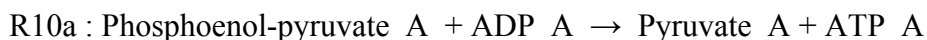
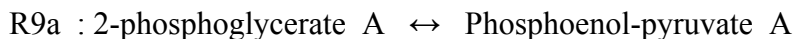
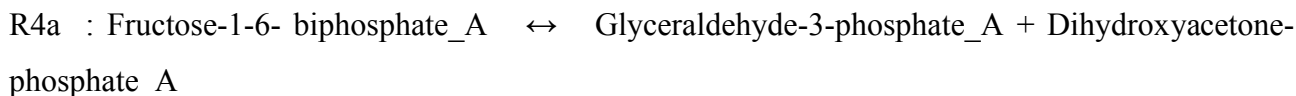
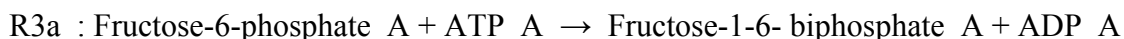


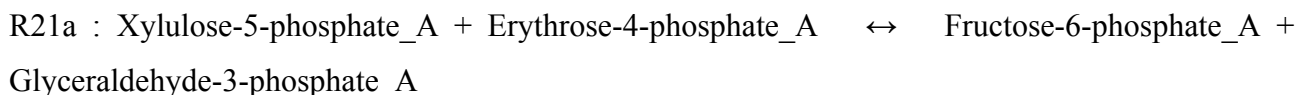
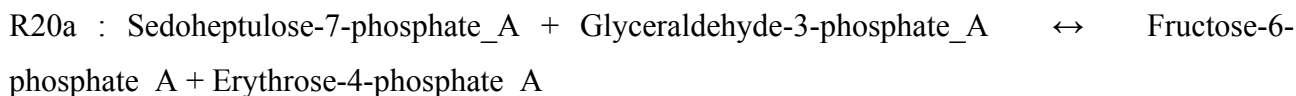
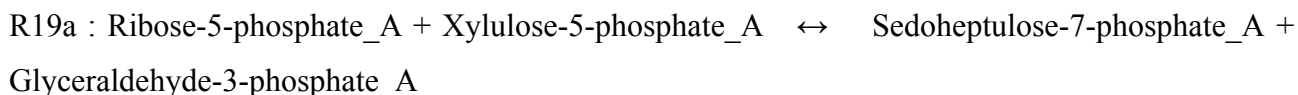
Additional File 1: Reaction Set of Metabolic Reconstruction for Astrocytes and Neurons.

In metabolite names as suffix, A: astrocytic, N: neuronal. For cofactors: M indicates mitochondrial localization of the corresponding reaction. If there is no M, this means that the reaction is located in cytosol. 'EX' as suffix for metabolite names indicates extracellular version of that metabolite.

GLYCOLYSIS (ASTROCYTES)



PENTOSE PHOSPHATE PATHWAY (ASTROCYTES)



#TCA CYCLE (ACTROCYTES)

R22a : Oxoloacetate_A + Acetyl-CoA_A $\rightarrow$ Citrate_A
R23a : Citrate_A $\leftrightarrow$ Isocitrate_A
R24a : Isocitrate_A + NAD_AM $\rightarrow$ alpha-ketoglutarate_A + NADH_AM + CO2_A
R25a : Isocitrate_A + NADP_A $\rightarrow$ alpha-ketoglutarate_A + NADPH_A + CO2_A
R26a : Isocitrate_A + NADP_AM $\rightarrow$ alpha-ketoglutarate_A + NADPH_AM + CO2_A
R27a : alpha-ketoglutarate_A + NAD_AM $\rightarrow$ Succinyl-CoA_A + NADH_AM + CO2_A
R28a : Succinyl-CoA_A + ADP_A $\leftrightarrow$ Succinate_A + ATP_A
R29a : Succinate_A + FAD_AM $\leftrightarrow$ Fumarate_A + FADH2_AM
R30a : Fumarate_A $\leftrightarrow$ Malate_A
R31a : Malate_A + NAD_AM $\rightarrow$ Oxoloacetate_A + NADH_AM
R32a : Malate_A + NAD_A $\rightarrow$ Oxoloacetate_A + NADH_A
R33a : Malate_A + NADP_A $\rightarrow$ Pyruvate_A + NADPH_A + CO2_A
R34a : NADP_AM + NADH_AM $\rightarrow$ NADPH_AM + NAD_AM

