PC carboxylates PYR to OA

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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

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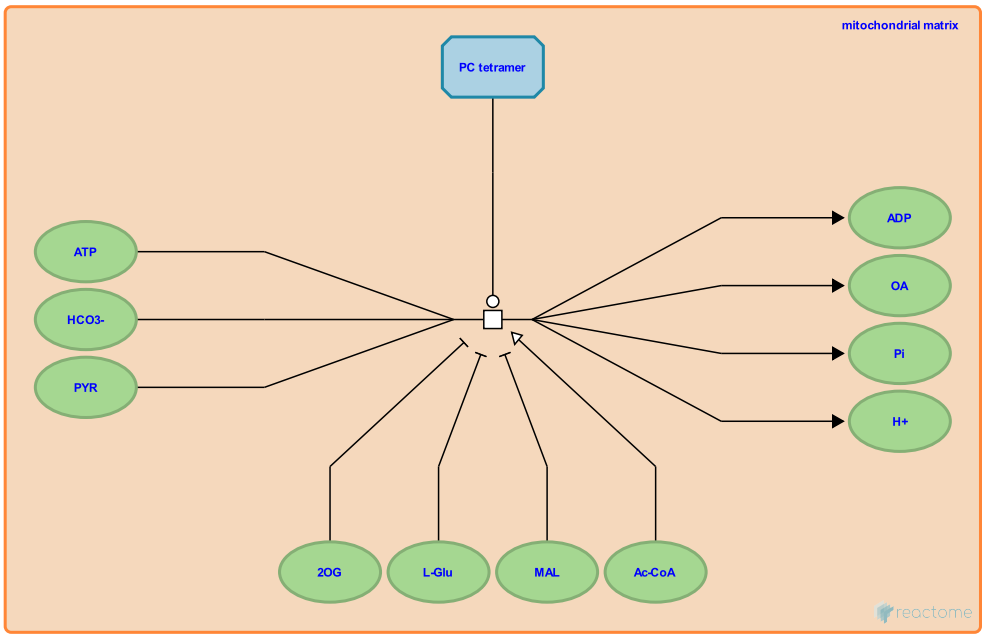
Stable identifier: R-HSA-70501

Type: transition

Compartments: mitochondrial matrix



Mitochondrial pyruvate carboxylase (PC) catalyzes the irreversible reaction of pyruvate (PYR), bicarbonate (HCO3-), and ATP to form oxaloacetate (OA), ADP, phosphate, (Pi), and H+. The enzyme is biotinylated and is active as a tetramer. The protein structure and function have been characterized in detail (Jitrapakdee et al., 2008; Jitrapakdee & Wallace, 1999; Lopez-Alonso et al., 2022). The reaction proceeds in two steps, with the biotin modification carboxylated first (Wexler et al., 1998). It is highly sensitive to activation by acetyl-CoA and gets inhibited by 2-oxoglutarate, L-malate, and L-glutamate (Scrutton & White, 1974; Jitrapakdee et al., 2008). Activation of PC by acetyl-CoA produced from lipolysis and leading to excess gluconeogenesis is the central mechanism of metabolic syndrome and diabetes (reviewed in Lao-On et al., 2018). Both normal and defective forms of the human enzyme have been described, with deficiency leading to lactic acidosis and potentially intellectual disability and death (MIM:266150; Carbone & Robinson, 2003; reviewed in Marin-Valencia et al., 2010).

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Editions

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