

**Supplementary Table 5. Number of reactions per subsystem present only in control models and GBA-PD models, respectively.**

Pathway	Rxn number in CTRL models	Pathway	Rxn number in GBA-PD models
Transport, extracellular	116	Transport, extracellular	292
Fatty acid oxidation	75	Exchange/demand reaction	275
Exchange/demand reaction	55	Peptide metabolism	242
Sphingolipid metabolism	26	Fatty acid oxidation	60
Transport, mitochondrial	17	Glycerophospholipid metabolism	19
Valine, leucine, and isoleucine metabolism	9	Nucleotide interconversion	16
Transport, golgi apparatus	9	Transport, mitochondrial	13
Miscellaneous	9	Keratan sulfate degradation	13
Transport, endoplasmic reticular	8	Keratan sulfate synthesis	11
Phosphatidylinositol phosphate metabolism	7	Transport, peroxisomal	9
NAD metabolism	6	Transport, endoplasmic reticular	9
Bile acid synthesis	5	Drug metabolism	7
Glycerophospholipid metabolism	5	Tryptophan metabolism	6
Transport, nuclear	5	Transport, lysosomal	6
Transport, peroxisomal	5	Folate metabolism	6
Glycosphingolipid metabolism	5	Eicosanoid metabolism	5
Folate metabolism	5	Transport, nuclear	4
Tyrosine metabolism	4	Chondroitin sulfate degradation	4
Transport, lysosomal	4	Pentose phosphate pathway	4
Nucleotide interconversion	4	Lysine metabolism	4
Steroid metabolism	4	Phosphatidylinositol phosphate metabolism	4
Urea cycle	4	Glycine, serine, alanine, and threonine metabolism	3
Vitamin B6 metabolism	4	Pyrimidine catabolism	3
C5-branched dibasic acid metabolism	4	O-glycan metabolism	3
Tryptophan metabolism	3	Glycosphingolipid metabolism	3
N-glycan synthesis	3	Inositol phosphate metabolism	3
Fructose and mannose metabolism	3	Bile acid synthesis	3
Glyoxylate and dicarboxylate metabolism	3	Aminosugar metabolism	2
Pentose phosphate pathway	3	Blood group synthesis	2
Phenylalanine metabolism	3	Sphingolipid metabolism	2
Fatty acid synthesis	3	Transport, golgi apparatus	2
Eicosanoid metabolism	3	Pyruvate metabolism	2
Butanoate metabolism	2	Phenylalanine metabolism	2
Propanoate metabolism	2	Purine catabolism	2
Aminosugar metabolism	2	Chondroitin synthesis	2

Cholesterol metabolism	2	Propanoate metabolism	1
Androgen and estrogen synthesis and metabolism	2	Glutathione metabolism	1
N-glycan metabolism	2	ROS detoxification	1
Inositol phosphate metabolism	2	Cholesterol metabolism	1
Purine catabolism	2	Purine synthesis	1
Methionine and cysteine metabolism	2	NAD metabolism	1
Ubiquinone synthesis	1	Pyrimidine synthesis	1
Glycolysis/gluconeogenesis	1	Starch and sucrose metabolism	1
Lysine metabolism	1	Heme degradation	1
Vitamin C metabolism	1	Glycolysis/gluconeogenesis	1
Oxidative phosphorylation	1		
Leukotriene metabolism	1		
Glycine, serine, alanine, and threonine metabolism	1		
Pyrimidine catabolism	1		
Vitamin B2 metabolism	1		
Triacylglycerol synthesis	1		
Chondroitin synthesis	1		
Galactose metabolism	1		