#OXIDATIVE PHOSPHORYLATION AND ATPASE (ASTROCYTES)

R35a : 6 ADP_A + 2 NADH_AM + 1 O2_A $\rightarrow$ 6 ATP_A + 2 NAD_AM
R36a : 4 ADP_A + 2 FADH2_AM + 1 O2_A $\rightarrow$ 4 ATP_A + 2 FAD_AM
R37a : ATP_A $\rightarrow$ ADP_A

GLYCOLYSIS (NEURONS)

R38n : Glucose_N + ATP_N $\rightarrow$ Glucose-6-phosphate_N + ADP_N
R39n : Glucose-6-phosphate_N $\leftrightarrow$ Fructose-6-phosphate_N
R40n : Fructose-6-phosphate_N + ATP_N $\rightarrow$ Fructose-1-6- biphosphate_N + ADP_N
R41n : Fructose-1-6- biphosphate_N $\leftrightarrow$ Glyceraldehyde-3-phosphate_N + Dihydroxyacetone-phosphate_N
R42n : Dihydroxyacetone-phosphate_N $\leftrightarrow$ Glyceraldehyde-3-phosphate_N
R43n : Glyceraldehyde-3-phosphate_N + NAD_N $\leftrightarrow$ 1-3-biphosphoglycerate_N + NADH_N
R44n : 1-3-biphosphoglycerate_N + ADP_N $\leftrightarrow$ 3-phosphoglycerate_N + ATP_N
R45n : 3-phosphoglycerate_N $\leftrightarrow$ 2-phosphoglycerate_N
R46n : 2-phosphoglycerate_N $\leftrightarrow$ Phosphoenol-pyruvate_N

R47n : Phosphoenol-pyruvate_N + ADP_N $\rightarrow$ Pyruvate_N + ATP_N

R48n : Pyruvate_N + NADH_N $\leftrightarrow$ Lactate_N + NAD_N

R49n : Pyruvate_N + NAD_NM $\rightarrow$ Acetyl-CoA_N + CO2_N + NADH_NM

PENTOSE PHOSPHATE PATHWAY (NEURONS)

R50n : Glucose-6-phosphate_N + NADP_N $\rightarrow$ 6-phosphoglucone_N + NADPH_N

R51n : 6-phosphoglucone_N $\leftrightarrow$ 6-phosphogluconate_N

R52n : 6-phosphogluconate_N + NADP_N $\rightarrow$ Ribulose-5-phosphate_N + NADPH_N + CO2_N

R53n : Ribulose-5-phosphate_N $\leftrightarrow$ Xylulose-5-phosphate_N

R54n : Ribulose-5-phosphate_N $\leftrightarrow$ Ribose-5-phosphate_N

R55n : Ribose-5-phosphate_N + Xylulose-5-phosphate_N $\leftrightarrow$ Sedoheptulose-7-phosphate_N + Glyceraldehyde-3-phosphate_N

R56n : Sedoheptulose-7-phosphate_N + Glyceraldehyde-3-phosphate_N $\leftrightarrow$ Fructose-6-phosphate_N + Erythrose-4-phosphate_N

R57n : Xylulose-5-phosphate_N + Erythrose-4-phosphate_N $\leftrightarrow$ Fructose-6-phosphate_N + Glyceraldehyde-3-phosphate_N

TCA CYCLE (NEURONS)

