

**Supplementary Table 9.** List of metabolites experimentally measured in the present work that are currently used as primary or secondary markers for Inborn errors of metabolism

URINARY MARKER	DISEASE	ABNORMAL CONCENTRATION ( $\mu\text{M}/\text{mM}$ creatinine)	REFERENCE
Glycine	Non-ketotic hyperglycinaemia	4753.0-6114.0	[1]
	Isovaleric acidemia	500.0 – 5000.0	[2]
	Propionic acidemia	2000.0-2500.0	[2]
	Ornithine transcarbamylase deficiency	2000.0-5000.0	[2]
	Arginosuccinic aciduria	2000.0-5000.0	[2]
	Transient immaturity of transporters	2000.0-6000.0	[2]
	MMA Cbl A deficiency	2000.0-5000.0	[2]
Alanine	Hartnup disease	400.0-1400.0	[2]
	Piruvate carboxylase deficiency	700.0-1400.0	[2]
	Ethylmalonic encephalopathy	70.0-1400.0	[2]
	Amish lethal microcephaly	427.6-681.4	[3]
Valine	Maple syrup urine disease (MSUD)	20.0-50.0	[2]
	Hartnup disease	40.0-500.0	[2]
Leucine	Hartnup disease	50.0-200.0	[2]
	Maple Sirup Urine disease	80.0-240.0	[2]
Isoleucine	Hartnup disease	50.0-500.0	[2]
	Maple Sirup Urine disease	50.0-500.0	[2]
Glutamine	Hartnup disease	300.0-3000.0	[2]
	Fumaric aciduria	154.0-512.0	[4]
	Glutamine deficiency, congenital	0.00-8.00	[5]

Phenylalanine	Phenylketonuria	> 414.76	[6]
Tyrosine	Tyrosinemia (Tyr)	> 150.0	[2]
	Methylmalonic aciduria	150.0-15500.0	[2]
	Hartnup disease	50.0-500.0	[2]
Tryptophan	Hartnup disease	80.0-240.0	[2]
Ornithine	Hyperdibasic aminoaciduria I	8.90-14.0	[7]
	Lysinuric protein intolerance	16.1-51.00	[8]
	Cystinuria	350.0 (200.0-500.0)	<a href="http://www.metagene.de">http://www.metagene.de</a>
Sarcosine	Sarcosinemia	100.0-5000.0	[2]
	Glutaric aciduria type II	25.0-100.0	[2]
Tyramine	Dihydropyriminidase deficiency	> 400.0	[2]
Betaine	Dimethylglycine dehydrogenase deficiency	1200.0-5000.0	[2]
	Homocistinuria	1200.0-5000.0	[2]
4-Hydroxyproline	Iminoglycinuria	0.00-250.0	[9]
	Hydroxyprolinemia	> 2960.0	[10]
Lactic acid	Primary lactic acidemia	500.0-3000.0	[2]
	3-Methyl-glutaconic aciduria type IV	500.0-1000.0	[2]
	Biotinidase deficiency	500.0-75000.0	[2]
	Pyruvate decarboxylase deficiency	500.0-3000.0	[2]
	Ethylmalonic encephalopathy	400.0-3000.0	[2]
beta-Hydroxybutyric acid	Propionic acidemia	100.0-5000.0	[2]
	Long Chain 3-HydroxyacylCoA Dehydrogenase deficiency	100.0-5000.0	[2]

	Maple Sirup Urine disease	200.0-1000.0	[2]
	Pyruvate Carboxylase efficiency	200.0-600.0	[2]
	b-Ketothiolase deficiency	50.0 – 200.0	[2]
	Fructose-1,6- biphosphatase deficiency	4.00– 48.0	[2]
	Glutaric aciduria type I	200.0 – 800.0	[2]
	Isovaleric acidemia	200.0 – 1000.0	[2]
Citric acid	3-Methylglutaconic aciduria	500.0-25000.0	[2]
Succinic acid	2-Ketoadipic acidemia	400.0-1200.0	[2]
	3-Methyl- glutaconic aciduria type II	400.0-1200.0	[2]
	Ethylmalonic encephalopathy	400.0-1200.0	[2]
	D-2-Hydroxyglutaric aciduria	> 86.16	[11]
	Pyruvate carboxylase deficiency	400.0-1200.0	[2]
	Fumaric aciduria	400.0-1200.0	[2]
Fumaric acid	2-Ketoadipic acidemia	100.0-1000.0	[2]
	Fumaric aciduria	3000.0-4000.0	[2]
	Ethylmalonic encephalopathy	> 100.0	[2]
Pyruvic acid	3-Methyl- glutaconic aciduria	50.0-200.0	[2]
Hippuric acid	Argininemia	200.0-5000.0	[2]
	Argininosuccinic aciduria	1000.0-15000.0	[2]
	Citrullinemia	200.0-50000.0	[2]
	Transient infantile liver failure	1000.0-15000.0	[2]
	Ornithine transcarbamylase deficiency	300.0-10000.0	[2]

