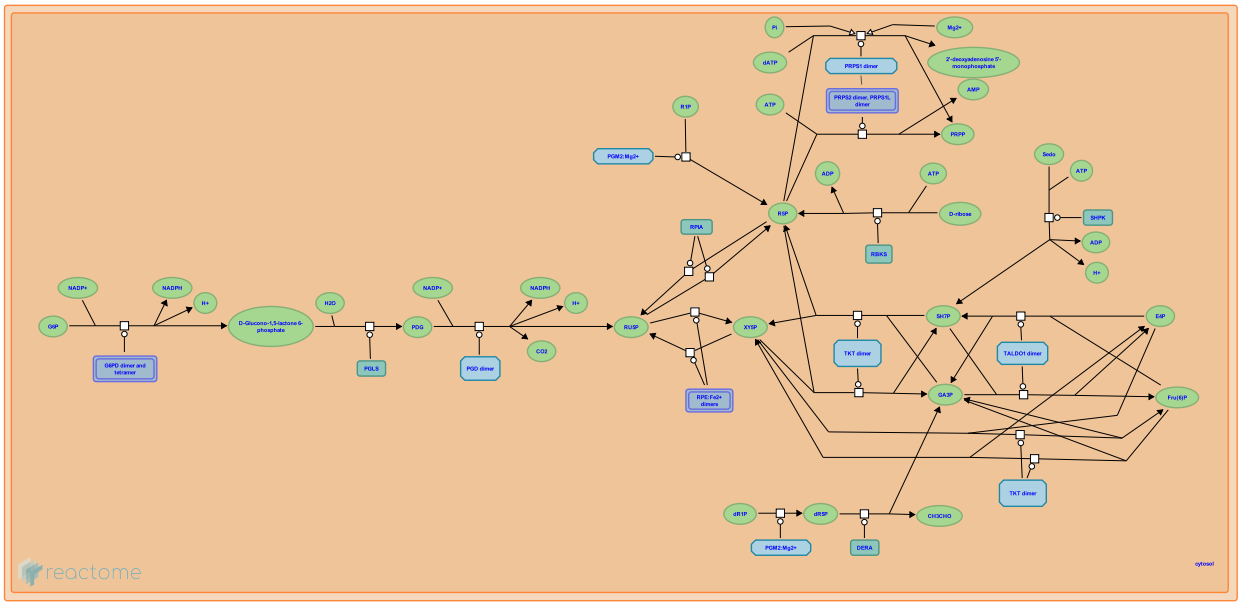
Pentose phosphate pathway



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19/11/2019

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. ↗

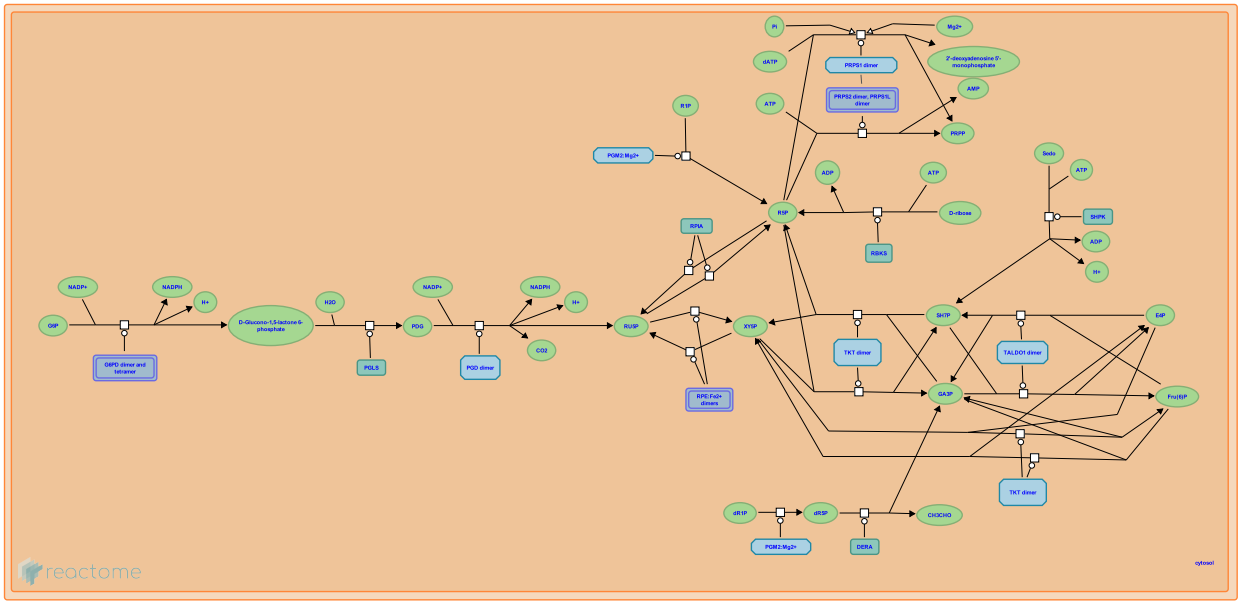
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Pentose phosphate pathway ↗

Stable identifier: R-HSA-71336

Compartments: cytosol



The pentose phosphate pathway is responsible for the generation of a substantial fraction of the cytoplasmic NADPH required for biosynthetic reactions, and for the generation of ribose 5-phosphate for nucleotide synthesis. Although the pentose phosphate pathway and glycolysis are distinct, they involve three common intermediates, glucose 6-phosphate, glyceraldehyde 3-phosphate, and fructose 6-phosphate, so the two pathways are interconnected. The pentose phosphate pathway consists of eight reactions:1. Conversion glucose 6-phosphate to D-glucono-1,5-lactone 6-phosphate, with the formation of NADPH; 2. Conversion of D-glucono-1,5-lactone 6-phosphate to 6-phospho-D-gluconate; 3. Conversion of 6-phospho-D-gluconate to ribulose 5-phosphate, with the formation of NADPH; 4. Conversion of ribulose 5-phosphate to xylulose 5-phosphate; 5. Conversion of ribulose 5-phosphate to ribose 5-phosphate; 6. Rearrangement of ribose 5-phosphate and xylulose 5-phosphate to form sedoheptulose 7-phosphate and glyceraldehyde 3-phosphate; 7. Rearrangement of sedoheptulose 7-phosphate and glyceraldehyde 3-phosphate to form erythrose 4-phosphate and fructose 6-phosphate; and 8. Rearrangement of xylulose 5-phosphate and erythrose 4-phosphate to form glyceraldehyde 3-phosphate and fructose-6-phosphate.

The oxidative branch of the pentose phosphate pathway, reactions 1-3, generates NADPH and pentose 5-phosphate. The non-oxidative branch of the pathway, reactions 4-8, converts pentose 5-phosphate to other sugars.

The overall pathway can operate to generate only NADPH (glucose 6-phosphate is converted to pentose 5-phosphates, which are directed to the synthesis of fructose 6-phosphate and glyceraldehyde 3-phosphate, which in turn are converted back to glucose 6-phosphate). The reactions of the non-oxidative branch can operate to generate net amounts of ribose 5-phosphate with no production of NADPH. Net flux through this network of reactions appears to depend on the metabolic state of the cell and the nature of the biosynthetic reactions underway (Casazza and Veech 1987).

G6PD, the enzyme that catalyzes the first reaction of the pathway, is more extensively mutated in human populations than any other enzyme, pehaps because these mutant alleles confer malaria resistance (Luzzatto and Afolayan 1968). Mutations affecting other parts of the pathway are rare, though several have been described and studies of their effects have contributed to our understanding of the normal flux of metabolites through this network of reactions (Wamelink et al. 2008).

Literature references

Luzzatto, L., Afolayan, A. (1968). Enzymic properties of different types of human erythrocyte glucose-6-phosphate dehydrogenase, with characterization of two new genetic variants. *J Clin Invest, 47*, 1833-42. ↗

Wamelink, MM., Struys, EA., Jakobs, C. (2008). The biochemistry, metabolism and inherited defects of the pentose phosphate pathway: a review. *J Inherit Metab Dis, 31*, 703-17. ↗

Casazza, JP., Veech, RL. (1987). The content of pentose-cycle intermediates in liver in starved, fed ad libitum and meal-fed rats. *Biochem J, 236*, 635-41. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