R58n : Oxaloacetate_N + Acetyl-CoA_N $\rightarrow$ Citrate_N

R59n : Citrate_N $\leftrightarrow$ Isocitrate_N

R60n : Isocitrate_N + NAD_NM $\rightarrow$ alpha-ketoglutarate_N + NADH_NM + CO2_N

R61n : Isocitrate_N + NADP_NM $\rightarrow$ alpha-ketoglutarate_N + NADPH_NM + CO2_N

R62n : Isocitrate_N + NADP_N $\rightarrow$ alpha-ketoglutarate_N + NADPH_N + CO2_N

R63n : alpha-ketoglutarate_N + NAD_NM $\rightarrow$ Succinyl-CoA_N + NADH_NM + CO2_N

R64n : Succinyl-CoA_N + ADP_N $\leftrightarrow$ Succinate_N + ATP_N

R65n : Succinate_N + FAD_NM $\leftrightarrow$ Fumarate_N + FADH2_NM

R66n : Fumarate_N $\leftrightarrow$ Malate_N

R67n : Malate_N + NAD_NM $\rightarrow$ Oxaloacetate_N + NADH_NM

R68n : Oxaloacetate_N + NADH_N $\rightarrow$ Malate_N + NAD_N

R69n : Malate_N + NADP_NM $\rightarrow$ Pyruvate_N + NADPH_NM + CO2_N

R70n : NADP_NM + NADH_NM $\rightarrow$ NADPH_NM + NAD_NM

OXIDATIVE PHOSPHORYLATION AND ATPASE (NEURONS)

R71n : $6 \text{ ADP_N} + 2 \text{ NADH_NM} + 1 \text{ O2_N} \rightarrow 6 \text{ ATP_N} + 2 \text{ NAD_NM}$

R72n : $4 \text{ ADP_N} + 2 \text{ FADH2_NM} + 1 \text{ O2_N} \rightarrow 4 \text{ ATP_N} + 2 \text{ FAD_NM}$

R73n : $\text{ATP_N} \rightarrow \text{ADP_N}$

GLUTAMATE – GLUTAMINE CYCLE

R74n : $\text{alpha-ketoglutarate_N} + \text{NH3_N} + \text{NADPH_NM} \leftrightarrow \text{Glutamate_N} + \text{NADP_NM}$

R75c : $\text{Glutamate_N} + \text{ATP_A} \rightarrow \text{Glutamate_A} + \text{ADP_A}$

R76a : $\text{alpha-ketoglutarate_A} + \text{NH3_A} + \text{NADPH_AM} \leftrightarrow \text{Glutamate_A} + \text{NADP_AM}$

R77a : $\text{Glutamate_A} + \text{NH3_A} + \text{ATP_A} \rightarrow \text{Glutamine_A} + \text{ADP_A}$

R78c : $\text{Glutamine_A} \rightarrow \text{Glutamine_N}$

R79n : $\text{Glutamine_N} \rightarrow \text{Glutamate_N} + \text{NH3_N}$

GABA CYCLE

R80n : $\text{Glutamate_N} \rightarrow \text{GABA_N} + \text{CO2_N}$

R81c : $\text{GABA_N} \leftrightarrow \text{GABA_A}$

R82a : $\text{GABA_A} + \text{alpha-ketoglutarate_A} \rightarrow \text{Glutamate_A} + \text{SuccinateSAL_A}$

R83a : $\text{SuccinateSAL_A} + \text{NAD_AM} \rightarrow \text{NADH_AM} + \text{Succinate_A}$

R84n : $\text{GABA_N} + \text{alpha-ketoglutarate_N} \rightarrow \text{Glutamate_N} + \text{SuccinateSAL_N}$

R85n : $\text{SuccinateSAL_N} + \text{NAD_NM} \rightarrow \text{NADH_NM} + \text{Succinate_N}$

ASPARTATE METABOLISM

R86n : $\text{Oxoloacetate_N} + \text{Glutamate_N} \leftrightarrow \text{Aspartate_N} + \text{alpha-ketoglutarate_N}$

