Supplementary material

Supplementary table 1.Metabolites observed in significantly different concentrations in urine samples obtained from slc26a6 null mice compared with wild-type control mice.

Metabolite	Chemical Shift. ppm	NMR RHO	NMR pval	CE_Variable	CE RHO	CE pval
METABOLITES POSITIVELY ASSOCIATED WITH SLC26A6-null MICE						
m-hppasulphate **	7.38(t)	0.662	2.03E-03	Var_6718	0.817	1.93E-05
	7.21(m)	0.817	1.93E-05			
	2.91(t)	0.817	1.93E-05			
	2.51(t)	0.817	1.93E-05			
	7.16(dd)	0.817	1.93E-05			
Scyllo inositol	3.36(s)	0.428	6.74E-02			
TMAO **	3.27(s)	0.292	2.25E-01			
Creatine **	3.04(s)	0.448	5.46E-02	Var_3587	0.428	6.74E-02
	3.93(s)	0.214	3.79E-01			
Lactate	1.33(d)	0.701	8.34E-04			
Glycerolphosphorylcholine	3.23 (s)	0.817	1.93E-05			
Alanine *	1.48 (d)	0.214	3.79E-01			
Oxalate				Var_5727	0.701	8.34E-04
Chlorides				Var_5164	0.467	4.38E-02
Allantoin **				Var_2122	0.428	6.74E-02
Glycolate				Var_7036	0.37	1.19E-01
Uric/inosine *				Var_2910	0.214	3.79E-01
METABOLITES NEGATIVELY ASSOCIATED WITH SLC26A6-null MICE						
Hippurate	7.84(d)	-0.856	2.89E-06	Var_2220	-0.72	5.07E-04
	7.64(t)	-0.856	2.89E-06			
	7.56(t)	-0.856	2.89E-06	Var_9726	-0.701	8.34E-04
	3.97(d)	-0.856	2.89E-06			
Taurine	3.43(t)	-0.35	1.41E-01			
	3.27 (t)	-0.545	1.58E-02			
TMA *	2.88(s)	-0.428	6.74E-02			
Succinate	2.41(s)	-0.35	1.41E-01			
Methionine *	2.14(s)	-0.195	4.25E-01			
Citrate	2.68(d)	-0.331	1.66E-01	Var_6653	-0.291	2.25E-01
	2.54 (d)	-0.545	1.58E-02			

** Metabolites positively associated with male. ** Metabolites positively associated with female*

Supplementary table 2. The changes of metabolites observed in urines obtained from female mice compared with male mice.

Metabolite	Chemical Shift. ppm	NMR RHO	NMR pval	CE_Variable	CE RHO	CE pval
METABOLITES NEGATIVELY ASSOCIATED WITH FEMALE						
TMA	2.88(s)	0.856	2.89E-06			
Alanine	1.48(d)	0.778	8.64E-05			
Methionine	2.15(s)	0.058	8.12E-01			
Urea				Var_340	0.058	8.12E-01
Phenylalanine				Var_1338	0.058	8.12E-01
PAG	3.68(s)	0.856	2.89E-06	Var_2057	0.058	8.12E-01
	7.35 (m)	0.856	2.89E-06			
	7.43 (m)	0.856	2.89E-06			
Uridine				Var_2286	0.097	6.92E-01
Uric/ inosine				Var_2910	0.039	8.74E-01
Spermine	3.12 (m)	0.856	2.89E-06			
	2.13 (m)	0.856	2.89E-06			
METABOLITES POSITIVELY ASSCIATED WITH FEMALE						
m-hppasulphate	7.38(t)	0.778	8.64E-05	Var_6718	-0.039	8.74E-01
	7.21(m)	0.72	5.07E-04			
	2.91(t)	0.448	5.46E-02			
	2.51(t)	0.817	1.93E-05			
	7.16(dd)	0.545	1.58E-02			
Formate	8.46(s)	0.817	1.93E-05			
TMAO	3.27(s)	0.856	2.89E-06			
Creatine	3.04(s)	0.642	3.03E-03	Var_3587	0.545	1.58E-02
	3.93(s)	0.759	1.64E-04			
Creatinine	3.045(s)	0.856	2.89E-06	Var_3598	0.136	5.78E-01
	4.05(s)	0.856	2.89E-06			
2-oxoisocaproate	0.94(d)	0.856	2.89E-06			
3-methyl-	1.11(d)	0.117	6.34E-01			

