***Supplementary Table 1*** *- Reactions and transporters in human galactose metabolism and kinetic parameters.*

| Id | Information | Kinetics |
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| **GLUT2** | **Facilitated glucose transporter member 2**<br>D-glucose (disse) [**glc_dis**] ↔ D-glucose (cytosol) [**glc**]<br>D-galactose (disse) [**gal_dis**] ↔ D-galactose (cytosol) [**gal**]<br><br>**Mechanism**<br>TCDB:2.A.1.1 (glucose transporter subfamily)<br>**Protein/Structure**<br>UniProt:P11168 (GTR2_HUMAN)<br>**Gene**<br>SLC2A2, GLUT2<br>**Disease**<br>OcMIM:227810 (Fanconi-Bickel syndrome; FBS)<br><br>Galactose and glucose transported via GLUT2 (competitive inhibition kinetics) (Brown, 2000; Colville, et al., 1993)<br><br>Deficient transport of galactose into hepatocytes in human patients with defective GLUT2 transporters (Fanconi-Bickel syndrome) resulting in galactose malabsorption/intolerance (Brown, 2000; Leslie, 2003). | **km(D-glc)=21.7 ± 1.8mM** (rat liver) (Ciaraldi, et al., 1986)<br>**km(D-glc)=66±14mM** (rat hepatocytes) (Elliott and Craik, 1982)<br>**km(D-glc)=17mM** (perfused rat liver, cited) (Elliott and Craik, 1982)<br>**km(D-glc)=30mM** (rat hepatocytes, cited) (Elliott and Craik, 1982)<br>km(3-O-MG)=42.3±4.1mM (human liver) (Gould, et al., 1991; Walmsley, et al., 1998)<br>km(3-O-Methyl glc)=17.3 ± 4.3mM (rat liver) (Ciaraldi, et al., 1986)<br>**$V_{max}$(D-glc)=220±19**mmol/min/l of cell H2O (rat hepatocytes) (Elliott and Craik, 1982)<br>**$V_{max}$(D-glc)=345**mmol/min/l of cell H2O (perfused rat liver, cited) (Elliott and Craik, 1982)<br>**$V_{max}$(D-glc)=70**mmol/min/l of cell H2O (rat hepatocytes, cited) (Elliott and Craik, 1982)<br><br>**km(D-gal)=174±48mM** (rat hepatocytes) (Elliott and Craik, 1982)<br>**km(D-gal)=100mM** (rat hepatocytes, cited) (Elliott and Craik, 1982)<br>**km(D-gal)>50mM** (GLUT2 enderocytes) (Walmsley, et al., 1998)<br>**km(D-gal)=85.5 ± 10.7mM** (human, liver-type GLUT2) (Colville, et al., 1993)<br>**km(D-gal)=92 ± 8.4mM** (human, liver-type GLUT2) (Arbuckle, et al., 1996)<br>**km(D-gal)~27.7mM** (dog liver, multiple indicator dilution curves (Goresky, et al., 1973)<br>**$V_{max}$ (D-gal)=288±48** mmol/min/l of cell H2O (rat hepatocytes) (Elliott and Craik, 1982)<br>**$V_{max}$ (D-gal)=160**mmol/min/l of cell H2O (rat hepatocytes, cited) (Elliott and Craik, 1982)<br><br>Km(D-fru)=66mM (Walmsley, et al., 1998)<br>Km(D-fru)=67mM (perfused rat liver, cited) (Elliott and Craik, 1982)<br>Km(D-fru)=>100mM (rat hepatocytes, cited) (Elliott and Craik, 1982)<br>v(D-fru)=291±26 mmol/min/l of cell H2O (rat hepatocytes) (Elliott and Craik, 1982)<br>$V_{max}$ (D-fru)=50mmol/min/l of cell H2O (perfused rat liver, cited) (Elliott and Craik, 1982)<br>$V_{max}$ (D-fru)=>160mmol/min/l of cell H2O (rat hepatocytes, cited) (Elliott and Craik, 1982)<br><br>**Accumulation rate** (human GLUT2) |

