

Text S2. Overview reactions and transporters.

Full Name	Short Name		Compartiment	V _{max} [μmol/ min/kg]	References
GLUT2 glucose transporter	GLUT2	eq.4	pm	250	[1-5]
Glucokinase	GK	eq.5	cyto	15	[4,6-11]
Glucose-6-phosphatase	G6PASE	eq.6	cyto	11.25	[12-14]
Glucose-6-phosphate isomerase	GPI	eq.7	cyto	250	[15,16]
Glucose-1-phosphate 1,6-phosphomutase	G16PI	eq.8	cyto	200	[17]
UTP:Glucose-1-phosphate uridylyltransferase	UGT	eq.9	cyto	160	[18-20]
Pyrophosphate phosphohydrolase	PPASE	eq.10	cyto	4.8	[21,22]
Glycogen synthase	GS	eq.11	cyto	26.4	[23-27]
Glycogen phosphorylase	GP	eq.12	cyto	13.6	[28-33]
Nucleosid diphosphate kinase (GTP)	NDK	eq.13	cyto	1750	[34-36]
Nucleosid diphosphate kinase (UTP)	NDK	eq.14	cyto	1750	[34-36]
Adenylat kinase	AK	eq.15	cyto	500	[16,37,38]
Phosphofructo kinase 2	PFK2	eq.16	cyto	0.0025	[39-43]
Fructose-2,6-bisphosphatase	FBP2	eq.17	cyto	0.075	[39-43]
Phosphofructo kinase 1	PFK1	eq.18	cyto	0.525	[44-46]
Fructose-1,6-bisphosphatase	FBP1	eq.19	cyto	2.575	[47,48]
Aldolase	ALD	eq.20	cyto	250	[16,49-51]
Triosephosphate isomerase	TPI	eq.21	cyto	250	[16,52,53]
Glyceraldehydepsophosphate dehydrogenase	GAPDH	eq.22	cyto	250	[16]
Phosphoglycerate kinase	PGK	eq.23	cyto	250	[16]
3-Phosphoglycerate mutase	PGM	eq.24	cyto	250	[16]
Enolase	EN	eq.25	cyto	21.43	[16]
Pyruvate kinase	PK	eq.26	cyto	20	[54-57]
Phosphoenolpyruvate carboxykinase	PEPCK	eq.28	cyto	325	[58,59]
Phosphoenolpyruvate carboxykinase	PEPCK	eq.28	mito	325	[58,59]
Pyruvate Carboxylase	PC	eq.29	mito	100	[60,61]
Lactate dehydrogenase	LDH	eq.30	cyto	7.5	[62-64]
Lactate transporter	LACT	eq.31	pm	33	
Pyruvate transporter	PYRT	eq.32	mm	25	
PEP transporter	PEPT	eq.33	mm	20	
Pyruvate dehydrogenase	PDH	eq.34	mito	2.5	[65-68]
Citrate synthase	CS	eq.35	mito	2.5	[4,69-71]
Nucleosid diphosphate kinase (GTP)	NDK	eq.36	mito	250	[34-36]
Oxalacetate flux	OAAFLX	eq.37	mito	0	
Acetyl-CoA flux	ACOAFLX	eq.38	mito	0	
Citrate flux	CITFLX	eq.39	mito	0	