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Methylmalonic acid	Isovaleric aciduria	50.0-500.0	[2]
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## References for Supplementary Table 9

1. Brandt, N.J.; Brandt, S.; Rasmussen, K.; Schnoheyder, F. Letter: Hyperglycericacidaemia with hyperglycinaemia: a new inborn error of metabolism. *Br Med J* **1974**, *4*, 344, doi:10.1136/bmj.4.5940.344-a.
2. Embade, N.; Cannet, C.; Diercks, T.; Gil-Redondo, R.; Bruzzzone, C.; Anso, S.; Echevarria, L.R.; Ayucar, M.M.M.; Collazos, L.; Lodoso, B., et al. NMR-based newborn urine screening for optimized detection of inherited errors of metabolism. *Sci Rep* **2019**, *9*, 13067, doi:10.1038/s41598-019-49685-x.
3. Kelley, R.I.; Robinson, D.; Puffenberger, E.G.; Strauss, K.A.; Morton, D.H. Amish lethal microcephaly: a new metabolic disorder with severe congenital microcephaly and 2-ketoglutaric aciduria. *Am J Med Genet* **2002**, *112*, 318-326, doi:10.1002/ajmg.10529.
4. Allegri, G.; Fernandes, M.J.; Scalco, F.B.; Correia, P.; Simoni, R.E.; Llerena, J.C., Jr.; de Oliveira, M.L. Fumaric aciduria: an overview and the first Brazilian case report. *J Inherit Metab Dis* **2010**, *33*, 411-419, doi:10.1007/s10545-010-9134-2.
5. Haberle, J.; Gorg, B.; Rutsch, F.; Schmidt, E.; Toutain, A.; Benoist, J.F.; Gelot, A.; Suc, A.L.; Hohne, W.; Schliess, F., et al. Congenital glutamine deficiency with glutamine synthetase mutations. *N Engl J Med* **2005**, *353*, 1926-1933, doi:10.1056/NEJMoa050456.
6. Swarna, M.; Jyothy, A.; Usha Rani, P.; Reddy, P.P. Amino acid disorders in mental retardation: a two-decade study from Andhra Pradesh. *Biochem Genet* **2004**, *42*, 85-98, doi:10.1023/b:bigi.0000020464.05335.79.
7. Whelan, D.T.; Sriver, C.R. Hyperdibasicaminoaciduria: an inherited disorder of amino acid transport. *Pediatr Res* **1968**, *2*, 525-534, doi:10.1203/00006450-196811000-00011.
8. Habib, A.; Azize, N.A.; Yakob, Y.; Md Yunus, Z.; Wee, T.K. Biochemical and molecular characteristics of Malaysian patients with lysinuric protein intolerance. *Malays J Pathol* **2016**, *38*, 305-310.
9. Broer, S.; Bailey, C.G.; Kowalczyk, S.; Ng, C.; Vanslambrouck, J.M.; Rodgers, H.; Auray-Blais, C.; Cavanaugh, J.A.; Broer, A.; Rasko, J.E. Iminoglycinuria and hyperglycinuria are discrete human phenotypes resulting from complex mutations in proline and glycine transporters. *J Clin Invest* **2008**, *118*, 3881-3892, doi:10.1172/JCI36625.
10. la Marca, G.; Malvagia, S.; Pasquini, E.; Donati, M.A.; Gasperini, S.; Procopio, E.; Zammarchi, E. Hyperhydroxyprolinaemia: a new case diagnosed during neonatal screening with tandem mass spectrometry. *Rapid Commun Mass Spectrom* **2005**, *19*, 863-864, doi:10.1002/rcm.1861.
11. Chalmers, R.A.; Lawson, A.M.; Watts, R.W.; Tavill, A.S.; Kamerling, J.P.; Hey, E.; Ogilvie, D. D-2-hydroxyglutaric aciduria: case report and biochemical studies. *J Inherit Metab Dis* **1980**, *3*, 11-15, doi:10.1007/bf02312516.