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| | | v(deoxy-D-glc) = 4.33±0.15 pmol/min/oocyte<br>v(D-gal) = 1.68±0.09 pmol/min/oocyte<br>v(D-fru) = 0.78±0.09 pmol/min/oocyte |
| **GALK** | **Galactokinase**<br>D-galactose [**gal**] + ATP [**atp**] ↔ D-galactose 1-phosphate [**gal1p**] + ADP [**adp**] + H+ [**hydron**]<br><br>**Reaction**<br>EC:2.7.1.6<br>RHEA:13556<br>KEGG:R01092<br>MetaCyc:GALACTOKIN-RXN<br>**Protein**<br>UniProt:P51570 (GALK1_HUMAN)<br>homodimer P51570*2<br>**Gene**<br>GALK, GALK1<br>**Disease**<br>MIM:230200 (GALCT2 Galactosemia II)<br><br>Galactokinase being rate limiting for galactose clearance (Schirmer, et al., 1986) | **Two-substrate ordered, ternary complex reaction** (Timson and Reece, 2003)<br><br>**kcat(gal) = 8.7±5 1/s** (SABIORK:14785)(Timson and Reece, 2003)<br><br>**km(atp) = 0.034±0.004mM** (SABIORK:14792)(Timson and Reece, 2003)<br>**km(atp) = 0.12mM** (adult, rat liver){Cuatrecasas1965}<br><br>**km(gal)=0.97±0.22mM** (SABIORK:14785) (Timson and Reece, 2003)<br>**km(gal) = 0.436mM** (SABIORK:45367), (Sangiuolo, et al., 2004)<br>**km(gal) = 0.15mM** (adult, rat liver){Cuatrecasas1965}<br>km(gal) = 0.65mM (newborn, rat liver){Cuatrecasas1965}<br>km(gal) = 0.91mM (18 day fetal, rat liver){Cuatrecasas1965}<br>**km(gal) = 0.14±0.01mM** (SEM, N=6, adult rat liver) {Walker1968}<br>km(gal) = 0.15±0.01mM (SEM, N=4, neonatal rat liver) {Walker1968}<br>km(gal) = 0.14±0.01mM (SEM, N=4, foetal rat liver) {Walker1968}<br><br>**Uncompetitive product inhibition** of GALK (adult rat liver) by gal1p with both 1mM and 5mM gal1p altering the Km for galactose from 0.150mM to 0.800mM (1mM gal1p caused 15% inhibition, 5mM gal1p 50% inhibition)<br>**ki(gal1p) = 5.3mM (5.0-5.7mM)** (adult rat liver) (Cuatrecasas and Segal, 1965)<br><br>**km(gal)<0.83mM** (dog liver, multiple indicator dilution curves) (Goresky, et al., 1973) |
| **IMP** | **Inositol monophosphatase**<br>D-galactose 1-phosphate [**gal1p**] ↔ D-galactose [**gal**] + phosphate [**pi**]<br><br>**Reaction**<br>EC:3.1.3.25<br>**Protein**<br>UniProt:P29218 (IMPA1_HUMAN)<br>homodimer P29218*2<br>**Gene**<br>IMPA1, IMPA | **Competitive inhibition model**<br>Kinetic analysis demonstrated that gal1p competitively inhibited human IMP1 by increasing Km for inositol-1p (ino1p) from 320±50µM to 980±70µM without changing the Vmax (Slepak, et al., 2007)<br>**km(ino1p) = 0.320±0.050mM** (Slepak, et al., 2007)<br>**km(gal1p) = 0.35mM** (similar kinetics gal1p to ino1p in vitro) (Parthasarathy, et al., 1997) |