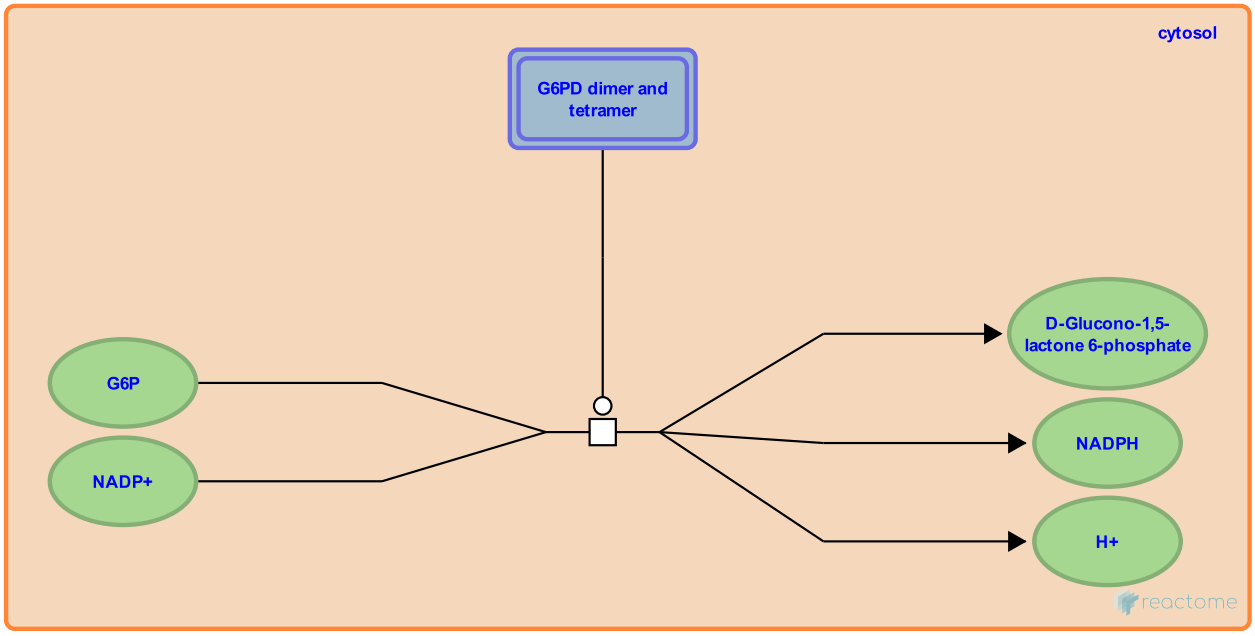
alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+ ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-70377

Type: transition

Compartments: cytosol



Cytosolic glucose-6-phosphate dehydrogenase (G6PD) catalyzes the reaction of glucose 6-phosphate and NADP+ to form D-glucono-1,5-lactone 6-phosphate and NADPH + H+. This constitutes the first committed step of the pentose phosphate pathway and it is critical to the maintenance of NAPDH pool and redox homeostasis. For this reason, anti-cancer therapies are making this step as a prominent target in cancer therapy (Zhang et al. 2014). The reaction is inhibited by high ADP/AMP concentration, and by high NAPDH concentration. Biochemical studies indicate that both G6PD dimers and tetramers are catalytically active and present under physiological conditions in vivo (Au et al. 2000). Mutations that reduce the catalytic efficiency of G6PD are remarkably common in human populations; these appear to have a protective effect against malaria (e.g., Luzzatto and Afolayan 1968).

Followed by: D-glucono-1,5-lactone 6-phosphate + H2O => 6-phospho-D-gluconate

Literature references

Luzzatto, L., Afolayan, A. (1968). Enzymic properties of different types of human erythrocyte glucose-6-phosphate dehydrogenase, with characterization of two new genetic variants. *J Clin Invest, 47*, 1833-42. ↗

Au, SW., Gover, S., Lam, VM., Adams, MJ. (2000). Human glucose-6-phosphate dehydrogenase: the crystal structure reveals a structural NADP(+) molecule and provides insights into enzyme deficiency. *Structure, 8*, 293-303. ↗

Zhang, C., Zhang, Z., Zhu, Y., Qin, S. (2014). Glucose-6-phosphate dehydrogenase: a biomarker and potential therapeutic target for cancer. *Anticancer Agents Med Chem, 14*, 280-9. ↗

Editions

2003-06-25	Authored	D'Eustachio, P.
2010-01-24	Edited, Revised	D'Eustachio, P.
2016-02-04	Reviewed	Inga, A., Zaccara, S.

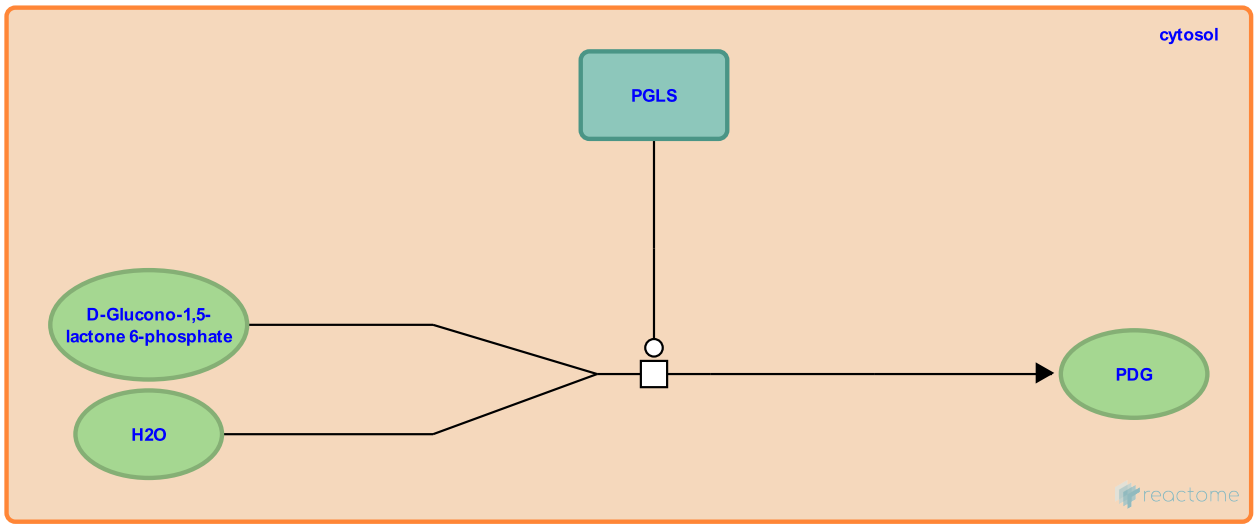
D-glucono-1,5-lactone 6-phosphate + H2O => 6-phospho-D-gluconate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71296

Type: transition

Compartments: cytosol



Cytosolic 6-phosphogluconolactonase (PGLS) catalyzes the hydrolysis of D-glucono-1,5-lactone 6-phosphate to form 6-phospho-D-gluconate (Beutler and Kuhl 1985; Collard et al. 1999).

Preceded by: alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+

Followed by: 6-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate + CO2 + NADPH + H+

Literature references

Beutler, E., Kuhl, W. (1985). Limiting role of 6-phosphogluconolactonase in erythrocyte hexose monophosphate pathway metabolism. *J Lab Clin Med, 106*, 573-7. ↗

Collard, F., Collet, JF., Gerin, I., Veiga-da-Cunha, M., Van Schaftingen, E. (1999). Identification of the cDNA encoding human 6-phosphogluconolactonase, the enzyme catalyzing the second step of the pentose phosphate pathway(1). *FEBS Lett, 459*, 223-6. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

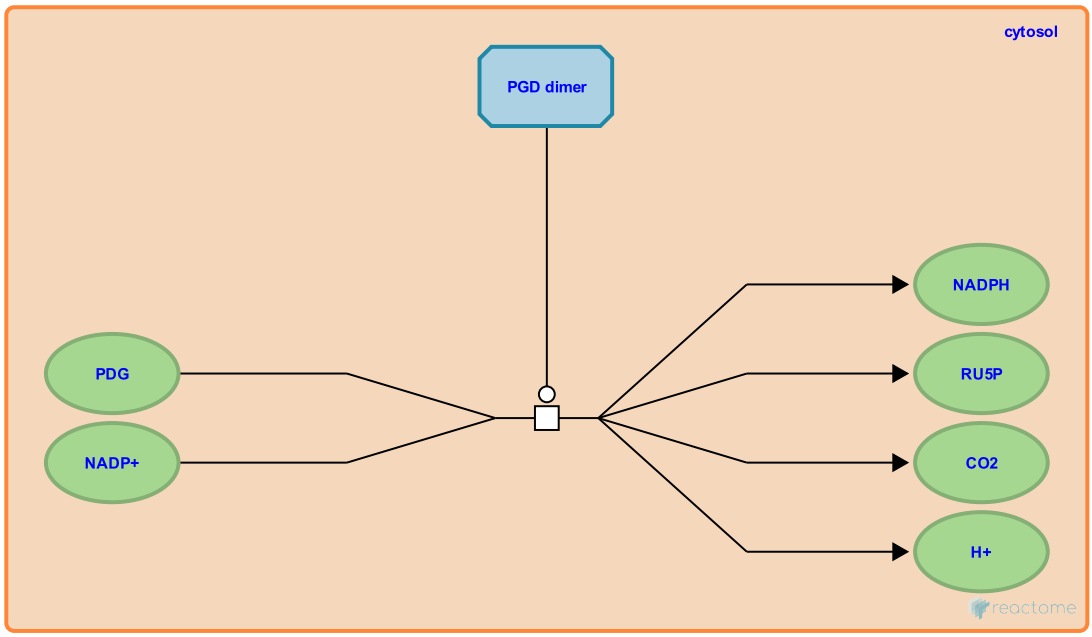
6-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate + CO2 + NADPH + H+ ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71299

Type: transition

Compartments: cytosol



Cytosolic phosphogluconate dehydrogenase (PGD) catalyzes the reaction of 6-phospho-D-gluconate and NADP+ to form D-ribulose 5-phosphate, CO2, and NADPH + H+ (Beutler and Kuhl 1985; Rippa et al. 1998). The PGD enzyme is dimeric (Dallocchio et al. 1985).