R87c : $\text{Aspartate_N} \leftrightarrow \text{Aspartate_A}$

R88a : $\text{Aspartate_A} + \text{alpha-ketoglutarate_A} \leftrightarrow \text{Oxoloacetate_A} + \text{Glutamate_A}$

ALANINE METABOLISM

R89n : $\text{Pyruvate_N} + \text{Glutamate_N} \leftrightarrow \text{alpha-ketoglutarate_N} + \text{Alanine_N}$

R90c : $\text{Alanine_N} \leftrightarrow \text{Alanine_A}$

R91a : $\text{Alanine_A} + \text{alpha-ketoglutarate_A} \leftrightarrow \text{Pyruvate_A} + \text{Glutamate_A}$

GLYCINE-SERINE METABOLISM (tetrahydrofolate and methylenetetrahydrofolate are not included in the stoichiometric matrix)

R92a : 3-phosphoglycerate_A + Glutamate_A + NAD_A → Serine_A + alpha-ketoglutarate_A + NADH_A

R93a : Serine_A → Pyruvate_A + NH3_A

R94c : Serine_A → Serine_N

R95n : Serine_N → Glycine_N

R96c : Glycine_N → Glycine_A

R97a : Glycine_A + NAD_AM → CO2_A + NH3_A + NADH_AM

R98a : Glycine_A → Serine_A

LEUCINE METABOLISM

R99a : Leucine_A + alpha-ketoglutarate_A → KIC_A + Glutamate_A

R100a : KIC_A + NAD_AM → Isovaleryl-CoA_A + CO2_A + NADH_AM

R101a : Isovaleryl-CoA_A + FAD_AM + CO2_A + ATP_A → Acetoacetate_A + Acetyl-CoA_A + FADH2_AM + ADP_A

R102a : Acetoacetate_A + Succinyl-CoA_A → Acetoacetyl-CoA_A + Succinate_A

R103a : Acetoacetyl-CoA_A → 2 Acetyl-CoA_A

R104c : KIC_A → KIC_N

R105n : KIC_N + Glutamate_N → Leucine_N + alpha-ketoglutarate_N

R106c : Leucine_N → Leucine_A

VALINE METABOLISM (r110a is shared with isoleucine metabolism)

R107a : Valine_A + alpha-ketoglutarate_A → KIV_A + Glutamate_A

R108a : KIV_A + NAD_AM → Isobutyryl-CoA_A + CO2_A + NADH_AM

R109a : Isobutyryl-CoA_A + FAD_AM + 2 NAD_AM → FADH2_AM + 2 NADH_AM + CO2_A + Propionyl-CoA_A

R110a : Propionyl-CoA_A + CO2_A + ATP_A → Succinyl-CoA_A + ADP_A

R111c : KIV_A → KIV_N

R112n : KIV_N + Glutamate_N → Valine_N + alpha-ketoglutarate_N

R113c : Valine_N → Valine_A

ISOLEUCINE METABOLISM

R114a : Isoleucine_A + alpha-ketoglutarate_A $\rightarrow$ KMV_A + Glutamate_A

R115a : KMV_A + NAD_AM $\rightarrow$ Methylbutyryl-CoA_A + CO2_A + NADH_AM

R116a : Methylbutyryl-CoA_A + FAD_AM + NAD_AM $\rightarrow$ FADH2_AM + NADH_AM + Propionyl-CoA_A + Acetyl-CoA_A

R117c : KMV_A $\rightarrow$ KMV_N

R118n : KMV_N + Glutamate_N $\rightarrow$ Isoleucine_N + alpha-ketoglutarate_N

R119c : Isoleucine_N $\rightarrow$ Isoleucine_A

LYSINE METABOLISM

R120n : Lysine_N + alpha-ketoglutarate_N + NADPH_N $\rightarrow$ Saccharopine_N + NADP_N

