein closely similar to components of the human MCT:basigin complex have been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Editions

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

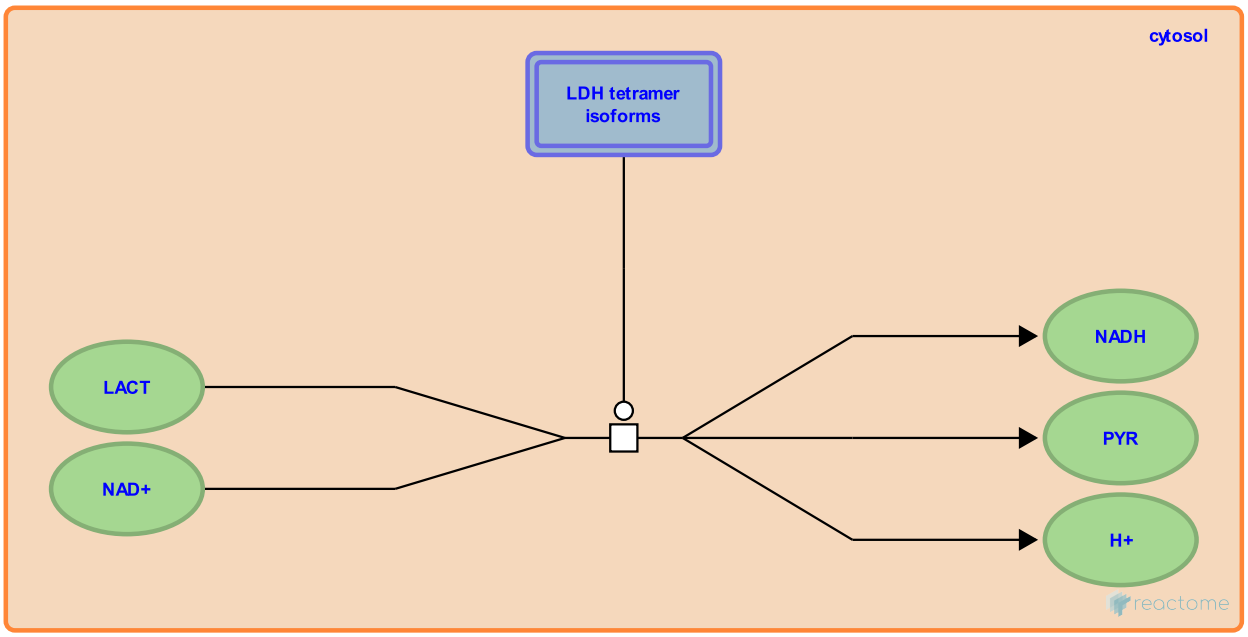
lactate + NAD+ <=> pyruvate + NADH + H+ ↗

Location: Pyruvate metabolism

Stable identifier: R-GGA-372903

Type: transition

Compartments: cytosol



Cytosolic lactate dehydrogenase catalyzes the reversible reaction of lactate and NAD+ to form pyruvate and NADH + H+. There are two isoforms of lactate dehydrogenase encoded by two different genes whose expression levels vary from tissue to tissue and as a function of developmental stage. The active form of the enzyme is a tetramer, whose composition in a tissue appears to be determined by the relative abundances of the two monomer isoforms. All five possible lactate dehydrogenase isoforms have been described; no functional differences among them have been found (Lindsay 1963; Hirota et al. 1990).

Followed by: pyruvate + H+ [cytosol] => pyruvate + H+ [mitochondrial matrix]

Literature references

Hirota, Y., Katsumata, A., Takeya, T. (1990). Nucleotide and deduced amino acid sequences of chicken lactate dehydrogenase-A. *Nucl Acids Res, 18*, 6432. ↗

Lindsay, DT. (1963). Isozymic patterns and properties of lactate dehydrogenase from developing tissues of the chicken. *J Exp Zool, 152*, 75-89. ↗

