

**Supplementary Table 2:** Results of pathway enrichment analysis between cluster 1 (-like status) and 2 (-like status).

A

Results of pathway enrichment analysis between cluster 1 and 2 in human PPGLs.

metabolites	fold change	<i>P</i> -value
<b>Purine metabolism</b>		
Pyrophosphate	0.445	3.47.E-09
10-Formyltetrahydrofolate	2.122	8.18.E-05
AMP	0.091	2.64.E-04
GTP	0.270	4.25.E-04
Ribose 1-phosphate	0.443	4.35.E-04
ATP	0.192	0.002
GDP	0.389	0.006
dGTP	0.408	0.007
Guanosine 2',3'-cyclic phosphate	0.470	0.007
dAMP	0.439	0.019
ADP	0.257	0.022
Cyclic AMP	0.438	0.024
<b>Tryptophan metabolism</b>		
5-Methoxyindoleacetate	0.352	4.03.E-11
8-Methoxykynurenate	0.318	5.06.E-11
Indolepyruvate	0.440	4.04.E-10
Indoleacetic acid	0.467	5.51.E-10
Xanthurenic acid	0.434	2.35.E-09
Pyrophosphate	0.445	3.47.E-09
4,6-Dihydroxyquinoline	0.496	3.50.E-09
5-Hydroxyindoleacetic acid	0.446	9.91.E-09
ATP	0.192	0.002
4-(2-Amino-3-hydroxyphenyl)-2,4-dioxobutanoic acid	0.369	0.020
<b>Pyruvate metabolism</b>		
Pyrophosphate	0.445	3.47.E-09
GSH	0.327	1.27.E-07
Biotin	0.489	1.46.E-04
Acetyl adenylate	0.439	1.63.E-04
AMP	0.091	2.64.E-04
GTP	0.270	4.25.E-04
GDP	0.389	0.006
ADP	0.257	0.022
<b>Inositol metabolism</b>		
Pyrophosphate	0.445	3.47.E-09
ATP	0.192	0.002
Myo-inositol biphosphate	0.344	0.002
Myo-inositol hexakisphosphate	0.236	0.004
Myo-inositol tetrakisphosphate	0.329	0.007
Inositol 1,3,4,5,6-pentakisphosphate	0.251	0.007
ADP	0.257	0.022
<b>Pyrimidine metabolism</b>		
Pyrophosphate	0.445	3.47.E-09
Uridine 5'-monophosphate	0.327	3.75E-05
dCTP	0.418	1.31E-05
Ribose 1-phosphate	0.443	4.35.E-04
Uridine 5'-diphosphate	0.338	0.002
ATP	0.192	0.002
ADP	0.257	0.022
<b>Pantothenate and CoA biosynthesis</b>		
Pyrophosphate	0.445	3.47.E-09
Pantetheine 4'-phosphate	0.309	8.14E-06
Pantetheine	0.362	2.65E-05
AMP	0.091	2.64.E-04
ATP	0.192	0.002
ADP	0.257	0.022
<b>Nicotinate and nicotinamide metabolism</b>		
Pyrophosphate	0.445	3.47.E-09
Nicotinate D-ribonucleoside	0.240	4.60.E-08
N1-Methyl-4-pyridone-3-carboxamide	0.186	3.71.E-04
Ribose 1-phosphate	0.443	4.35.E-04
ATP	0.192	0.002

	ADP	0.257	0.022
Amino sugar metabolism			
	Pyrophosphate	0.445	3.47.E-09
	Uridine 5'-diphosphate	0.338	0.002
	ATP	0.192	0.002
	ADP	0.257	0.022
Tyrosine metabolism			
	L-Dopachrome	0.396	6.89E-08
	L-Dopa	0.481	2.09E-07
	Dopaquinone	0.428	5.86E-06

fold changes; divided cluster 1 by 2.

B

Results of pathway enrichment analysis between cluster 1-like status: knockdown of *Sdhb* or *Vhl* gene, and cluster 2-like status: scrambled siRNA, in PC12 cells.

metabolites	siSdhb/ scrambled siRNA		siVhl/ scrambled siRNA	
	fold change	<i>P</i> -value	fold change	<i>P</i> -value
Purine metabolism				
Hypoxanthin	0.579	5.98.E-07	0.785	0.022
Cyclic AMP	1.808	4.84.E-06	1.506	5.69.E-04
Adenosine	1.647	9.71.E-04	0.637	0.002
Uric acid	0.442	0.002	0.703	0.019
Inosine	0.789	0.006	0.789	0.006
Pyrimidine metabolism				
Uridine	0.328	0.002	0.364	0.002
Amino sugar metabolism				
<i>N</i> -Acetylneuraminic acid	0.327	0.001	0.265	4.19.E-04
Glucosamine	0.297	0.012	0.197	0.002
Fatty acid biosynthesis				
3-Oxohexadecanoic acid	0.523	0.002	0.699	0.006
Myristic acid	0.666	0.011	0.837	0.045
Betaine metabolism / methionine metabolism				
Adenosine	1.647	0.001	0.637	0.002
Choline	0.727	0.031	0.625	0.004

Abbreviations AMP, adenosine monophosphate; dAMP, deoxyadenosine monophosphate; ADP, adenosine diphosphate; ATP, adenosine triphosphate; GDP, guanosine diphosphate; dGTP, deoxyguanosine triphosphate; dCTP, deoxycytidine triphosphate; dCTP, deoxycytidine triphosphate; GSH, glutathione.