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| | Normal substrate inositol-1p (ino1p) | |
| **GALT** | **Galactose-1-phosphate uridyl transferase**<br>UDP-D-glucose [**udpglc**] + D-galactose 1-phosphate [**gal1p**] ↔ D-glucose 1-phosphate [**glc1p**] + UDP-D-galactose [**udpgal**].<br><br>**Reaction**<br>EC:2.7.7.12<br>RHEA:13992<br>KEGG:R00955<br>**Protein**<br>UniProt:P07902 (GALT_HUMAN)<br>homodimer P07902*2<br>**Gene**<br>GALT<br>**Disease**<br>OMIM:230400 (GALCT Galactosemia) | The catalytic mechanism of GALT is **ping-pong kinetics** with covalent intermediate UMP-enzyme (Facchiano and Marabotti, 2010).<br><br>**Mutation analysis** (Quimby, et al., 1996)<br>**km(gal1p) = 0.57±0.14mM** (human, wildtype) (Quimby, et al., 1996)<br>**km(udpglc) = 0.21±0.04mM** (human, wildtype) (Quimby, et al., 1996)<br><br>**Mutation analysis** (Tang, et al., 2012)<br>**km(gal1p) = 1.25±0.36mM** (human, wildtype) (Tang, et al., 2012)<br>**km(udpglc) = 0.43±0.09mM** (human, wildtype) (Tang, et al., 2012)<br><br>(?species, 4°C) (Geeganage and Frey, 1998)<br>**km(udpglc) = 0.5±0.1mM**<br>**v(glc1p)** = **281± 18 1/s**<br>**km(glc1p) = 0.37±0.18mM**<br>**v(glc1p)** = **226± 10 1/s**<br>**km(gal1p) = 0.061±0.020mM**<br>**v(glc1p)** = **166± 13 1/s**<br><br>**Potent linear competent inhibitors UTP and UDP of UDP-glucose** (Segal and Rogers, 1971)**:**<br>**Ki(UTP) = 0.13mM** (rat, liver)<br>**Ki(UDP) = 0.35mM** (rat, liver)<br>Ki(UMP) = 2.3mM (rat, liver)<br>Ki(UDP-glucuronic acid)=0.40mM (rat, liver) |
| **GALE** | **UDP-glucose 4-epimerase**<br>UDP-D-glucose [**udpglc**] ↔ UDP-D-galactose [**udpgal**]<br><br>**Reaction**<br>EC:5.1.3.2<br>RHEA:22171<br>KEGG:R00291<br>**Protein**<br>UniProt:Q14376 (GALE_HUMAN)<br>homodimer Q14376*2<br>**Gene**<br>GALE<br>**Disease**<br>OMIM:230350 (GALE deficiency) | **Mutation analysis** (Timson, 2005)<br>**km(udpgal)=0.069±0.012mM** (human, wildtype) (Timson, 2005)<br>**kcat(udpgal) = 36±1.4 1/s** (human, wildtype) (Timson, 2005)<br><br>**km(udpgal) = 0.15 ± 0.02mM** (human, wildtype) (Wohlers and Fridovich-Keil, 2000)<br>km(udpgal, V94M) = 0.27 ± 0.01mM (human, V94M) (Wohlers and Fridovich-Keil, 2000)<br>**km(udpgal)=0.140± 0.007mM** (human, wildtype) (SABIORK:19823) (Winans and Bertozzi, 2002)<br>**km(udpgal)=0.120± 0.04mM** (human, wildtype) (SABIORK:46260) (Wasilenko, et al., 2005)<br>**kcat= 33.8±11.2** (human, wildtype) (SABIORK:16222) (Thoden, et al., 2002)<br>**km(udpgal) = 0.230±0.06mM** (human, wildtype) (SABIORK:46263) (Quimby, et |

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| | | al., 1997) |
| | Alternative activity with GlcNAc:<br>UDP-GalNAc ↔ UDP-GlcNAc<br><br>“Ethanol treatment increases the NADH/NAD ratio in liver and by this inhibits the GALE. Under these conditions oxidation and elimination of galactose are impaired. Combined galactose+ethanol treatment results in accumulation of gal1p and udpgal in rat liver. The formation of high amounts of udpgal leads to a change in the distribution of liver uracil nucleotides. A marked decrease of udpglc, utp, udp and ump is followed by an increase of the sum of uracil nucleotides.” (Keppler, et al., 1970)<br>“The GALE reaction is indicated as the rate-limiting step of galactose metabolism in rat liver by the ratio of galactose metabolites.“ (Keppler, et al., 1970)<br>“The almost 4-fold increase of gal1p and updgal and the even stronger drop of the udpglc content in the ethanol treated liver after a galactose load demonstrates the ethanol-induced inhibition of the GALE.” (Keppler, et al., 1970).<br>“Galactose provokes pronounced alterations of the uracil nucleotide contents in the liver, which are intensified by an inhibition of the GALE” (Keppler, et al., 1970) | |
| **UGP** | **UDP-glucose pyrophosphorylase**<br>D-glucose 1-phosphate [**glc1p**] + UTP [**utp**] + H+[**hydron**] ↔ UDP-glucose [**udglc**]+ diphosphate [**ppi**]<br><br>**Reaction**<br>EC:2.7.7.9<br>RHEA:19892<br>KEGG:R00289<br>**Protein**<br>UniProt:Q16851 (UGPA_HUMAN)<br>homooctamer Q16851*8<br>**Gene**<br>UGP2, UGP1 | Enzyme displays simple Michaelis-Menten kinetics in both directions (Chang, et al., 1996)<br>MgUTP is a product inhibitor that shows competitive inhibition with respect to UDP-Glc (Chang, et al., 1996)<br><br>(human, liver, wildtype) (Chang, et al., 1996)<br>**km(udpglc) = [0.031 - 0.051]mM**<br>**km(pp) = [0.172 - 0.210] mM**<br>**km(glc1p) = [0.172 - 0.174] mM**<br>**km(utp) = [0.563 - 0.692] mM**<br>**ki(utp) = 0.477± 41 mM** (competitive inhibition with respect to UDP-glc)<br>**$V_{fwd}/V_{rev}$ = 0.260**<br>(human, liver, wildtype) (Duggleby, et al., 1996)<br>**km(udpglc) = 0.049±0.004mM**<br>**km(pp) = 0.166±0.013 mM**<br>**km(glc1p) = 0.172±0.010 mM**<br>**km(utp) = 0.563±0.115 mM**<br>**ki(utp) = 0.643± 0.047 mM** (competitive inhibition with respect to UDP-glc) |
| **UGALP** | **UDP-galactose pyrophosphorylase**<br>D-galactose-1-phosphate [**gal1p**] + UTP [**utp**] + H+[**hydron**] ↔ UDP-D-galactose [**udpgal**] pyrophosphate [**pp**] | |