References

1. Ciaraldi TP, Horuk R, Matthaei S (1986) Biochemical and functional characterization of the rat liver glucose-transport system. Comparisons with the adipocyte glucose-transport system. *Biochem J* 240: 115-123.
2. Gould GW, Thomas HM, Jess TJ, Bell GI (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.
3. Leturque A, Brot-Laroche E, Le Gall M (2009) GLUT2 mutations, translocation, and receptor function in diet sugar managing. *Am J Physiol Endocrinol Metab* 296: E985-992.
4. Nelson DL, Cox MM, Lehninger AL (2008) Principles of biochemistry. New York: Freeman. getr. Zählung. p.
5. Thorens B (1996) Glucose transporters in the regulation of intestinal, renal, and liver glucose fluxes. *Am J Physiol* 270: G541-553.
6. Agius L (2008) Glucokinase and molecular aspects of liver glycogen metabolism. *Biochem J* 414: 1-18.
7. Agius L, Peak M (1993) Intracellular binding of glucokinase in hepatocytes and translocation by glucose, fructose and insulin. *Biochem J* 296 (Pt 3): 785-796.
8. Brocklehurst KJ, Davies RA, Agius L (2004) Differences in regulatory properties between human and rat glucokinase regulatory protein. *Biochem J* 378: 693-697.
9. Morita H, Yano Y, Niswender KD, May JM, Whitesell RR, et al. (1994) Coexpression of glucose transporters and glucokinase in *Xenopus* oocytes indicates that both glucose transport and phosphorylation determine glucose utilization. *J Clin Invest* 94: 1373-1382.
10. Storer AC, Cornish-Bowden A (1976) Kinetics of rat liver glucokinase. Co-operative interactions with glucose at physiologically significant concentrations. *Biochem J* 159: 7-14.
11. Van Schaftingen E (1989) A protein from rat liver confers to glucokinase the property of being antagonistically regulated by fructose 6-phosphate and fructose 1-phosphate. *Eur J Biochem* 179: 179-184.
12. Arion WJ, Wallin BK, Carlson PW, Lange AJ (1972) The specificity of glucose 6-phosphatase of intact liver microsomes. *J Biol Chem* 247: 2558-2565.
13. Nordlie RC (1969) Some properties and possible physiological functions of phosphotransferase activities of microsomal glucose-6-phosphatase. *Ann N Y Acad Sci* 166: 699-718.
14. Reczek PR, Villee CA, Jr. (1982) A purification of microsomal glucose-6-phosphatase from human tissue. *Biochem Biophys Res Commun* 107: 1158-1165.
15. Kahana SE, Lowry OH, Schulz DW, Passonneau JV, Crawford EJ (1960) The kinetics of phosphoglucoisomerase. *J Biol Chem* 235: 2178-2184.
16. Schuster R, Holzhutter HG (1995) Use of mathematical models for predicting the metabolic effect of large-scale enzyme activity alterations. Application to enzyme deficiencies of red blood cells. *Eur J Biochem* 229: 403-418.
17. Kashiwaya Y, Sato K, Tsuchiya N, Thomas S, Fell DA, et al. (1994) Control of glucose utilization in working perfused rat heart. *J Biol Chem* 269: 25502-25514.

18. Chang HY, Peng HL, Chao YC, Duggleby RG (1996) The importance of conserved residues in human liver UDPglucose pyrophosphorylase. *Eur J Biochem* 236: 723-728.
19. Duggleby RG, Chao YC, Huang JG, Peng HL, Chang HY (1996) Sequence differences between human muscle and liver cDNAs for UDPglucose pyrophosphorylase and kinetic properties of the recombinant enzymes expressed in Escherichia coli. *Eur J Biochem* 235: 173-179.
20. Turnquist RL, Gillett TA, Hansen RG (1974) Uridine diphosphate glucose pyrophosphorylase. Crystallization and properties of the enzyme from rabbit liver and species comparisons. *J Biol Chem* 249: 7695-7700.
21. Reichert WH, Lauter CJ, Trams EG (1974) Inorganic pyrophosphatase in cultured cells. *Biochim Biophys Acta* 370: 556-563.
22. Tamura T, Shiraki H, Nakagawa H (1980) Purification and characterization of adenylate kinase isozymes from rat muscle and liver. *Biochim Biophys Acta* 612: 56-66.
23. Bosch F, Ciudad CJ, Guinovart JJ (1983) Different effects of glucagon and epinephrine on the kinetic properties of liver glycogen synthase. *FEBS Lett* 151: 76-78.
24. Ferrer JC, Favre C, Gomis RR, Fernandez-Novell JM, Garcia-Rocha M, et al. (2003) Control of glycogen deposition. *FEBS Lett* 546: 127-132.
25. Rawat AK (1968) Effects of ethanol infusion on the redox state and metabolite levels in rat liver in vivo. *Eur J Biochem* 6: 585-592.
26. Rothman DL, Magnusson I, Katz LD, Shulman RG, Shulman GI (1991) Quantitation of hepatic glycogenolysis and gluconeogenesis in fasting humans with ¹³C NMR. *Science* 254: 573-576.
27. Westphal SA, Nuttall FQ (1992) Comparative characterization of human and rat liver glycogen synthase. *Arch Biochem Biophys* 292: 479-486.
28. Ercan-Fang N, Gannon MC, Rath VL, Treadway JL, Taylor MR, et al. (2002) Integrated effects of multiple modulators on human liver glycogen phosphorylase a. *Am J Physiol Endocrinol Metab* 283: E29-37.
29. Lederer B, Stalmans W (1976) Human liver glycogen phosphorylase. Kinetic properties and assay in biopsy specimens. *Biochem J* 159: 689-695.
30. Maddaiah VT, Madsen NB (1966) Kinetics of purified liver phosphorylase. *J Biol Chem* 241: 3873-3881.
31. Stalmans W, Gevers G (1981) The catalytic activity of phosphorylase b in the liver. With a note on the assay in the glycogenolytic direction. *Biochem J* 200: 327-336.
32. Stalmans W, Hers HG (1975) The stimulation of liver phosphorylase b by AMP, fluoride and sulfate. A technical note on the specific determination of the a and b forms of liver glycogen phosphorylase. *Eur J Biochem* 54: 341-350.
33. Tan AW, Nuttall FQ (1975) Characteristics of the dephosphorylated form of phosphorylase purified from rat liver and measurement of its activity in crude liver preparations. *Biochim Biophys Acta* 410: 45-60.
34. Fukuchi T, Shimada N, Hanai N, Ishikawa N, Watanabe K, 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. *Biochim Biophys Acta* 1205: 113-122.

