

Supplemental Table 1. Unique\_changes\_WT\_KO

Reaction	Span	WT vs KO	Name	Equation	Subsystem	
3MOBt2im	500000	WT Unique	3-methyl-2-oxobutanoate	3mob[c] + h	Transport, Mitochondrial	
3MOPt2im	500000	WT Unique	3-Methyl-2-oxopentanoate	3mop[c] + h	Transport, Mitochondrial	
4MOPt2im	500000	WT Unique	4-methyl-2-oxopentanoate	4mop[c] + h	Transport, Mitochondrial	
4PYRDX	1	WT Unique	4-Pyridoxal secretion	4pyrdx[c] +	Transport, Extracellular	
ARACHDt2	1000000	WT Unique	fatty acid transport via diarachd[e]	<	Transport, Extracellular	
ARACHt	1000000	WT Unique	fatty acid transport via diarach[e]	<=	Transport, Extracellular	
ATPaseI	12.86041	WT Unique	V-type ATPase, H+ transp	atp[c] + (3)	Transport, Lysosomal	
CHOLATe2	258.922917	WT Unique	cholate transport via sod	cholate[e] +	Transport, Extracellular	
CHOLATe3	258.922917	WT Unique	ABC bile acid transporter	atp[c] + cho	Transport, Extracellular	
DOPAt4(2)r	500000	WT Unique	Dopamine reversible trar	dopa[e] + (2)	Transport, Extracellular	
EX_4pyrdx(e)	1	WT Unique	4-Pyridoxate Demand		Transport	
EX_ha(e)	8.319895	WT Unique	Hyaluronan Demand		Transport	
EX_ha_pre1(e)	16.639789	WT Unique	Hyaluronan biosynthesis, precursor	1	Transport	
FATP4t	1000000	WT Unique	fatty acid electroneutral	arach[c] + n	Transport, Extracellular	
FATP5t	1000000	WT Unique	fatty acid electroneutral	arachd[c] +	Transport, Extracellular	
GLCAASE8ly	25.72082	WT Unique	beta-glucuronidase, lyso	[I] : h2o + h	Hyaluronan Metabolism	
GLCAASE9ly	25.72082	WT Unique	beta-glucuronidase, lyso	[I] : (2) h2o	Hyaluronan Metabolism	
GLCURtly	51.441639	WT Unique	glucuronate transport int	glcur[c] + h	Transport, Lysosomal	
HAS1	26.452804	WT Unique	hyaluronan synthase	uacgam[c] +	Hyaluronan Metabolism	
HAS2	25.72082	WT Unique	hyaluronan synthase	ha_pre1[e]	Hyaluronan Metabolism	
HAtly	25.72082	WT Unique	hyaluronan transport, ex	ha[e] -->	ha	Transport, Lysosomal
HMGCOASim	293.497396	WT Unique	Hydroxymethylglutaryl C	[m] : acoa	Cholesterol Metabolism	
ILETA	500000	WT Unique	isoleucine transaminase	[c] : ak	g + i	Valine, Leucine, and Isoleucine Metabolism
ILETA <sub>m</sub>	500000	WT Unique	isoleucine transaminase,	[m] : ak	g + i	Valine, Leucine, and Isoleucine Metabolism
ILEt5m	500000	WT Unique	Isoleucine mitochondrial	ile-L[c] <==>	Transport, Mitochondrial	
LEUTA	500000	WT Unique	leucine transaminase	[c] : ak	g + l	Valine, Leucine, and Isoleucine Metabolism
LEUTA <sub>m</sub>	500000	WT Unique	leucine transaminase, mi	[m] : ak	g + l	Valine, Leucine, and Isoleucine Metabolism
LEUt5m	500000	WT Unique	leucine mitochondrial tra	leu-L[c] <==	Transport, Mitochondrial	
MALTe	1	WT Unique	alpha-glucosidase, extrac	[e] : h2o + r	Starch and Sucrose Metabolism	
NACHEX27ly	25.72082	WT Unique	beta-N-acetylhexosamini	[I] : h2o + h	Hyaluronan Metabolism	
NRPPHRt4(2)r	500000	WT Unique	Norepinephrine reversibl	(2) na1[e] +	Transport, Extracellular	
PYDXDH	1	WT Unique	pyridoxal dehydrogenase	[c] : h2o + o	Vitamin B6 Metabolism	