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| | **Reaction**<br>EC:2.7.7.10<br>RHEA:14212<br>KEGG:R00502<br>**Protein**<br>UniProt:Q16851 (UGPA_HUMAN)<br>homooctamer Q16851*8<br>**Gene**<br>UGP2, UGP1<br><br>"The formation of UDP-glucose is the major physiological function of UGP, however at slow rates, the enzyme also catalyzes the phosphorylation of UDP-galactose." (Knop and Hansen, 1970) [Segal1968].<br><br>"Not significant in normal physiological conditions, but in galactosemic patients could circumvent GALT deficiency. Stable transfection of human UGP (hUGP2) rescued galactose GALT deficient yeast from "galactose toxicity." [Lai2002]. | **ki(udpglc) = 0.013± 4 mM** (competitive inhibition with respect to UTP?) (human, liver, wildtype) (Knop and Hansen, 1970)<br>**keq**([udpglc][pp]/([UTP][glc1p])) = **0.15 – 0.16**<br>**km(udpglc) = 50mM**<br>**km(utp) = 48 mM**<br>**km(glc1p) = 95±10 mM**<br><br>**keq**([UTP][glc1p]/([udpglc][pp])) = 4.55±0.1 (Guynn, et al., 1974) (**0.22**)<br><br>The saturating concentration for UDP-galactose is 10 times that of UDP-glucose:<br>**km(udpgal)** = 10*km(udpglc) ~ **0.5mM** (human, liver, wildtype) (Knop and Hansen, 1970)<br>**km(udpgal) = 0.420mM** (rabbit, liver, wildtype) (Turnquist, et al., 1974)<br>udpgal was an adequate substrate at 10 times the concentration of udpglc, showing 14.3% of udpglc (Calf) and 12.0% (Human).<br>activity with udpgal 2-12% of udpglc (12% with 3mM udpgal) (human liver) (Turnquist, et al., 1974)<br><br>"The activity of UDPG:galactose-1-phosphate uridylyltransferase from rat liver under optimal conditions in vitro is less than 5% of the UDPG pyrophosphorylase activity." (Keppler, et al., 1970)[Keppler1970 ->39,40]<br><br>**gal1p as competitive inhibitor of glc1p**<br>"Previously, we showed that galactose-1-phosphate competitively inhibited UDP-glucose pyrophosphorylase, leading to 66% reduction in UDP-glucose/galactose contents in GALT-deficient cells under galactose challenge" [Slepak2007->Lai2002]. |
| **ALDR** | **Aldose reductase (galactitol NAD 1-oxidoreductase)**<br>D-galactose [**gal**] + NADPH [**nadph**] + H ↔ galactitol [**galtol**] + NADP [**nadp**]<br><br>**Reaction**<br>EC:1.1.1.21<br>RHEA:37967<br>KEGG:R01095<br>**Protein**<br>UniProt:P15121 (ALDR_HUMAN)<br>monomer P15121*1<br>**Gene**<br>AKR1B1, ALDR1 | **km(gal) = 40.0mM** (human brain) (SABIORK:22893) (Wermuth, et al., 1982)<br>**kcat(gal) = 0.40 1/s** (human brain) (SABIORK:22893) (Wermuth, et al., 1982)<br><br>**km(gal) = 110.0mM** (human brain) (SABIORK:15695) (Wermuth and von Wartburg, 1982) |