Editions

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

pyruvate + H+ [cytosol] => pyruvate + H+ [mitochondrial matrix] ↗

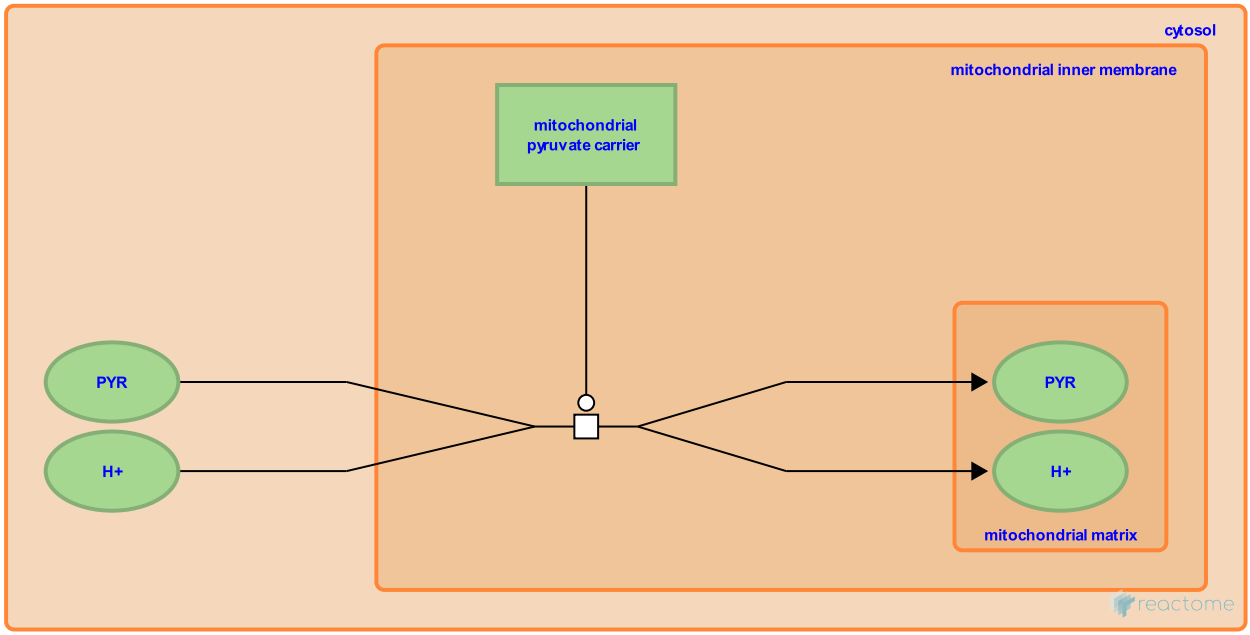
Location: Pyruvate metabolism

Stable identifier: R-GGA-372359

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix, cytosol

Inferred from: Cytosolic PYR is transported to the mitochondrial matrix (Rattus norvegicus)



The mitochondrial uptake of pyruvate is inferred from the process worked out in studies of isolated rat mitochondria (Papa et al. 1971).

Preceded by: lactate + NAD+ <=> pyruvate + NADH + H+

Followed by: pyruvate + CoASH + NAD+ => acetylCoA + CO2 + NADH + H+

Editions

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

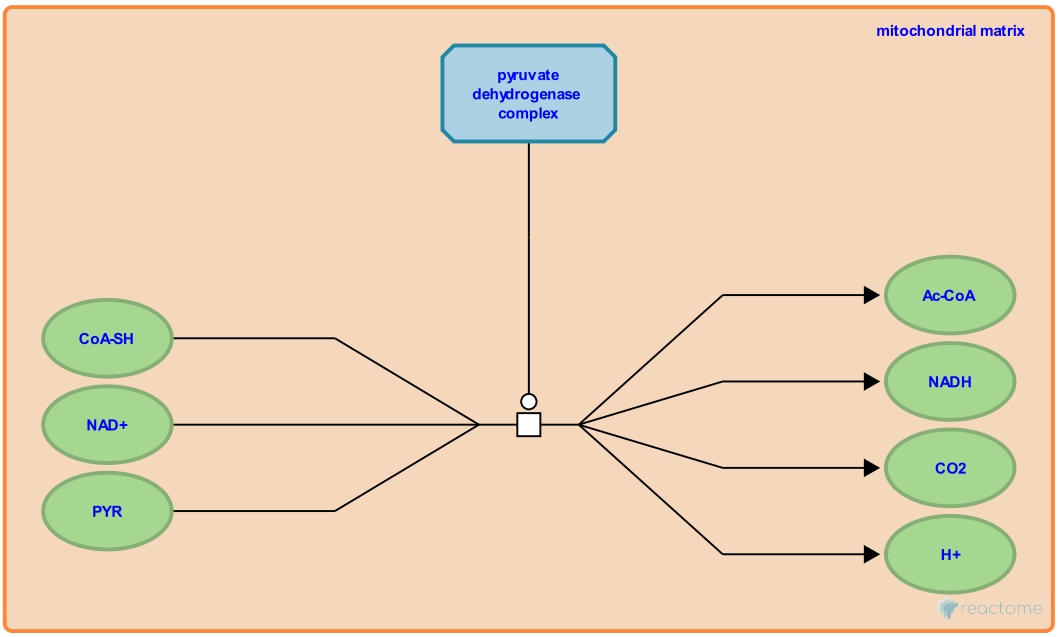
pyruvate + CoASH + NAD+ => acetylCoA + CO2 + NADH + H+ ↗

Location: Pyruvate metabolism

Stable identifier: R-GGA-373177

Type: transition

Compartments: mitochondrial matrix



Mitochondrial pyruvate dehydrogenase complex catalyzes the reaction of pyruvate, CoASH, and NAD+ to form acetylCoA, CO2, and NADH + H+. No chicken enzyme complex capable of catalyzing this reaction has been identified, although open reading frames capable of encoding proteins closely similar to each of the three authentic human pyruvate dehydrogenase E1, E2, and E3 subunits have been identified computationally in the ENSEMBL chicken gene set. This reaction is inferred from its human counterpart.

Preceded by: pyruvate + H+ [cytosol] => pyruvate + H+ [mitochondrial matrix]

Literature references

Reed, LJ., Hackert, ML. (1990). Structure-function relationships in dihydrolipoamide acyltransferases. *J Biol Chem, 265*, 8971-4. ↗

Editions

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

Table of Contents