Preceded by: D-glucono-1,5-lactone 6-phosphate + H2O => 6-phospho-D-gluconate

Followed by: D-ribulose 5-phosphate <=> ribose 5-phosphate, RPE dimers isomerise RU5P to XY5P

Literature references

Beutler, E., Kuhl, W. (1985). Limiting role of 6-phosphogluconolactonase in erythrocyte hexose monophosphate pathway metabolism. *J Lab Clin Med, 106*, 573-7. ↗

Dallocchio, F., Matteuzzi, M., Bellini, T. (1985). Half-site reactivity in 6-phosphogluconate dehydrogenase from human erythrocytes. *Biochem J, 227*, 305-10. ↗

Rippa, M., Giovannini, PP., Barrett, MP., Dallocchio, F., Hanau, S. (1998). 6-Phosphogluconate dehydrogenase: the mechanism of action investigated by a comparison of the enzyme from different species. *Biochim Biophys Acta, 1429*, 83-92. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

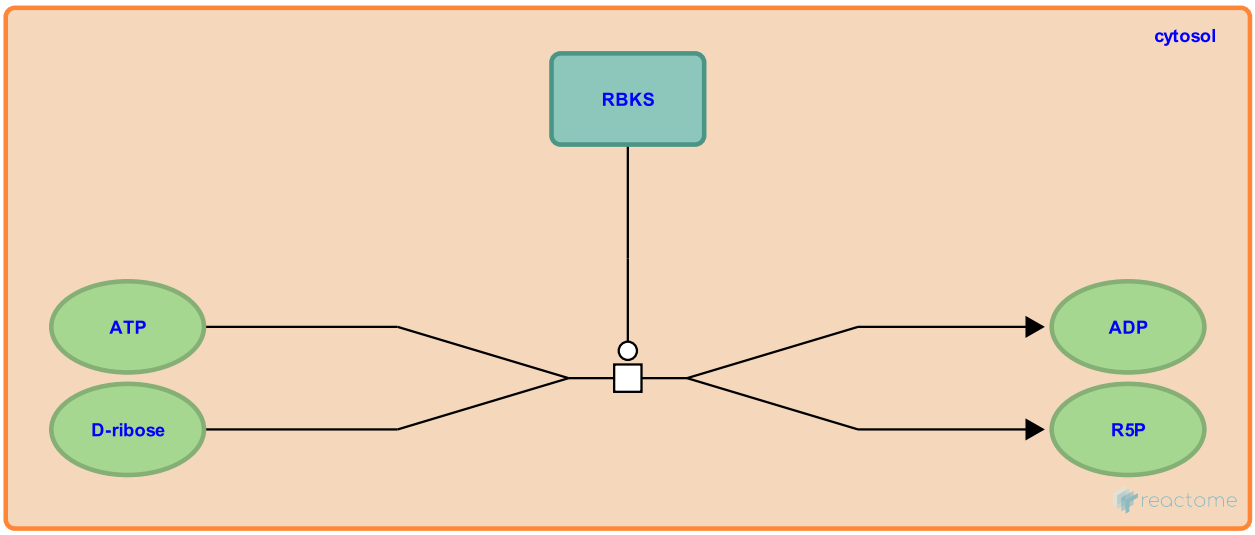
RBKS phosphorylates ribose to R5P ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-8955844

Type: transition

Compartments: cytosol



In order for D-ribose to be incorporated into ATP or other high energy phosphorylated derivatives, ribose must first be converted into ribose-5-phosphate (R5P), which can then be used either for sythesis of nucleotides, histidine, and tryptophan, or as a component of the pentose phosphate pathway. Cytosolic ribokinase (RBKS) catalyses this reaction in the presence of ATP (Park et al. 2007). Other pentoses and simple sugars were either not or poorly phosphorylated by RBKS. RBKS belongs to the PfkB family of carbohydrate kinases which includes adenosine kinase (AK) and fructokinase. RBKS shares high structural similarity to AK and its catalytic mechanism is very similar to AK (Park & Gupta 2008).

Followed by: ribose 5-phosphate + xylulose 5-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate

Literature references

Park, J., van Koeverden, P., Singh, B., Gupta, RS. (2007). Identification and characterization of human ribokinase and comparison of its properties with E. coli ribokinase and human adenosine kinase. *FEBS Lett., 581*, 3211-6. ↗

Park, J., Gupta, RS. (2008). Adenosine kinase and ribokinase--the RK family of proteins. *Cell. Mol. Life Sci., 65*, 2875-96 . ↗

Editions

2017-01-13	Authored, Edited	Jassal, B.
2017-01-30	Reviewed	D'Eustachio, P.

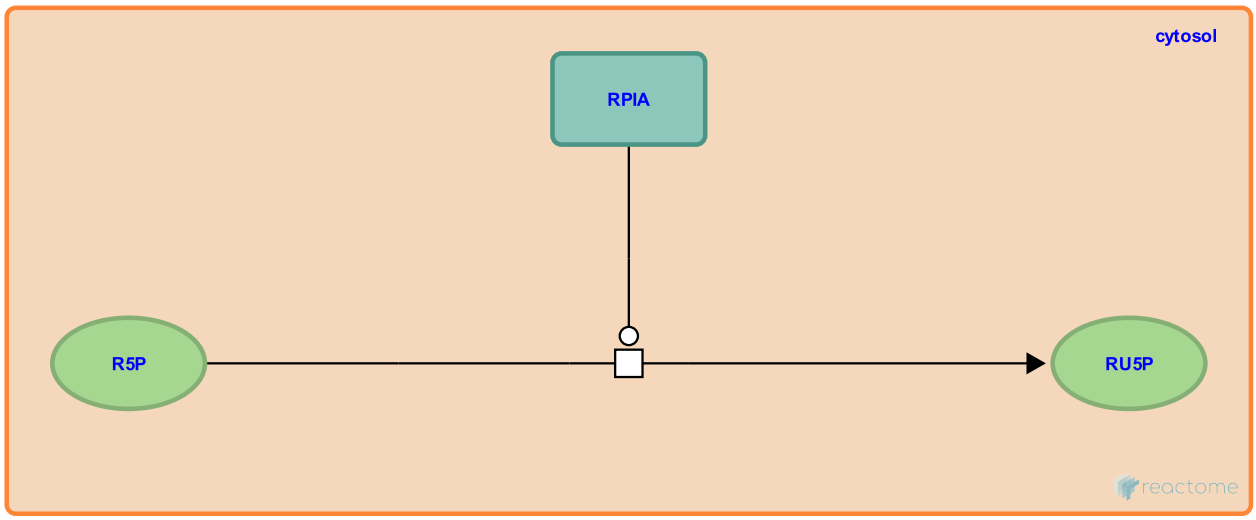
ribose 5-phosphate <=> D-ribulose 5-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-177784

Type: transition

Compartments: cytosol



The reversible interconversion of ribose 5-phosphate and ribulose 5-phosphate is catalyzed by cytosolic ribose 5-phosphate isomerase (Huck et al. 2004).

Literature references

Huck, JHJ., Verhoeven, NM., Struys, EA., Salomons, GS., Jakobs, C., van der Knaap, MS. (2004). Ribose-5-phosphate isomerase deficiency: new inborn error in the pentose phosphate pathway associated with a slowly progressive leukoencephalopathy. *Am J Hum Genet, 74*, 745-51. ↗

Editions

2006-04-05	Edited	D'Eustachio, P.
2010-01-24	Revised	D'Eustachio, P.

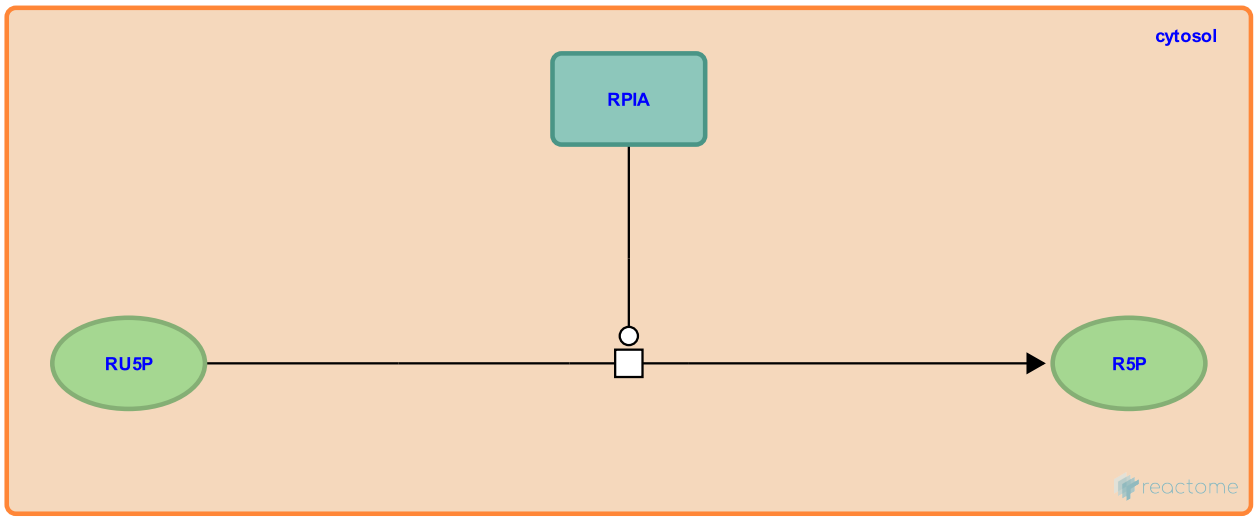
D-ribulose 5-phosphate <=> ribose 5-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71306

Type: transition

Compartments: cytosol



The reversible interconversion of ribulose 5-phosphate and ribose 5-phosphate is catalyzed by cytosolic ribose 5-phosphate isomerase (Huck et al. 2004).