TCHOLAt	258.922917	WT Unique	taurocholate transport via hco3[c] + tc	Transport, Extracellular
TCHOLAt3	258.922917	WT Unique	ABC bile acid transporter atp[c] + h2c	Transport, Extracellular
TRPt	1	WT Unique	L-tryptophan transport trp-L[e] <==	Transport, Extracellular
VALTA	500000	WT Unique	valine transaminase [c] : ak + v	Valine, Leucine, and Isoleucine Metabolism
VALTAm	500000	WT Unique	valine transaminase, mitochondrial [m] : ak + v	Valine, Leucine, and Isoleucine Metabolism
VALt5m	500000	WT Unique	Valine reversible mitochondrial val-L[c] <==	Transport, Mitochondrial
sink_3mob(c)	1	WT Unique	3-Methyl-2-oxobutanoate Demand	Transport
sink_3mop	1	WT Unique	(S)-3-Methyl-2-oxopentanoate Demand	Transport
sink_4mop	1	WT Unique	4-Methyl-2-oxopentanoate Demand	Transport
AHCYStr	3	KO Unique	S-Adenosyl-L-homocysteine ahcys[c] <==	Transport, Endoplasmic Reticular
AMETr	3	KO Unique	S-Adenosyl-L-methionine amet[c] <==	Transport, Endoplasmic Reticular
AMETt2m	3	KO Unique	S-Adenosyl-L-methionine ahcys[m] +	Transport, Mitochondrial
ARGt4	1	KO Unique	L-arginine transport in via arg-L[e] + n	Transport, Extracellular
ASPCTr	49.980399	KO Unique	aspartate carbamoyltransferase [c] : asp-L +	Pyrimidine Biosynthesis
BTNt3i	259.722917	KO Unique	Biotin transport via sodium atp[c] + btn	Transport, Extracellular
CBPS	49.980399	KO Unique	carbamoyl-phosphate synthase [c] : (2) atp	Pyrimidine Biosynthesis
CYSt4	500000	KO Unique	L-cysteine reversible transmembrane cys-L[e] + n	Transport, Extracellular
CYTDn	65.005729	KO Unique	cytidine deaminase, nuclear [n] : cytd +	Nucleotides
CYTDtn	65.005729	KO Unique	cytidine transport in nuclear cytd[c] <==>	Transport, Nuclear
DHORD9	49.980399	KO Unique	dihydroorotic acid dehydratase dhor-S[c] +	Pyrimidine Biosynthesis
DHORTS	49.980399	KO Unique	dihydroorotase [c] : dhor-S	Pyrimidine Biosynthesis
EX_tyr-L(e)	1	KO Unique	L-tyrosine transport in via sodium syr	L-tyrosine transport in via sodium symport
GHMT2r	29.264607	KO Unique	glycine hydroxymethyltransferase [c] : ser-L +	Glycine, Serine, and Threonine Metabolism
GLCtly	2	KO Unique	glucose efflux from lysosomes glc-D[l] -->	Transport, Lysosomal
GMPS2	86.907639	KO Unique	GMP synthase [c] : atp + g	Nucleotides
ILEt4	500000	KO Unique	L-isoleucine transport in via ile-L[e] + n	Transport, Extracellular
IMPD	86.907639	KO Unique	IMP dehydrogenase [c] : h2o + i	Nucleotides
MALTly	1	KO Unique	alpha-glucosidase, lysosomal [l] : h2o + n	Starch and Sucrose Metabolism
MALTt1r	1	KO Unique	maltose transport (unipolar) malt[e] <==	Transport, Extracellular
NH4tn	65.005729	KO Unique	ammonia nuclear transport nh4[c] <==>	Transport, Nuclear
OMPDC	45.991031	KO Unique	orotidine-5'-phosphate decarboxylase [c] : h + o	Pyrimidine Biosynthesis
ORPT	45.991031	KO Unique	orotate phosphoribosyltransferase [c] : orot5p	Pyrimidine Biosynthesis
PCFLOPm	1	KO Unique	phosphatidylcholine flippase atp[c] + h2c	Transport, Mitochondrial
PETOHMm_hs	1	KO Unique	phosphatidylethanolamine phosphatase [m] : (3) am	Glycerophospholipid Metabolism

PETOHMr_hs	1 KO Unique	phosphatidylethanolamir [r] : (3) ame	Glycerophospholipid Metabolism
PE_HSter	1 KO Unique	phosphatidylethanolamir pe_hs[c] <=	Transport, Endoplasmic Reticular
PGCD	40.05 KO Unique	phosphoglycerate dehyd [c] : 3pg + n	Glycine, Serine, and Threonine Metabolism
PSERT	40.05 KO Unique	phosphoserine transamir [c] : 3php +	Glycine, Serine, and Threonine Metabolism
PSP_L	40.05 KO Unique	phosphoserine phosphat [c] : h2o + p	Glycine, Serine, and Threonine Metabolism
TRPt4	1 KO Unique	L-tryptophan transport ir na1[e] + trp	Transport, Extracellular
TYRt4	1 KO Unique	L-tyrosine transport in vi: na1[e] + tyr	Transport, Extracellular
Uritn	65.005729 KO Unique	uridine transport in nucl: uri[c] <==>	Transport, Nuclear
VALt4	500000 KO Unique	L-valine transport in via s na1[e] + val	Transport, Extracellular
sink_orot(c)	20.025 KO Unique	Orotate demand	Transport

MULTISPECIFIC DRUG TRANSPORTER Slc22a8 (Oat3) REGULATES MULTIPLE METABOLIC PATHWAYS. Wei Wu, Neema Jamshidi, Satish A. Eraly, Henry C. Liu, Kevin T. Bush, Bernhard O. Palsson and Sanjay K. Nigam. DRUG METABOLISM AND DISPOSITION.