35. Kimura N, Shimada N (1988) Membrane-associated nucleoside diphosphate kinase from rat liver. Purification, characterization, and comparison with cytosolic enzyme. *J Biol Chem* 263: 4647-4653.
36. Lam SC, Packham MA (1986) Isolation and kinetic studies of nucleoside diphosphokinase from human platelets and effects of cAMP phosphodiesterase inhibitors. *Biochem Pharmacol* 35: 4449-4455.
37. Blair JM (1970) Magnesium, potassium, and the adenylate kinase equilibrium. Magnesium as a feedback signal from the adenine nucleotide pool. *Eur J Biochem* 13: 384-390.
38. Tsuboi KK, Chervenka CH (1975) Adenylate kinase of human erythrocyte. Isolation and properties of the predominant inherited form. *J Biol Chem* 250: 132-140.
39. Richards CS, Furuya E, Uyeda K (1981) Regulation of fructose 2,6-P₂ concentration in isolated hepatocytes. *Biochem Biophys Res Commun* 100: 1673-1679.
40. Richards CS, Yokoyama M, Furuya E, Uyeda K (1982) Reciprocal changes in fructose-6-phosphate,2-kinase and fructose-2,6-bisphosphatase activity in response to glucagon and epinephrine. *Biochem Biophys Res Commun* 104: 1073-1079.
41. Sakakibara R, Kitajima S, Uyeda K (1984) Differences in kinetic properties of phospho and dephospho forms of fructose-6-phosphate, 2-kinase and fructose 2,6-bisphosphatase. *J Biol Chem* 259: 41-46.
42. Sakata J, Abe Y, Uyeda K (1991) Molecular cloning of the DNA and expression and characterization of rat testes fructose-6-phosphate,2-kinase:fructose-2,6-bisphosphatase. *J Biol Chem* 266: 15764-15770.
43. Van Schaftingen E, Jett MF, Hue L, Hers HG (1981) Control of liver 6-phosphofructokinase by fructose 2,6-bisphosphate and other effectors. *Proc Natl Acad Sci U S A* 78: 3483-3486.
44. Brand IA, Soling HD (1974) Rat liver phosphofructokinase. Purification and characterization of its reaction mechanism. *J Biol Chem* 249: 7824-7831.
45. Dunaway GA, Segal HL (1976) Purification and physiological role of a peptide stabilizing factor of rat liver phosphofructokinase. *J Biol Chem* 251: 2323-2329.
46. Durante P, Raleigh X, Gomez ME, Campos G, Ryder E (1995) Isozyme analysis of human normal polymorphonuclear leukocyte phosphofructokinase. *Biochem Biophys Res Commun* 216: 898-905.
47. Adams A, Redden C, Menahem S (1990) Characterization of human fructose-1,6-bisphosphatase in control and deficient tissues. *J Inher Metab Dis* 13: 829-848.
48. Dzugaj A, Kochman M (1980) Purification of human liver fructose-1,6-bisphosphatase. *Biochim Biophys Acta* 614: 407-412.
49. Bais R, James HM, Rofe AM, Conyers RA (1985) The purification and properties of human liver ketohexokinase. A role for ketohexokinase and fructose-bisphosphate aldolase in the metabolic production of oxalate from xylitol. *Biochem J* 230: 53-60.
50. Doyle SA, Tolan DR (1995) Characterization of recombinant human aldolase B and purification by metal chelate chromatography. *Biochem Biophys Res Commun* 206: 902-908.
51. Malay AD, Procious SL, Tolan DR (2002) The temperature dependence of activity and structure for the most prevalent mutant aldolase B associated with hereditary