Preceded by: 6-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate + CO2 + NADPH + H+

Followed by: 5-Phosphoribose 1-diphosphate biosynthesis, ribose 5-phosphate + xylulose 5-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate

Literature references

Huck, JHJ., Verhoeven, NM., Struys, EA., Salomons, GS., Jakobs, C., van der Knaap, MS. (2004). Ribose-5-phosphate isomerase deficiency: new inborn error in the pentose phosphate pathway associated with a slowly progressive leukoencephalopathy. *Am J Hum Genet, 74*, 745-51. ↗

Editions

2006-04-05	Edited	D'Eustachio, P.
2010-01-24	Revised	D'Eustachio, P.

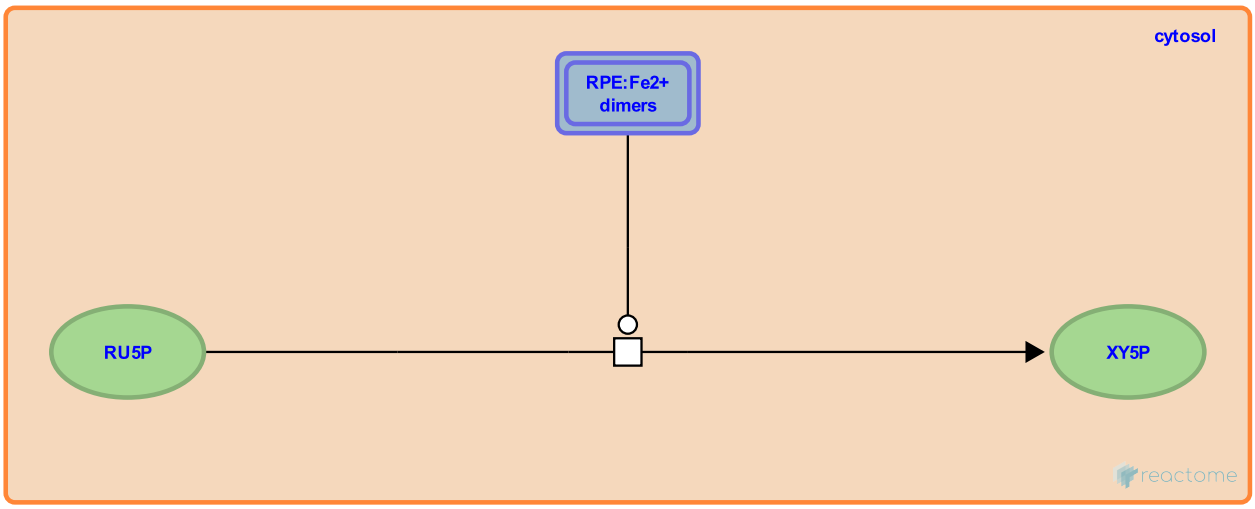
RPE dimers isomerise RU5P to XY5P ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71303

Type: transition

Compartments: cytosol



Cytosolic ribulose-5-phosphate-3-epimerase (RPE), using Fe2+ as cofactor, catalyzes the reversible interconversion of D-ribulose 5-phosphate (RU5P) and D-xylulose 5-phosphate (XY5P) (Bose & Pilz 1985, Liang et al. 2011). The electrophoretic properties of RPE activity detected in extracts of mouse-human somatic cell hybrids suggest that the active form of the enzyme is a homodimer (Spencer & Hopkinson 1980). Ribulose-phosphate 3-epimerase-like protein 1 (RPEL1), based on sequence similarity, is suggested to function as RPE.

Preceded by: 6-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate + CO2 + NADPH + H+

Followed by: xylulose 5-phosphate + D-erythrose 4-phosphate <=> D-glyceraldehyde 3-phosphate + D-fructose 6-phosphate, ribose 5-phosphate + xylulose 5-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate

Literature references

Boss, GR., Pilz, RB. (1985). Phosphoribosylpyrophosphate synthesis from glucose decreases during amino acid starvation of human lymphoblasts. *J Biol Chem, 260*, 6054-9. ↗

Spencer, N., Hopkinson, DA. (1980). Biochemical genetics of the pentose phosphate cycle: human ribose 5-phosphate isomerase (RPI) and ribulose 5-phosphate 3-epimerase (RPE). *Ann Hum Genet, 43*, 335-42. ↗

Liang, W., Ouyang, S., Shaw, N., Joachimiak, A., Zhang, R., Liu, ZJ. (2011). Conversion of D-ribulose 5-phosphate to D-xylulose 5-phosphate: new insights from structural and biochemical studies on human RPE. *FASEB J., 25*, 497-504. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.
2017-01-25	Edited, Revised	Jassal, B.

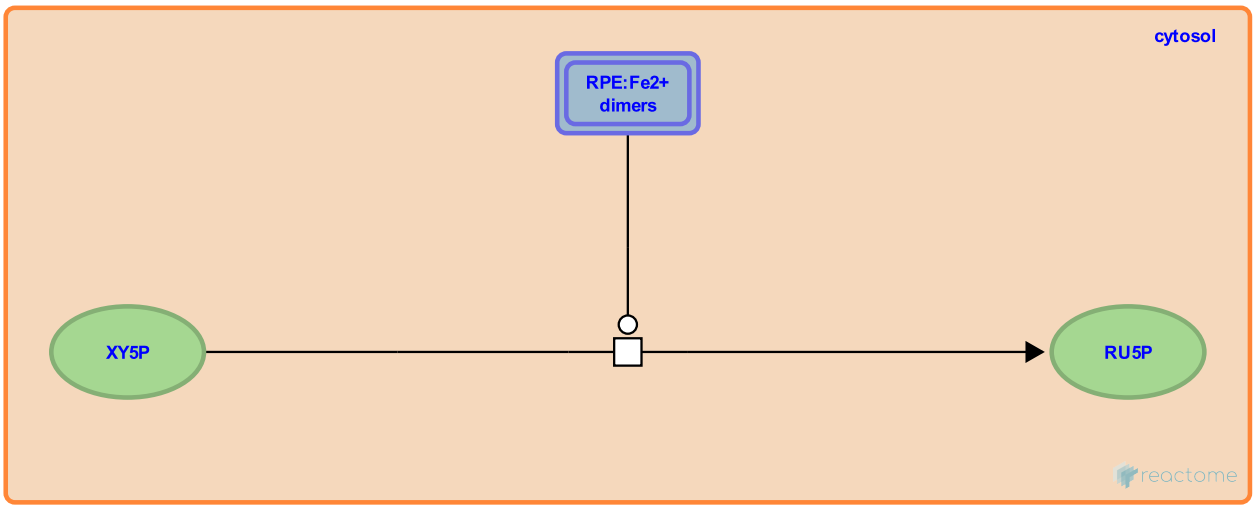
xylulose 5-phosphate <=> D-ribulose 5-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-199803

Type: transition

Compartments: cytosol



Cytosolic ribulose-5-phosphate-3-epimerase (RPE) catalyzes the reversible interconversion of D-xylulose 5-phosphate and D-ribulose 5-phosphate (Bose and 1985). The electrophoretic properties of RPE activity detected in extracts of mouse-human somatic cell hybrids suggest that the active form of the enzyme is a homodimer (Spencer and Hopkinson 1980).

Literature references

Boss, GR., Pilz, RB. (1985). Phosphoribosylpyrophosphate synthesis from glucose decreases during amino acid starvation of human lymphoblasts. *J Biol Chem, 260*, 6054-9. ↗

Spencer, N., Hopkinson, DA. (1980). Biochemical genetics of the pentose phosphate cycle: human ribose 5-phosphate isomerase (RPI) and ribulose 5-phosphate 3-epimerase (RPE). *Ann Hum Genet, 43*, 335-42. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

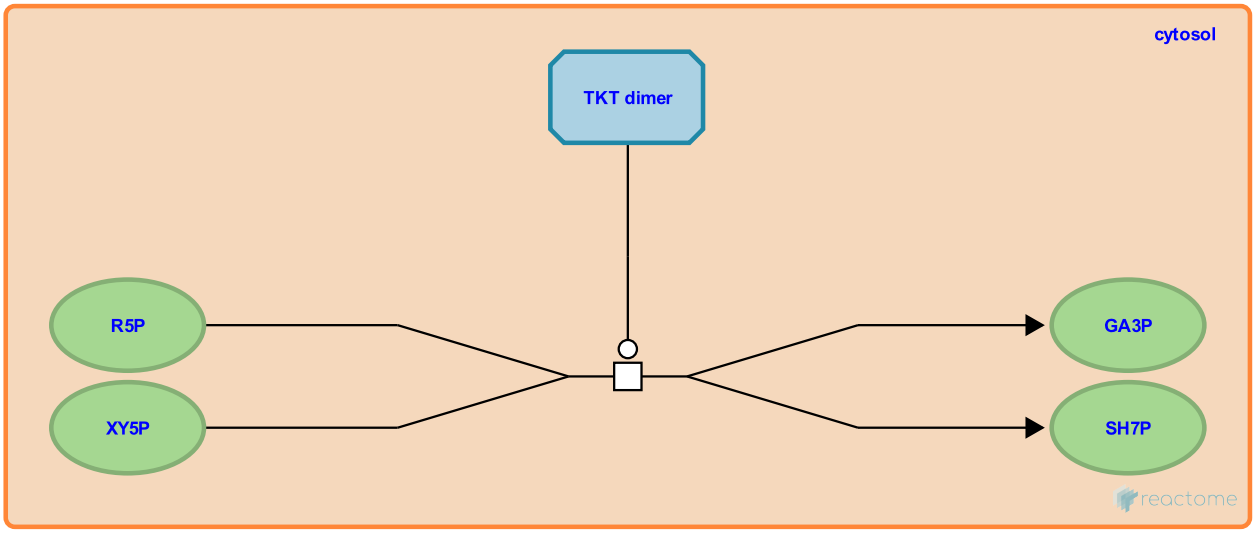
ribose 5-phosphate + xylulose 5-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71324

Type: transition

Compartments: cytosol



Cytosolic transketolase (TKT) catalyzes the reversible reaction of D-xylulose 5-phosphate and D-ribose 5-phosphate to form D-glyceraldehyde 3-phosphate and sedoheptulose 7-phosphate. The active transketolase enzyme is a homodimer with one molecule of thiamine pyrophosphate and magnesium bound to each monomer (Wang et al. 1997).