R121n : Saccharopine_N + NAD_N $\rightarrow$ Glutamate_N + NADH_N + 2-aminoadipate semialdehyde_N

R122n : 2-aminoadipate semialdehyde_N + alpha-ketoglutarate_N + 1 NAD_N $\rightarrow$ alpha-ketoadipate_N + Glutamate_N + 1 NADH_N

R123n : alpha-ketoadipate_N + 2 NAD_NM + FAD_NM $\rightarrow$ Acetoacetyl-CoA_N + 2 NADH_NM + FADH2_NM + 2 CO2_N

R124n : Acetoacetyl-CoA_N $\rightarrow$ 2 Acetyl-CoA_N

PHENYLALANINE-TYROSINE METABOLISM

R125n : Phenylalanine_N + O2_N + NADPH_N $\rightarrow$ Tyrosine_N + NADP_N

R126n : Tyrosine_N + O2_N $\rightarrow$ L-DOPA_N

R127n : L-DOPA_N $\rightarrow$ Dopamine_N + CO2_N

R128n : Dopamine_N + O2_N $\rightarrow$ Norepinephrine_N

R129n : Norepinephrine_N $\rightarrow$ Epinephrine_N

R130c : Dopamine_N $\rightarrow$ Dopamine_A

R131a : Dopamine_A $\rightarrow$ Norepinephrine_A

TRYPTOPHAN METABOLISM

R132n : Tryptophan_N + O2_N $\rightarrow$ 5- hydroxytryptophan_N

R133n : 5- hydroxytryptophan_N $\rightarrow$ Serotonin_N + CO2_N

R134n : Serotonin_N $\rightarrow$ Melatonin_N

ACETYLCHOLINE METABOLISM

R135n : Choline_N + Acetyl-CoA_N $\leftrightarrow$ Acetylcholine_N

CHOLESTEROL SYNTHESIS (Astrocyte Only)

R136a: 18 Acetyl-CoA_A + 18 ATP_A + 11 O2_A + 29 NADPH_A + 2 NAD_A $\rightarrow$ 9 CO2_A + Cholesterol_A + 2 NADH_A + 18 ADP_A + 29 NADP_A

R137c: Cholesterol_A $\rightarrow$ Cholesterol_N

FATTY ACID SYNTHESIS

R138a : 8 Acetyl-CoA_A + 7 ATP_A + 14 NADPH_A $\rightarrow$ Palmitate_A + 7 ADP_A + 14 NADP_A

R139a : 9 Acetyl-CoA_A + 8 ATP_A + 16 NADPH_A $\rightarrow$ Stearate_A + 8 ADP_A + 16 NADP_A

R140a : 9 Acetyl-CoA_A + 8 ATP_A + 15 NADPH_A $\rightarrow$ Oleate_A + 8 ADP_A + 15 NADP_A

R141a : Linoleate_A + 2 O2_A + 2 NADH_A + ATP_A + CO2_A + Acetyl-CoA_A $\rightarrow$ Arachidonate_A + ADP_A + 2 NAD_A

R142a : Linolenate_A + 3 O2_A + 3 NADH_A + 2 ATP_A + 2 CO2_A + 2 Acetyl-CoA_A $\rightarrow$ Decosahexenoate_A + 2 ADP_A + 3 NAD_A

R143n : 8 Acetyl-CoA_N + 7 ATP_N + 14 NADPH_N $\rightarrow$ Palmitate_N + 7 ADP_N + 14 NADP_N

R144n : 9 Acetyl-CoA_N + 8 ATP_N + 16 NADPH_N $\rightarrow$ Stearate_N + 8 ADP_N + 16 NADP_N

R145n : 9 Acetyl-CoA_N + 8 ATP_N + 15 NADPH_N $\rightarrow$ Oleate_N + 8 ADP_N + 15 NADP_N

R146c : Arachidonate_A $\rightarrow$ Arachidonate_N

R147c : Decosahexenoate_A $\rightarrow$ Decosahexenoate_N

LIPID SYNTHESIS (Astrocytes & Neurons)