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| | Aldolase reductase is specific for NADPH as cofactor (NADH ~10% of NADPH-dependent activity) (Wermuth and von Wartburg, 1982).<br>"Aldolase reductase catalyzes the conversion of aldoses and a number of other aldehydes to the corresponding alcohol metabolites. It is one of several cytosolic, monomeric, NADPH-dependent aldehyde and ketone reductases of wide substrate specificity" (Wermuth, et al., 1982)". | |
| **PGM1** | **Phosphoglucomutase-1**<br>D-glucose 1-phosphate [**glc1p**] ↔ D-glucose 6-phosphate [**glc6p**]<br><br>**Reaction**<br>EC:5.4.2.2<br>RHEA:23539<br>KEGG:R00959<br>**Protein (multiple isoforms PGM1, PGM2)**<br>UniProt:P36871 (PGM1_HUMAN)<br>monomer P36871*1<br>main isoform for glc1p ↔ glc6p reaction<br>**Gene**<br>PGM1<br>**Disease**<br>OMIM:612934 (Glycogen storage disease 14)<br>OMIM:614921 (Congenital disorder of glycosylation 1T CDG1T)<br><br>**Protein**<br>UniProt:Q96G03 (PGM2_HUMAN)<br>**Gene**<br>PGM2<br><br>CDG1T - A multisystem disorder caused by a defect in glycoprotein biosynthesis and characterized by under-glycosylated serum glycoproteins. | The equilibrium lies strongly toward glc6p and reaction proceeds through **ping-pong mechanism** (Guynn, et al., 1974)<br>The kinetic properties of PGM1 and PGM2 are essentially the same. PGM1 is specific for mutation of glucose, whereas PGM2 also has phosphoribomutase activities. (human, RBC) (Accorsi, et al., 1989)<br><br>**[glc6p]/[glc1p] ~10-12** (Guynn, et al., 1974)<br>DeltaG =-7.1 kJ/mol (König, et al., 2012)<br><br>**km(glc1p) = 0.049mM** (human, RBC) (Quick, et al., 1974)<br><br>**km(glc1p) = 0.045mM** (rat, heart) (Kashiwaya, et al., 1994)<br>**km(glc6p) = 0.67mM** (rat, heart) (Kashiwaya, et al., 1994)<br><br>**km(glc1p) = 0.083mM** (human, RBC, PGM1) (Accorsi, et al., 1989)<br>ki(fru16bp) = 0.092mM (human, RBC, PGM1) (Accorsi, et al., 1989) |
| **PPASE** | **Pyrophosphatase**<br>Pyrophosphate [**pp**] + H2O [**h2o**] → 2 phosphate [**phos**] + H+ [**hydron**] | **km(pp) = 0.005mM** (rat liver) (Yoshida, et al., 1982)<br>**km(pp) = 0.14mM** (human erythrocyte) (Thuillier, 1978)<br>**km(pp) = 0.07mM** (rat liver) (Irie, et al., 1970)<br>**Delta G0 = -23.56 kJ/mol** (Thuillier, 1978) |

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| | **Reaction**<br>EC:3.6.1.1<br>RHEA:24579<br>KEGG:R00004<br>**Protein**<br>UniProt:Q15181 (IPYR_HUMAN)<br>homodimer Q15181*2<br>**Gene**<br>PPA1, IOPPP, PP | **Delta G0 = -19.2 kJ/mol** (Guynn, et al., 1974) |
| **NDKU** | **Nucleoside diphosphokinase (ATP:UDP phosphotransferase)**<br>ATP [**atp**] + UDP [**udp**] ↔ ADP [**adp**] + UTP [**udp**]<br><br>**Reaction**<br>EC: 2.7.4.6<br>RHEA:25101<br>KEGG:R00156<br>**Protein**<br>Multitude of isoforms | Compulsory-order substituted-enzyme (**Ping Pong Bi Bi**) mechanism (Lam and Packham, 1986)<br><br>**km(atp) = 0.38mM** (human, platelets) (Lam and Packham, 1986)<br>**km(adp) = 0.024mM** (human, platelets) (Lam and Packham, 1986)<br>**km(gtp) = 0.12mM** (human, platelets) (Lam and Packham, 1986)<br><br>**km(atp) = 1.33mM** (rat, liver) (Kimura and Shimada, 1988)<br>**km(adp) = 0.042mM** (rat, liver) (Kimura and Shimada, 1988)<br>**km(udp) = 0.19mM**(rat, liver) (Kimura and Shimada, 1988)<br><br>**km(atp) = 1.80 mM** (rat, liver) (Fukuchi, et al., 1994)<br>**km(adp) = 0.066 mM** (rat, liver) (Fukuchi, et al., 1994)<br>**km(utp) = 27.00mM** (rat, liver) (Fukuchi, et al., 1994)<br>km(gtp) = 0.15mM (rat, liver) (Fukuchi, et al., 1994)<br>km(gdp) = 0.049mM (rat, liver) (Fukuchi, et al., 1994) |
| **NADPR** | **NADP reductase**<br>NADP [**nadp**] + H2→NADPH [**nadph**]<br><br>Modeled via glucose-6-phosphate dehydrogenase in pentose phosphate pathway<br>D-glucose 6-phosphate [**glc6p**] + NADP [**nadp**] → 6-phospho-D-glucono-1,5-lactone + NADPH [**nadph**] + H<br><br>**Reaction**<br>EC: 1.1.1.49<br>RHEA:15844<br>KEGG:R00835<br>**Protein**<br>UniProt:P11413 (G6PD_HUMAN)<br>homotetramer (dimer of dimer) P11413*4 | Delta G0 = -19.6 kJ/mol [Schuster1995]<br><br>**km(glc6p) = 0.040±0.008 mM** (human, placenta) (Ozer, et al., 2001)<br>**km(nadp) = 0.020±0.010 mM** (human, placenta) (Ozer, et al., 2001)<br>**ki(nadph) = 0.0171±0.0032 mM** (human, placenta) (Ozer, et al., 2001)<br><br>**km(glc6p) = 0.072 mM** (human, RBC) (Bautista, et al., 1992)<br>**km(glc6p) = 0.069±0.003 mM** (human, recombinant) (Bautista, et al., 1992)<br>**km(nadp) = 0.013 mM** (human, RBC) (Bautista, et al., 1992)<br>**km(nadp) = 0.012±0.002 mM** (human, recombinant) (Bautista, et al., 1992)<br>**km(nadph) = 0.015±0.002 mM** (human, RBC) (Bautista, et al., 1992)<br>**km(nadph) = 0.014±0.003 mM** (human, recombinant) (Bautista, et al., 1992)<br><br>**km(glc6p) = 0.326mM** (rat, liver)<br>**km(glc6p) = 0.157mM** (rat, liver) |