Preceded by: D-ribulose 5-phosphate <=> ribose 5-phosphate, RPE dimers isomerise RU5P to XY5P, RBKS phosphorylates ribose to R5P

Followed by: sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate <=> D-erythrose 4-phosphate + D-fructose 6-phosphate

Literature references

Wang, JJ., Martin, PR., Singleton, CK. (1997). Aspartate 155 of human transketolase is essential for thiamine diphosphate-magnesium binding, and cofactor binding is required for dimer formation. *Biochim Biophys Acta, 1341*, 165-72. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

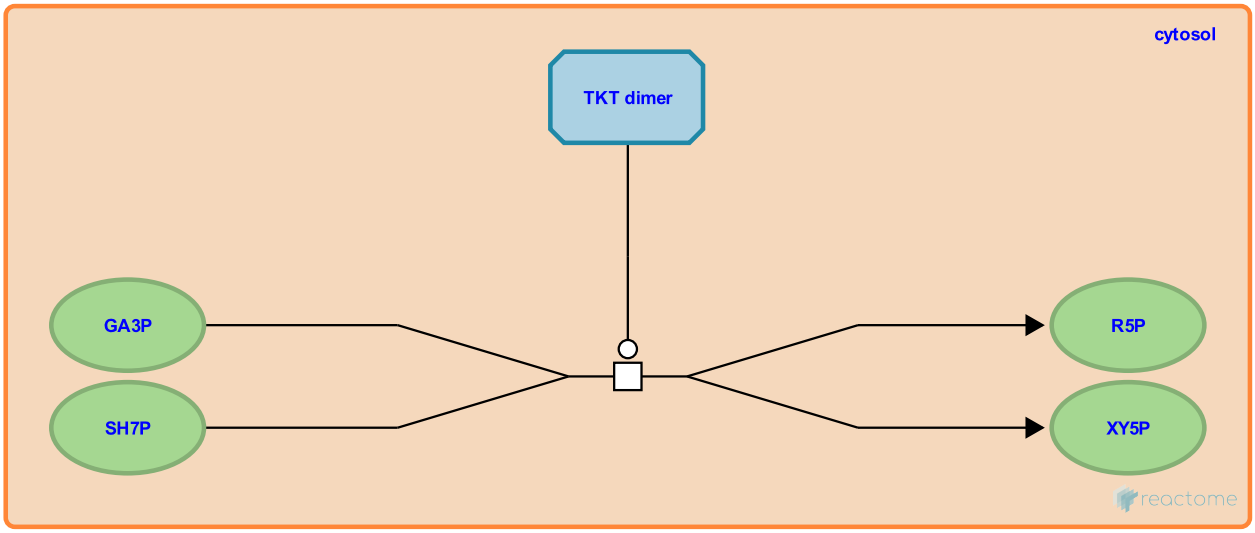
D-glyceraldehyde 3-phosphate + sedoheptulose 7-phosphate<=> xylulose 5-phosphate+ribose 5-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-163741

Type: transition

Compartments: cytosol



Cytosolic transketolase (TKT) catalyzes the reversible reaction of D-glyceraldehyde 3-phosphate and sedoheptulose 7-phosphate to form D-xylulose 5-phosphate and D-ribose 5-phosphate. The active transketolase enzyme is a homodimer with one molecule of thiamine pyrophosphate and magnesium bound to each monomer (Wang et al. 1997).

Preceded by: D-fructose 6-phosphate + D-erythrose 4-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate

Literature references

Wang, JJ., Martin, PR., Singleton, CK. (1997). Aspartate 155 of human transketolase is essential for thiamine diphosphate-magnesium binding, and cofactor binding is required for dimer formation. *Biochim Biophys Acta, 1341*, 165-72. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

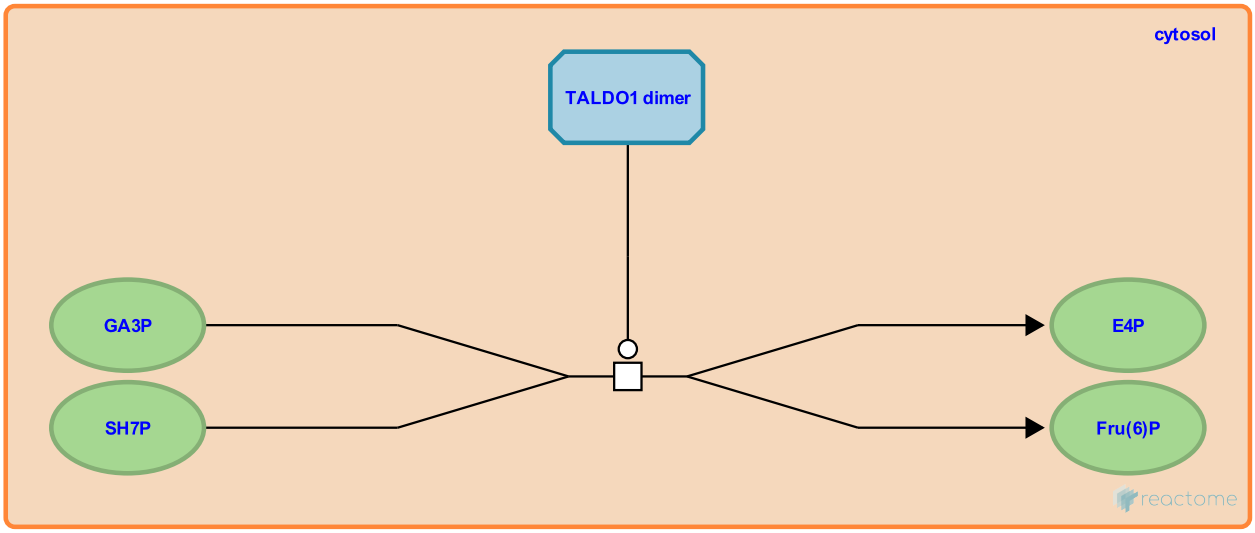
sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate <=> D-erythrose 4-phosphate + D-fructose 6-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71334

Type: transition

Compartments: cytosol



Dimeric cytosolic transaldolase (TALDO1) catalyzes the reversible reaction of D-glyceraldehyde 3-phosphate and sedoheptulose 7-phosphate to form D-erythrose 4-phosphate and D-fructose 6-phosphate. Protein expressed from the cloned gene has been characterized biochemically and crystallographically (Banki et al. 1994; Thorell et al. 2000) and transaldolase deficiency in a patient has been correlated with a mutation in the TALDO1 gene (Verhoeven et al. 2001).

Preceded by: ribose 5-phosphate + xylulose 5-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate

Followed by: xylulose 5-phosphate + D-erythrose 4-phosphate <=> D-glyceraldehyde 3-phosphate + D-fructose 6-phosphate

Literature references

Banki, K., Halladay, D., Perl, A. (1994). Cloning and expression of the human gene for transaldolase. A novel highly repetitive element constitutes an integral part of the coding sequence. *J Biol Chem, 269*, 2847-51. ↗

Thorell, S., Gergely, P., Banki, K., Perl, A., Schneider, G. (2000). The three-dimensional structure of human transaldolase. *FEBS Lett., 475*, 205-8. ↗

Verhoeven, NM., Huck, JHJ., Roos, B., Struys, EA., Salomons, GS., Douwes, AC. et al. (2001). Transaldolase deficiency: liver cirrhosis associated with a new inborn error in the pentose phosphate pathway. *Am J Hum Genet, 68*, 1086-92. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

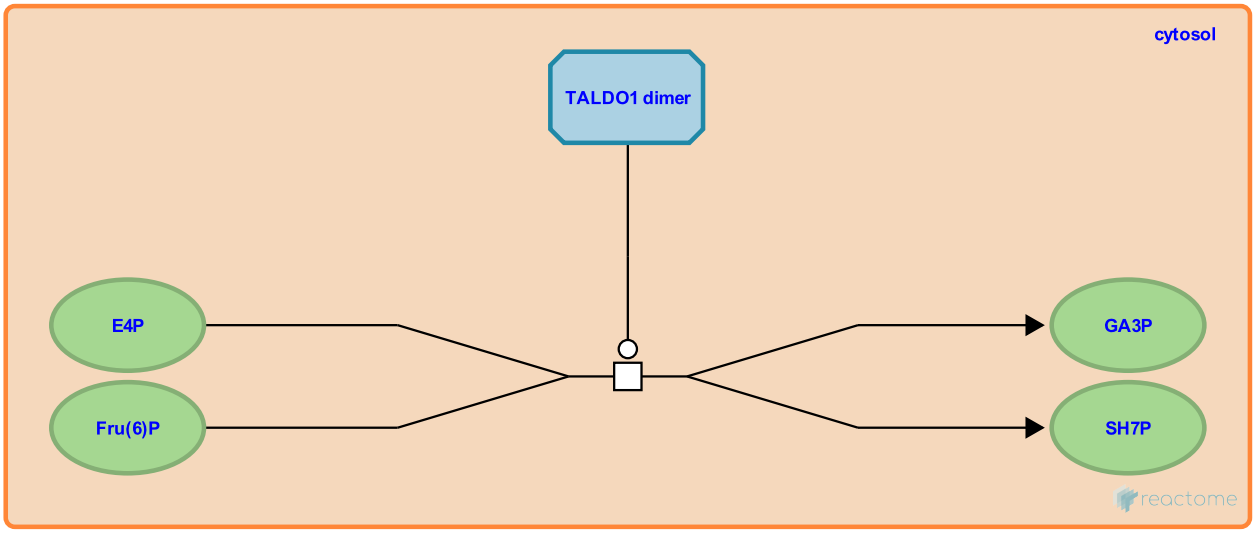
D-fructose 6-phosphate + D-erythrose 4-phosphate <=> sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-163764