- fructose intolerance. *Arch Biochem Biophys* 408: 295-304.
52. Snyder R, Lee EW (1975) Triosephosphate isomerase from human and horse liver. *Methods Enzymol* 41: 430-434.
53. Yuan PM, Dewan RN, Zaun M, Thompson RE, Gracy RW (1979) Isolation and characterization of triosephosphate isomerase isozymes from human placenta. *Arch Biochem Biophys* 198: 42-52.
54. Flory W, Peczon BD, Koeppe RE, Spivey HO (1974) Kinetic properties of rat liver pyruvate kinase at cellular concentrations of enzyme, substrates and modifiers. *Biochem J* 141: 127-131.
55. Ishibashi H, Cottam GL (1978) Glucagon-stimulated phosphorylation of pyruvate kinase in hepatocytes. *J Biol Chem* 253: 8767-8771.
56. Reynard AM, Hass LF, Jacobsen DD, Boyer PD (1961) The correlation of reaction kinetics and substrate binding with the mechanism of pyruvate kinase. *J Biol Chem* 236: 2277-2283.
57. Van Berkel TJ, Kruijt JK, Van den Berg GB, Koster JF (1978) Difference in the effect of glucagon and starvation upon L-type pyruvate kinase from rat liver. *Eur J Biochem* 92: 553-561.
58. Case CL, Mukhopadhyay B (2007) Kinetic characterization of recombinant human cytosolic phosphoenolpyruvate carboxykinase with and without a His10-tag. *Biochim Biophys Acta* 1770: 1576-1584.
59. Yang J, Kalhan SC, Hanson RW (2009) What is the metabolic role of phosphoenolpyruvate carboxykinase? *J Biol Chem* 284: 27025-27029.
60. Jitrapakdee S, Walker ME, Wallace JC (1999) Functional expression, purification, and characterization of recombinant human pyruvate carboxylase. *Biochem Biophys Res Commun* 266: 512-517.
61. Scrutton MC, White MD (1974) Purification and properties of human liver pyruvate carboxylase. *Biochem Med* 9: 217-292.
62. Ketchum CH, Robinson CA, Hall LM, Grizzle WE (1988) Lactate dehydrogenase isolated from human liver mitochondria: its purification and partial biochemical characterization. *Clin Biochem* 21: 231-237.
63. Pettit SM, Nealon DA, Henderson AR (1981) Purification of lactate dehydrogenase isoenzyme-5 from human liver. *Clin Chem* 27: 88-93.
64. Saad LO, Mirandola SR, Maciel EN, Castilho RF (2006) Lactate dehydrogenase activity is inhibited by methylmalonate in vitro. *Neurochem Res* 31: 541-548.
65. Hamada M, Koike K, Nakaula Y, Hiraoka T, Koike M (1975) A kinetic study of the alpha-keto acid dehydrogenase complexes from pig heart mitochondria. *J Biochem* 77: 1047-1056.
66. Holness MJ, MacLennan PA, Palmer TN, Sugden MC (1988) The disposition of carbohydrate between glycogenesis, lipogenesis and oxidation in liver during the starved-to-fed transition. *Biochem J* 252: 325-330.
67. Kiselevsky YV, Ostrovtsova SA, Strumilo SA (1990) Kinetic characterization of the pyruvate and oxoglutarate dehydrogenase complexes from human heart. *Acta Biochim Pol* 37: 135-139.
68. Korotchkina LG, Sidhu S, Patel MS (2006) Characterization of testis-specific isoenzyme of human pyruvate dehydrogenase. *J Biol Chem* 281: 9688-9696.
69. Matsuoka Y, Srere PA (1973) Kinetic studies of citrate synthase from rat kidney and

- rat brain. *J Biol Chem* 248: 8022-8030.
70. Shepherd D, Garland PB (1969) The kinetic properties of citrate synthase from rat liver mitochondria. *Biochem J* 114: 597-610.
71. Smitherman TC, Mukherjee A, Robinson JB, Jr., Butsch RW, Richards EG, et al. (1979) Human heart citrate synthase: purification, properties, kinetic and immunologic studies. *J Mol Cell Cardiol* 11: 149-160.