2oxoisovalerate	0.90 (t)	0.856	2.89E-06			
Glycerate	3.83(dd)	0.856	2.89E-06			
Allantoin *				Var_2120	0.117	6.34E-01
Guanidino acetate	3.86(s)	0.856	2.89E-06			
Methyl malonate	1.25(d)	0.72	5.07E-04			

* Allantoin signals appear in the region, corresponding to water and urea resonances (δ 4.5-6.5), has been removed

Supplementary table 3. Summary of the metabolites that are positively and negatively associated with Oxalate (variable 5727), based on Pearson correlation.

Metabolite	Chemical Shift. ppm	Correlation coeffcient *r*	pval	CE_Variable	Correlation coeffcient *r*	pval
m-hppasulphate	7.38(t)	0.497	3.03E-02	Var_6718	0.886	4.93 E -007
	7.21(m)	0.559	1.90E-02			
	2.91(t)	0.561	1.63E-02			
	2.51(t)	0.563	1.21E-02			
	7.16(dd)	0.6	3.23E-02			
TMAO	3.27(s)	0.6	5.61E-03			
Lactate	1.33(d)	0.61	5.86E-03			
Chlorides				Var_5164	0.549	2.46E-03
Nitrate				Var_5228	0.718	1.86E-03
Oxalate *				Var_5727 *	1	0.00E+00
Fumarate				Var_6168	0.58	4.07E-03
2-oxoglutarate				Var_6308	0.619	4.07E-03
Glutamate				Var_6528	0.73	1.06E-03
Citrate				Var_ 6628	0.757	3.00E-04
Glycolate				Var_7038	0.825	4.09E-05
Benzoate/ Glycerate				Var_8968	0.64	1.61E-02
Hippurate	7.84(d)	-0.599	-0.762	Var_2220	-0.762	0.000159
	7.64(t)	-0.595	-0.723			
	7.56(t)	-0.596	-0.701	Var_9726	-0.701	0.0175
	3.97(d)	-0.6	6.63E-03			
Taurine	3.43(t)	-0.49	4.40E-02			
	3.27 (t)	-0.516	1.97E-02			

* Variable selected for driving the correlation from.

Supplementary table 4. Summary of the metabolites that are positively and negatively associated with m-HPPS (2.51 (t) ppm) based on Pearson correlation.

Metabolite	Chemical Shift. ppm	Correlation coefficient *r*	pval	CE_Variable	Correlation coefficient *r*	pval
m-hppasulphate *	7.38(t)	0.959	7.36E-11	Var_6718	0.751	0.000000494
	7.21(m)	0.987	2.44E-15			
	2.91(t)	0.995	0.00E+00			
	2.51(t)*	1	0.00E+00			
	7.16(dd)	0.988	2.88E-15			
TMAO	3.27(s)	0.629	3.90E-03			
Creatine	3.04(s)	0.687	9.70E-03			
	3.93(s)	0.573	1.28E-02			
Creatinine	3.045(s)	0.738	3.10E-04			
	4.05(s)	0.753	2.00E-04			
Scyllo inositol	3.37(s)	0.492	1.98E-02			
α-Ketoisocaproate	0.94(d)	0.535	1.84E-02			
	2.62(d)	0.655	2.36E-03			
Methylmalonate	1.25(d)	0.734	3.40E-04			
α-Keto-β-methyl-N-valerate	1.11(d)	0.573	1.03E-02			
Indoxylsulphate	7.71(d)	0.661	2.00E-03			
	7.50(d)	0.673	1.58E-03			
	7.36(s)	0.576	6.01E-03			
Chlorides				Var_5164	0.178	2.28E-02
Oxalate				Var_5727	0.483	3.63E-02
Hippurate	7.84(d)	-0.693	4.50E-04	Var_2220	-0.739	4.60E-04
	7.64(t)	-0.669	1.74E-03			
	7.56(t)	-0.666	1.90E-03	Var_9726	-0.76	4.60E-04
	3.97(d)	-0.592	7.54E-03			
TMA	2.88 (s)	-0.649	2.62E-03			
Methionine	2.14(s)	-0.564	1.79E-02			

* Variable selected for driving the correlation from