Type: transition

Compartments: cytosol



Dimeric cytosolic transaldolase (TALDO1) catalyzes the reversible reaction of D-erythrose 4-phosphate and D-fructose 6-phosphate to form D-glyceraldehyde 3-phosphate and sedoheptulose 7-phosphate. Protein expressed from the cloned gene has been characterized biochemically and crystallographically (Banki et al. 1994; Thorell et al. 2000) and transaldolase deficiency in a patient has been correlated with a mutation in the TALDO1 gene (Verhoeven et al. 2001).

Followed by: D-glyceraldehyde 3-phosphate + sedoheptulose 7-phosphate<=> xylulose 5-phosphate+ribose 5-phosphate

Literature references

Banki, K., Halladay, D., Perl, A. (1994). Cloning and expression of the human gene for transaldolase. A novel highly repetitive element constitutes an integral part of the coding sequence. *J Biol Chem, 269*, 2847-51. ↗

Thorell, S., Gergely, P., Banki, K., Perl, A., Schneider, G. (2000). The three-dimensional structure of human transaldolase. *FEBS Lett., 475*, 205-8. ↗

Verhoeven, NM., Huck, JHJ., Roos, B., Struys, EA., Salomons, GS., Douwes, AC. et al. (2001). Transaldolase deficiency: liver cirrhosis associated with a new inborn error in the pentose phosphate pathway. *Am J Hum Genet, 68*, 1086-92. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

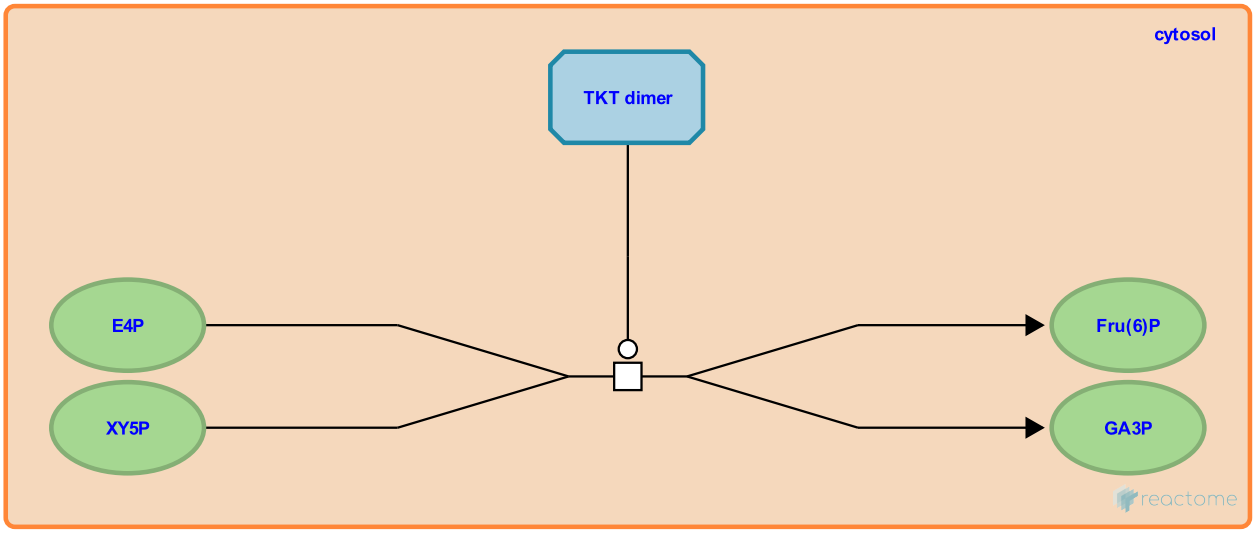
xylulose 5-phosphate + D-erythrose 4-phosphate <=> D-glyceraldehyde 3-phosphate + D-fructose 6-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-71335

Type: transition

Compartments: cytosol



Cytosolic transketolase (TKT) catalyzes the reaction of D-erythrose 4-phosphate and D-xylulose 5-phosphate to form D-glyceraldehyde 3-phosphate and D-fructose 6-phosphate. The active transketolase enzyme is a homodimer with one molecule of thiamine pyrophosphate and magnesium bound to each monomer (Wang et al. 1997).

Preceded by: RPE dimers isomerise RU5P to XY5P, sedoheptulose 7-phosphate + D-glyceraldehyde 3-phosphate <=> D-erythrose 4-phosphate + D-fructose 6-phosphate

Literature references

Wang, JJ., Martin, PR., Singleton, CK. (1997). Aspartate 155 of human transketolase is essential for thiamine diphosphate-magnesium binding, and cofactor binding is required for dimer formation. *Biochim Biophys Acta, 1341*, 165-72. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

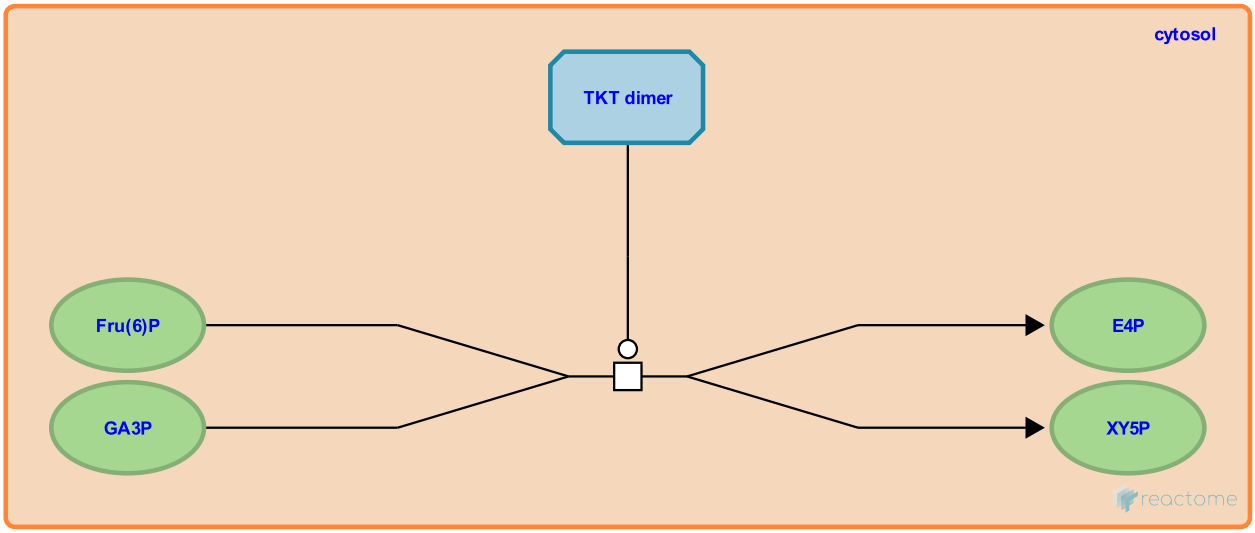
D-glyceraldehyde 3-phosphate + D-fructose 6-phosphate <=> xylulose 5-phosphate + D-erythrose 4-phosphate ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-163751

Type: transition

Compartments: cytosol



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Wang, JJ., Martin, PR., Singleton, CK. (1997). Aspartate 155 of human transketolase is essential for thiamine diphosphate-magnesium binding, and cofactor binding is required for dimer formation. *Biochim Biophys Acta, 1341*, 165-72. ↗

Editions

2010-01-24	Revised	D'Eustachio, P.