R148a : 0.270 Palmitate_A + 0.276 Stearate_A + 0.249 Oleate_A + 0.108 Arachidonate_A + 0.094 Decosahexenoate_A $\rightarrow$ 1 FattyAcid_A

R149n : 0.270 Palmitate_N + 0.276 Stearate_N + 0.249 Oleate_N + 0.108 Arachidonate_N + 0.094 Decosahexenoate_N $\rightarrow$ 1 FattyAcid_N

R150a : Dihydroxyacetone-phosphate_A + NADH_A $\rightarrow$ Glycerol-3-phosphate_A + NAD_A
 R151a : Glycerol-3-phosphate_A + FAD_AM $\rightarrow$ Dihydroxyacetone-phosphate_A + FADH2_AM
 R152a : Glycerol-3-phosphate_A + 2 FattyAcid_A $\rightarrow$ Phosphatidate_A
 R153a : Phosphatidate_A + 3 ATP_A + Ethanolamine_A $\rightarrow$ 3 ADP_A + Phosphatidyl-ethanolamine_A
 R154a : Phosphatidyl-ethanolamine_A $\rightarrow$ Phosphatidyl-choline_A
 R155a : Choline_A + 3 ATP_A + Phosphatidate_A $\rightarrow$ Phosphatidyl-choline_A + 3 ADP_A
 R156a : Phosphatidyl-ethanolamine_A + Serine_A $\rightarrow$ Ethanolamine_A + Phosphatidyl-serine_A
 R157a : Phosphatidyl-serine_A $\rightarrow$ Phosphatidyl-ethanolamine_A + CO2_A

R158n : Dihydroxyacetone-phosphate_N + FADH2_NM $\rightarrow$ Glycerol-3-phosphate_N + FAD_NM
 R159n : Glycerol-3-phosphate_N + 2 FattyAcid_N $\rightarrow$ Phosphatidate_N
 R160n : Phosphatidate_N + 3 ATP_N + Ethanolamine_N $\rightarrow$ 3 ADP_N + Phosphatidyl-ethanolamine_N
 R161n : Phosphatidyl-ethanolamine_N $\rightarrow$ Phosphatidyl-choline_N
 R162n : Choline_N + 3 ATP_N + Phosphatidate_N $\rightarrow$ Phosphatidyl-choline_N + 3 ADP_N
 R163n : Phosphatidyl-ethanolamine_N + Serine_N $\rightarrow$ Ethanolamine_N + Phosphatidyl-serine_N
 R164n : Phosphatidyl-serine_N $\rightarrow$ Phosphatidyl-ethanolamine_N + CO2_N

R165a : 0.52 Cholesterol_A + 0.24 Phosphatidyl-ethanolamine_A + 0.23 Phosphatidyl-choline_A + 0.09 Phosphatidyl-serine_A $\rightarrow$ Lipid_A
 R166n : 0.52 Cholesterol_N + 0.24 Phosphatidyl-ethanolamine_N + 0.23 Phosphatidyl-choline_N + 0.09 Phosphatidyl-serine_N $\rightarrow$ Lipid_N

REACTIVE oXYGEN SPECIES (ROS) PATHWAY

R167a : Cystine_A + NADH_A $\rightarrow$ 2 Cysteine_A + NAD_A
 R168a : Cysteine_A + Glutamate_A + Glycine_A + 2 ATP_A $\rightarrow$ ReducedGlutathione_A + 2 ADP_A
 R169a : O2_A $\rightarrow$ H2O2_A
 R170a : 2 ReducedGlutathione_A + H2O2_A $\rightarrow$ OxidizedGlutathione_A
 R171a : OxidizedGlutathione_A + NADPH_A $\rightarrow$ 2 ReducedGlutathione_A + NADP_A
 R172a : OxidizedGlutathione_A + NADPH_AM $\rightarrow$ 2 ReducedGlutathione_A + NADP_AM
 R173a : H2O2_A $\rightarrow$ O2_A