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| | **Gene**<br>G6PD | (Corpas, et al., 1995; Corpas, et al., 1995)<br>**km(nadp) = 0.108 mM** (rat, liver)<br>**km(nadp) = 0.258 mM** (rat, liver) (Corpas, et al., 1995; Corpas, et al., 1995)<br>**ki(nadhp) = 0.010 mM**(rat, liver)<br>**ki(nadhp) = 0.021 mM**(rat, liver) (Corpas, et al., 1995; Corpas, et al., 1995) |
| **ATPS** | **ATP synthesis**<br>ADP [**adp**] + phosphate [**phos**] + H+ [**hydron**] → ATP [**atp**] + H20 [**h2o**]<br><br>**Reaction**<br>RHEA:13068<br>KEGG:R00086<br><br>Modelled via general ATP producing reaction representative for ATP production via glycolysis and oxidative phosphorylation | |
| **GTFGAL**<br>**GTFGLC** | **Glycosyltransferase**<br>Acceptor + UDP-glucose [**udpglc**] → Acceptor-glucose + UDP [**udp**]<br><br>Acceptor + UDP-glucose [**udpgal**] → Acceptor-glucose + UDP [**udp**]<br><br>Enzymes that transfer mono- or oligosaccharides from donor molecules to growing oligosaccharide chains or proteins are called glycosyltransferases (Gtfs) | |
| **GLY** | **Glycolysis**<br>D-glucose 6-phosphate [**glc6p**] + 6 O2 [**o2**] → phosphate [**phos**] + 6 CO2 [**co2**] + 5 H2O [**h2o**]<br><br>Pseudo-reaction for using galactose in glycolysis freeing the phosphate. | |
| **GALDH** | **Galactose 1-dehydrogenase**<br>D-galactose + $NAD^+$ ↔ D-galactono-1,4-lactone + NADH + $H^+$<br>EC.1.1.1.48 (Brenda only bacteria)<br>D-galactose -> galactonate<br>(first enzyme in oxidative pathway)<br>[Segal1968 -> Cuatrecasas1966,15]<br>Alternative pathway to xylulose.<br><br>D-Galactose + Oxygen + H2O <=> D-Galactonate + Hydrogen | |

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| | peroxide<br>EC:1.1.3.9<br>KEGG:R01098<br>(only bacteria) |

## REFERENCES


Accorsi, A., *et al.* (1989) Isoenzymes of phosphoglucomutase from human red blood cells: isolation and kinetic properties, *Preparative biochemistry*, **19**, 251-271.

Arbuckle, M.I., *et al.* (1996) Structure-function analysis of liver-type (GLUT2) and brain-type (GLUT3) glucose transporters: expression of chimeric transporters in Xenopus oocytes suggests an important role for putative transmembrane helix 7 in determining substrate selectivity, *Biochemistry*, **35**, 16519-16527.

Bautista, J.M., Mason, P.J. and Luzzatto, L. (1992) Purification and properties of human glucose-6-phosphate dehydrogenase made in E. coli, *Biochimica et biophysica acta*, **1119**, 74-80.

Brown, G.K. (2000) Glucose transporters: structure, function and consequences of deficiency, *Journal of inherited metabolic disease*, **23**, 237-246.

Chang, H.Y., *et al.* (1996) The importance of conserved residues in human liver UDPglucose pyrophosphorylase, *European journal of biochemistry / FEBS*, **236**, 723-728.