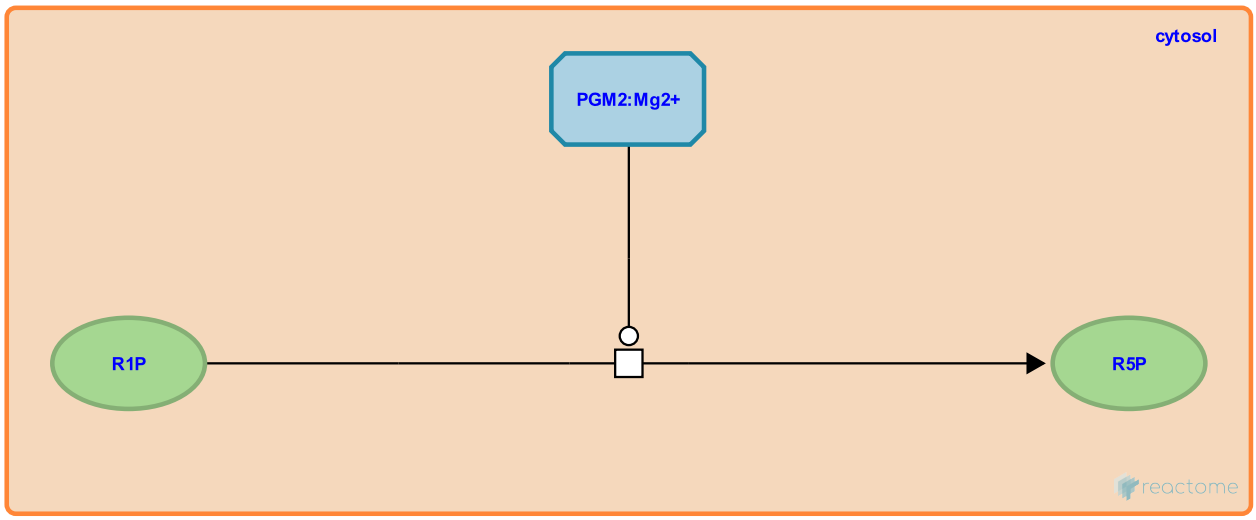
PGM2:Mg2+ isomerises R1P to R5P ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-6787329

Type: transition

Compartments: cytosol



The nucleoside breakdown product ribose-1-phosphate (R1P) can be used to produce energy during oxidative or mitochondrial stress to minimize or delay stress-induced damage. Two steps connect this nucleoside breakdown product to central carbon metabolism in mammals. In the first step, R1P is isomerised to the corresponding 5-phosphopentose, R5P, mediated by phosphoglucomutase-2 (PGM2). PGM2 is a cytosolic, M2+-dependent enzyme that acts ten times better as a phosphopentomutase (both on R1P and dR1P) than as a phosphoglucomutase (on glucose-1-phosphate) (Maliekal et al. 2007).

Literature references

Maliekal, P., Sokolova, T., Vertommen, D., Veiga-da-Cunha, M., Van Schaftingen, E. (2007). Molecular identification of mammalian phosphopentomutase and glucose-1,6-bisphosphate synthase, two members of the alpha-D-phosphohexomutase family. *J Biol Chem, 282*, 31844-51. ↗

Editions

2015-07-13	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

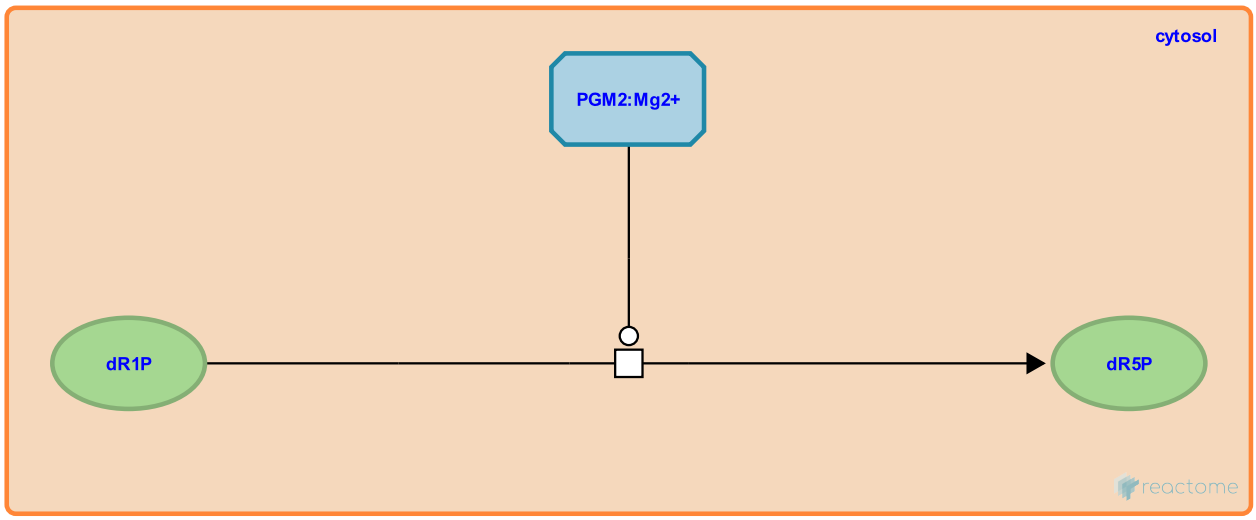
PGM2:Mg2+ isomerises dR1P to dR5P ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-8982667

Type: transition

Compartments: cytosol



The nucleoside breakdown product deoxyribose-1-phosphate (dR1P) can be used to produce energy during oxidative or mitochondrial stress to minimize or delay stress-induced damage. Two steps connect this nucleoside breakdown product to central carbon metabolism in mammals. In the first step, dR1P is isomerised to the corresponding 5-phosphopentose, dR5P, mediated by phosphoglucomutase-2 (PGM2). PGM2 is a cytosolic, M2+-dependent enzyme that acts ten times better as a phosphopentomutase (both on R1P and dR1P) than as a phosphoglucomutase (on glucose-1-phosphate) (Maliekal et al. 2007).

Literature references

Maliekal, P., Sokolova, T., Vertommen, D., Veiga-da-Cunha, M., Van Schaftingen, E. (2007). Molecular identification of mammalian phosphopentomutase and glucose-1,6-bisphosphate synthase, two members of the alpha-D-phosphohexomutase family. *J Biol Chem, 282*, 31844-51. ↗

Editions

2015-07-13	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

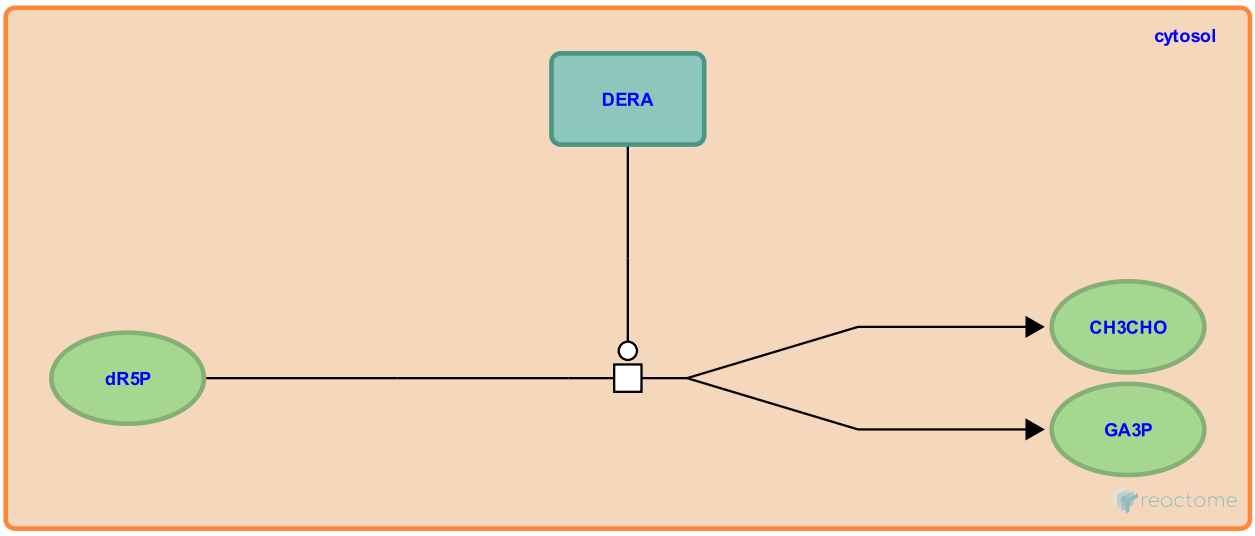
DERA cleaves dR5P to GA3P and CH3CHO ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-6787321

Type: transition

Compartments: cytosol



The nucleoside breakdown products ribose-1-phosphate (R1P) and deoxyribose-1-phosphate (dR1P) can be used to produce energy during oxidative or mitochondrial stress to minimize or delay stress-induced damage. Two steps connect these nucleoside breakdown products to central carbon metabolism in mammals. In the second step, deoxy-ribose5-phosphate (dR5P) is cleaved to glyceraldehyde-3-phosphate (GA3P, an intermediate in glycolysis) and acetaldehyde (CH3CHO) by deoxyribose-phosphate aldolase (DERA) (Salleron et al. 2014).

Literature references

Salleron, L., Magistrelli, G., Mary, C., Fischer, N., Bairoch, A., Lane, L. (2014). DERA is the human deoxyribose phosphate aldolase and is involved in stress response. *Biochim. Biophys. Acta, 1843*, 2913-25. ↗

Editions

2015-07-13	Authored, Edited	Jassal, B.
2015-09-14	Reviewed	D'Eustachio, P.