R174a : ReducedGlutathione_A + Glutamine_A $\rightarrow$ Glutamate_A + NH3_A + CysteinylGlycine_A
 R175c : CysteinylGlycine_A $\rightarrow$ CysteinylGlycine_N
 R176n : CysteinylGlycine_N $\rightarrow$ Cysteine_N + Glycine_N
 R177n : Cysteine_N + Glutamate_N + Glycine_N + 2 ATP_N $\rightarrow$ ReducedGlutathione_N + 2 ADP_N
 R178n : O2_N $\rightarrow$ H2O2_N
 R179n : 2 ReducedGlutathione_N + H2O2_N $\rightarrow$ OxidizedGlutathione_N
 R180n : OxidizedGlutathione_N + NADPH_N $\rightarrow$ 2 ReducedGlutathione_N + NADP_N
 R181n : OxidizedGlutathione_N + NADPH_NM $\rightarrow$ 2 ReducedGlutathione_N + NADP_NM
 R182n : H2O2_N $\rightarrow$ O2_N

GLYCOGEN DEGRADATION METABOLISM (active in stressed conditions)

R183a : Glycogen $\rightarrow$ Glucose-1-phosphate_A
 R184a : Glucose-1-phosphate_A $\rightarrow$ Glucose-6-phosphate_A

EXCHANGE REACTIONS

LACatr : Lactate_A $\rightarrow$ Lactate_AEX
 LACntr : Lactate_N $\rightarrow$ Lactate_NEX
 CO2atr : CO2_A $\rightarrow$ CO2_AEX
 CO2ntr : CO2_N $\rightarrow$ CO2_NEX
 GLNatr : Glutamine_A $\rightarrow$ Glutamine_AEX
 DOPntr : Dopamine_N $\rightarrow$ Dopamine_NEX
 NOREPntr : Norepinephrine_N $\rightarrow$ Norepinephrine_NEX
 EPntr : Epinephrine_N $\rightarrow$ Epinephrine_NEX
 NOREPatr : Norepinephrine_A $\rightarrow$ Norepinephrine_AEX
 SERTntr : Serotonin_N $\rightarrow$ Serotonin_NEX
 MELTntr : Melatonin_N $\rightarrow$ Melatonin_NEX
 CHLNtr : Acetylcholine_N $\rightarrow$ Acetylcholine_NEX
 LPDntr : Lipid_N $\rightarrow$ Lipid_NEX
 LPDatr : Lipid_A $\rightarrow$ Lipid_AEX
 LNLNtr : Linoleate_AEX $\rightarrow$ Linoleate_A
 LNLNtr : Linolenate_AEX $\rightarrow$ Linolenate_A
 CHLNtr : Choline_NEX $\rightarrow$ Choline_N

CHLatr : Choline_AEX $\rightarrow$ Choline_A

CYSatr : Cystine_AEX $\rightarrow$ Cystine_A

GSHntr : ReducedGlutathione_N $\rightarrow$ ReducedGlutathione_NEX

GLCatr : GLC_AEX $\rightarrow$ Glucose_A

GLCntr : GLC_NEX $\rightarrow$ Glucose_N

O2atr : O2_AEX $\rightarrow$ O2_A

O2ntr : O2_NEX $\rightarrow$ O2_N

LEUatr : LEU_AEX $\rightarrow$ Leucine_A

ILEatr : ILE_AEX $\rightarrow$ Isoleucine_A

VALatr : VAL_AEX $\rightarrow$ Valine_A

TYRntr : TYR_NEX $\rightarrow$ Tyrosine_N

TRPntr : TRP_NEX $\rightarrow$ Tryptophan_N

LYSntr : LYS_NEX $\rightarrow$ Lysine_N

PHEntr : PHE_NEX $\rightarrow$ Phenylalanine_N

NH3atr : NH3_AEX $\rightarrow$ NH3_A