Ciaraldi, T.P., Horuk, R. and Matthaei, S. (1986) Biochemical and functional characterization of the rat liver glucose-transport system. Comparisons with the adipocyte glucose-transport system, *The Biochemical journal*, **240**, 115-123.

Colville, C.A., *et al.* (1993) Kinetic analysis of the liver-type (GLUT2) and brain-type (GLUT3) glucose transporters in Xenopus oocytes: substrate specificities and effects of transport inhibitors, *The Biochemical journal*, **290 ( Pt 3)**, 701-706.

Corpas, F.J., *et al.* (1995) Kinetic properties of hexose-monophosphate dehydrogenases. II. Isolation and partial purification of 6-phosphogluconate dehydrogenase from rat liver and kidney cortex, *Molecular and cellular biochemistry*, **144**, 97-104.

Corpas, F.J., *et al.* (1995) Kinetic properties of hexose-monophosphate dehydrogenases. I. Isolation and partial purification of glucose-6-phosphate dehydrogenase from rat liver and kidney cortex, *Life sciences*, **56**, 179-189.

Cuatrecasas, P. and Segal, S. (1965) Mammalian Galactokinase. Developmental and Adaptive Characteristics in the Rat Liver, *The Journal of biological chemistry*, **240**, 2382-2388.

Duggleby, R.G., *et al.* (1996) Sequence differences between human muscle and liver cDNAs for UDPglucose pyrophosphorylase and kinetic properties of the recombinant enzymes expressed in Escherichia coli, *European journal of biochemistry / FEBS*, **235**, 173-179.

Elliott, K.R. and Craik, J.D. (1982) Sugar transport across the hepatocyte plasma membrane, *Biochemical Society transactions*, **10**, 12-13.

Facchiano, A. and Marabotti, A. (2010) Analysis of galactosemia-linked mutations of GALT enzyme using a computational biology

approach, *Protein engineering, design & selection : PEDS*, **23**, 103-113.
Fukuchi, T., *et al.* (1994) Recombinant rat nucleoside diphosphate kinase isoforms (alpha and beta): purification, properties and application to immunological detection of native isoforms in rat tissues, *Biochimica et biophysica acta*, **1205**, 113-122.
Geeganage, S. and Frey, P.A. (1998) Transient kinetics of formation and reaction of the uridylyl-enzyme form of galactose-1-P uridylyltransferase and its Q168R-variant: insight into the molecular basis of galactosemia, *Biochemistry*, **37**, 14500-14507.
Goresky, C.A., Bach, G.G. and Nadeau, B.E. (1973) On the uptake of materials by the intact liver. The transport and net removal of galactose, *The Journal of clinical investigation*, **52**, 991-1009.
Gould, G.W., *et al.* (1991) Expression of human glucose transporters in Xenopus oocytes: kinetic characterization and substrate specificities of the erythrocyte, liver, and brain isoforms, *Biochemistry*, **30**, 5139-5145.
Guynn, R.W., *et al.* (1974) The concentration and control of cytoplasmic free inorganic pyrophosphate in rat liver in vivo, *The Biochemical journal*, **140**, 369-375.
Irie, M., *et al.* (1970) Distribution and properties of alkaline pyrophosphatases of rat liver, *Journal of biochemistry*, **67**, 47-58.
Kashiwaya, Y., *et al.* (1994) Control of glucose utilization in working perfused rat heart, *The Journal of biological chemistry*, **269**, 25502-25514.
Keppler, D., Rudigier, J. and Decker, K. (1970) Trapping of uridine phosphates by D-galactose in ethanol-treated liver, *FEBS letters*, **11**, 193-196.
Keppler, D.O., *et al.* (1970) The trapping of uridine phosphates by D-galactosamine. D-glucosamine, and 2-deoxy-D-galactose. A study on the mechanism of galactosamine hepatitis, *European journal of biochemistry / FEBS*, **17**, 246-253.
Kimura, N. and Shimada, N. (1988) Membrane-associated nucleoside diphosphate kinase from rat liver. Purification, characterization, and comparison with cytosolic enzyme, *The Journal of biological chemistry*, **263**, 4647-4653.
Knop, J.K. and Hansen, R.G. (1970) Uridine diphosphate glucose pyrophosphorylase. IV. Crystallization and properties of the enzyme from human liver, *The Journal of biological chemistry*, **245**, 2499-2504.
König, M., Bulik, S. and Holzhütter, H.G. (2012) Quantifying the contribution of the liver to glucose homeostasis: a detailed kinetic model of human hepatic glucose metabolism, *PLoS computational biology*, **8**, e1002577.
Lam, S.C. and Packham, M.A. (1986) Isolation and kinetic studies of nucleoside diphosphokinase from human platelets and effects of cAMP phosphodiesterase inhibitors, *Biochemical pharmacology*, **35**, 4449-4455.
Leslie, N.D. (2003) Insights into the pathogenesis of galactosemia, *Annual review of nutrition*, **23**, 59-80.
Ozer, N., Aksoy, Y. and Ogus, I.H. (2001) Kinetic properties of human placental glucose-6-phosphate dehydrogenase, *The international journal of biochemistry & cell biology*, **33**, 221-226.
Parthasarathy, R., Parthasarathy, L. and Vadnal, R. (1997) Brain inositol monophosphatase identified as a galactose 1-phosphatase, *Brain research*, **778**, 99-106.
Quick, C.B., Fisher, R.A. and Harris, H. (1974) A kinetic study of the isozymes determined by the three human phosphoglucomutase loci PGM1, PGM2, and PGM3, *European journal of biochemistry / FEBS*, **42**, 511-517.
Quimby, B.B., *et al.* (1997) Characterization of two mutations associated with epimerase-deficiency galactosemia, by use of a yeast