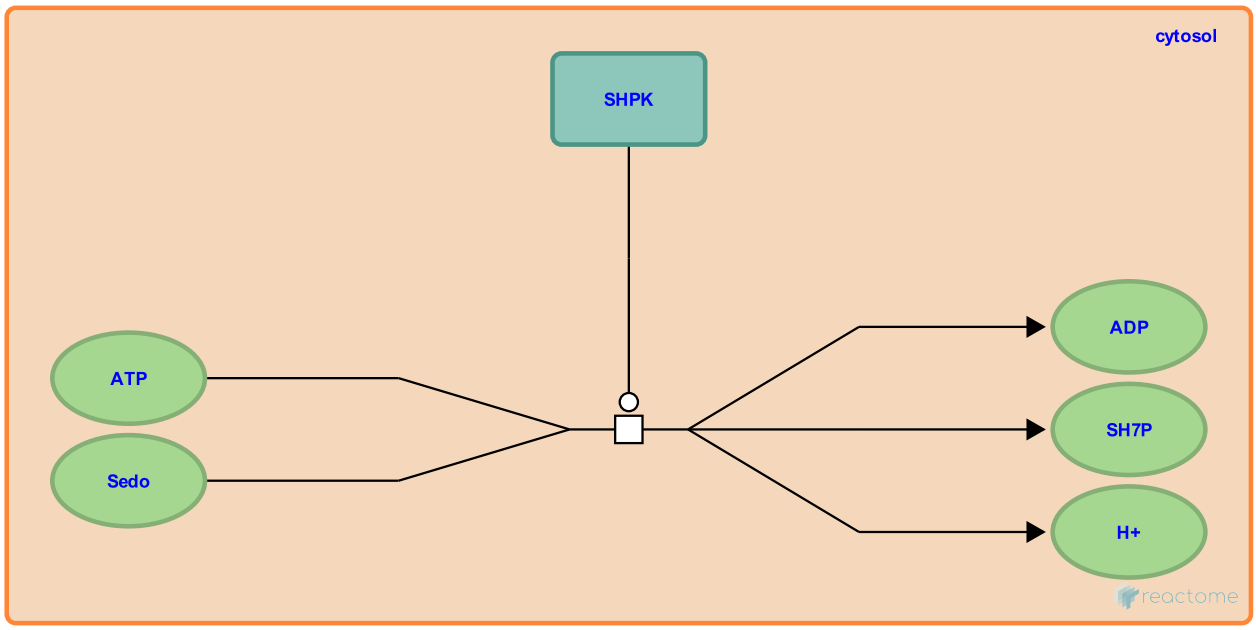
SHPK phosphorylates Sedo to Sedo7P ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-8959719

Type: transition

Compartments: cytosol



Cytosolic sedoheptulokinase (SHPK aka CARKL) catalyses an orphan reaction in the pentose phosphate pathway and is a novel regulator of glycolytic energy flux which is critical for macrophage activation (Haschemi et al. 2012). The most common mutation in the nephropathic cystinosis (CTNS) gene is a homozygous 57-kb deletion that also includes the adjacent gene SHPK. In nephropathic cystinosis patients, defects in SHPK can cause urinary accumulation of sedoheptulose and erythritol (Wamelink et al. 2008, Kardon et al. 2008).

Literature references

Haschemi, A., Kosma, P., Gille, L., Evans, CR., Burant, CF., Starkl, P. et al. (2012). The sedoheptulose kinase CARKL directs macrophage polarization through control of glucose metabolism. *Cell Metab., 15*, 813-26. ↗

Wamelink, MM., Struys, EA., Jansen, EE., Levtchenko, EN., Zijlstra, FS., Engelke, U. et al. (2008). Sedoheptulokinase deficiency due to a 57-kb deletion in cystinosis patients causes urinary accumulation of sedoheptulose: elucidation of the CARKL gene. *Hum. Mutat., 29*, 532-6. ↗

Kardon, T., Stroobant, V., Veiga-da-Cunha, M., Schaftingen, EV. (2008). Characterization of mammalian sedoheptulokinase and mechanism of formation of erythritol in sedoheptulokinase deficiency. *FEBS Lett., 582*, 3330-4. ↗

Editions

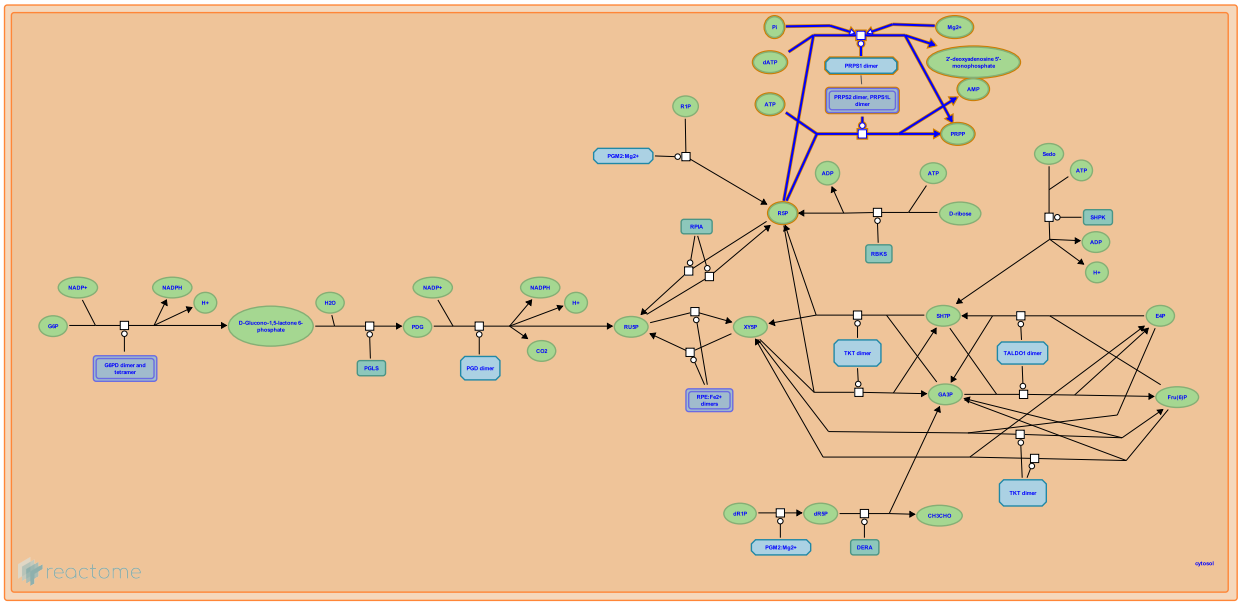
2017-01-30	Authored, Edited	Jassal, B.
2017-02-06	Reviewed	D'Eustachio, P.

5-Phosphoribose 1-diphosphate biosynthesis ↗

Location: Pentose phosphate pathway

Stable identifier: R-HSA-73843

Compartments: cytosol



5-Phospho-alpha-D-ribose 1-diphosphate (PRPP) is a key intermediate in both the de novo and salvage pathways of purine and pyrimidine synthesis. PRPP and the enzymatic activity responsible for its synthesis were first described by Kornberg et al. (1955). The enzyme, phosphoribosyl pyrophosphate synthetase 1, has been purified from human erythrocytes and characterized biochemically. The purified enzyme readily forms multimers; its smallest active form appears to be a dimer and for simplicity it is annotated as a dimer here. It specifically catalyzes the transfer of pyrophosphate from ATP or dATP to D-ribose 5-phosphate, and has an absolute requirement for Mg++ and orthophosphate (Fox and Kelley 1971; Roth et al. 1974). The significance of the reaction with dATP in vivo is unclear, as the concentration of cytosolic dATP is normally much lower than that of ATP. The importance of this enzyme for purine synthesis in vivo has been established by demonstrating excess phosphoribosyl pyrophosphate synthetase activity, correlated with elevated enzyme levels or altered enzyme properties, in individuals whose rates of uric acid production are constitutively abnormally high (Becker and Kim 1987; Roessler et al. 1993).

Molecular cloning studies have revealed the existence of two additional genes that encode phosphoribosyl pyrophosphate synthetase-like proteins, one widely expressed (phosphoribosyl pyrophosphate synthetase 2) and one whose expression appears to be confined to the testis (phosphoribosyl pyrophosphate synthetase 1-like 1) (Taira et al. 1989; 1991). Neither of these proteins has been purified and characterized enzymatically, nor have variations in the abundance or sequence of either protein been associated with alterations in human nucleotide metabolism (Roessler et al. 1993; Becker et al. 1996), so their dimerization and ability to catalyze the synthesis of PRPP from D-ribose 5-phosphate are inferred here on the basis of their predicted amino acid sequence similarity to phosphoribosyl pyrophosphate synthetase 1.

Literature references

Becker, MA., Kim, M. (1987). Regulation of purine synthesis de novo in human fibroblasts by purine nucleotides and phosphoribosylpyrophosphate. *J Biol Chem, 262,* 14531-14537. ↗

Becker, MA., Taylor, W., Smith, PR., Ahmed, M. (1996). Overexpression of the normal phosphoribosylpyrophosphate synthetase 1 isoform undelies catalytic superactivity of human phosphoribosylpyrophosphate synthetase. *J Biol Chem, 271*, 19894-19899. ↗

Fox, IH., Kelley, WN. (1971). Human phosphoribosylpyrophosphate synthetase. *J Biol Chem, 246*, 5739-5748. ↗

Kornberg, A., Lieberman, I., Simms, ES. (1955). Enzymatic synthesis and properties of 5-phosphoribosylpyrophosphate. *J Biol Chem, 215*, 389-402. ↗

Roessler, BJ., Nosal, JM., Smith, PR., Heidler, SA., Palella, TD., Switzer, RL. et al. (1993). Human X-linked phosphoribosylpyrophosphate synthetase superactivity is associated with distinct point mutations in the PRPS1 gene. *J Biol Chem, 268*, 26476-26481. ↗

Editions

2004-02-09	Authored	D'Eustachio, P.
2010-01-24	Revised	D'Eustachio, P.
2019-08-16	Edited	D'Eustachio, P.

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6-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate + CO2 + NADPH + H+ 6

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