expression system for human UDP-galactose-4-epimerase, *American journal of human genetics*, **61**, 590-598.
Quimby, B.B., *et al.* (1996) Functional requirements of the active site position 185 in the human enzyme galactose-1-phosphate uridylyltransferase, *The Journal of biological chemistry*, **271**, 26835-26842.
Sangiuolo, F., *et al.* (2004) Biochemical characterization of two GALK1 mutations in patients with galactokinase deficiency, *Human mutation*, **23**, 396.
Schirmer, W.J., *et al.* (1986) Galactose clearance as an estimate of effective hepatic blood flow: validation and limitations, *The Journal of surgical research*, **41**, 543-556.
Segal, S. and Rogers, S. (1971) Nucleotide inhibition of mammalian liver galactose-I-phosphate uridylyltransferase, *Biochimica et biophysica acta*, **250**, 351-360.
Slepak, T.I., *et al.* (2007) Involvement of endoplasmic reticulum stress in a novel Classic Galactosemia model, *Molecular genetics and metabolism*, **92**, 78-87.
Tang, M., *et al.* (2012) Correlation assessment among clinical phenotypes, expression analysis and molecular modeling of 14 novel variations in the human galactose-1-phosphate uridylyltransferase gene, *Human mutation*, **33**, 1107-1115.
Thoden, J.B., *et al.* (2002) Structural analysis of the Y299C mutant of Escherichia coli UDP-galactose 4-epimerase. Teaching an old dog new tricks, *The Journal of biological chemistry*, **277**, 27528-27534.
Thuillier, L. (1978) Purification and kinetic properties of human erythrocyte Mg2+-dependent inorganic pyrophosphatase, *Biochimica et biophysica acta*, **524**, 198-206.
Timson, D.J. (2005) Functional analysis of disease-causing mutations in human UDP-galactose 4-epimerase, *The FEBS journal*, **272**, 6170-6177.
Timson, D.J. and Reece, R.J. (2003) Functional analysis of disease-causing mutations in human galactokinase, *European journal of biochemistry / FEBS*, **270**, 1767-1774.
Turnquist, R.L., *et al.* (1974) Uridine diphosphate glucose pyrophosphorylase: differential heat inactivation and further characterization of human liver enzyme, *Biochimica et biophysica acta*, **364**, 59-67.
Walmsley, A.R., *et al.* (1998) Sugar transporters from bacteria, parasites and mammals: structure-activity relationships, *Trends in biochemical sciences*, **23**, 476-481.
Wasilenko, J., *et al.* (2005) Functional characterization of the K257R and G319E-hGALE alleles found in patients with ostensibly peripheral epimerase deficiency galactosemia, *Molecular genetics and metabolism*, **84**, 32-38.
Wermuth, B., *et al.* (1982) Purification and characterization of human-brain aldose reductase, *European journal of biochemistry / FEBS*, **127**, 279-284.
Wermuth, B. and von Wartburg, J.P. (1982) Aldose reductase from human tissues, *Methods in enzymology*, **89 Pt D**, 181-186.
Winans, K.A. and Bertozzi, C.R. (2002) An inhibitor of the human UDP-GlcNAc 4-epimerase identified from a uridine-based library: a strategy to inhibit O-linked glycosylation, *Chemistry & biology*, **9**, 113-129.
Wohlers, T.M. and Fridovich-Keil, J.L. (2000) Studies of the V94M-substituted human UDPgalactose-4-epimerase enzyme associated with generalized epimerase-deficiency galactosaemia, *Journal of inherited metabolic disease*, **23**, 713-729.

Yoshida, C., Shah, H. and Weinhouse, S. (1982) Purification and properties of inorganic pyrophosphatase of rat liver and hepatoma 3924A, *Cancer research*, **42**, 3526-3531.