Supplementary Table 1. Subject profiles

Case	Age	Sex	Epilepsy classification	Seizure types	Type of KD	Medication changes after starting the KD	Seizure reduction rate at 3 months after the start of the KD	Seizure reduction rate at the last follow-up
1	2 y 10 m	F	Dravet syndrome	Generalized tonic-clonic, atypical absence	Modified Atkins diet + MCT (carbohydrate 14 g/day)	None	>75%	Discontinuation at 5 months due to difficulty to maintain the KD; >75% before discontinuation
2	17 y 3 m	M	Focal epilepsy	Focal tonic	MCT KD (ketogenic ratio 3:1)	None	>75%	>75% at 4 years 2 months
3	7 y 7 m	M	Generalized epilepsy	Generalized tonic-clonic, tonic, myoclonic	MCT KD (1.5:1)	None	50–75%	50% at 2 years 6 months
4	7 y 1 m	M	Dravet syndrome	Focal impaired awareness, focal to bilateral tonic-clonic	Modified Atkins diet +MCT (carbohydrate 10 g/day)	Citrate, L-carnitine, and allopurinol added	50–75%	25% at 1 year 10 months
5	1 y 5 m	F	West syndrome	Epileptic spasms	MCT KD (2.5:1)	L-Carnitine added	50–75%	Tapering off at 1 year 8 months due to ineffectiveness
6	12 y 11 m	F	Lennox–Gastaut syndrome	Generalized tonic, atonic, myoclonic	MCT KD (3:1)	L-Carnitine added	50–75%	Discontinuation at 1 year 3 months due to side effects; 50–75% before discontinuation
7	1 y 6 m	M	West syndrome	Epileptic spasms, generalized tonic	Modified Atkins diet + MCT (carbohydrate 15 g/day)	Citrate added; Topiramate, carbocysteine, and ambroxol (discontinued)	50–75%	100% at 1 year
8†	1 y 10 m	M	West syndrome	Generalized tonic	MCT KD (2.5:1)	L-Carnitine and vitamins‡ added	50–75%	>80% at 1 year
9	5 y 5 m	M	Dravet syndrome	Generalized tonic-clonic	MCT KD (3:1)	None	<50%	Discontinuation at 3 months
10	3 y 11 m	M	West syndrome	Epileptic spasms	MCT KD (2:1)	Citrate, L-carnitine, and biotin added	<50%	Discontinuation at 3 months
11	0 y 8 m	M	West syndrome	Epileptic spasms	MCT KD (2:1)	Vitamins‡ added	<50%	Discontinuation at 5 months; <50% before discontinuation

F, female; KD, ketogenic diet; M, male; MCT, medium-chain triglyceride; m, month(s); y, year(s).

†Samples of this case were analysed using GC/MS/MS alone.

‡Vitamins A, B1, B2, B3, B6, B12, C, D, and E, pantothenic acid, folic acid.

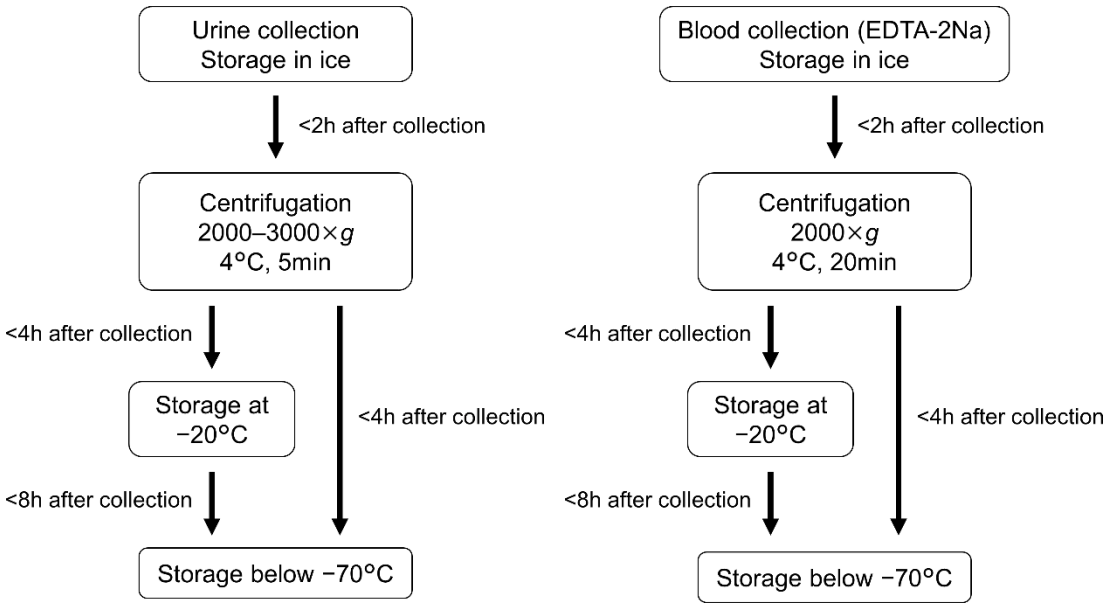
Supplementary Table 2. LC/MS/MS results for urine metabolite changes by the ketogenic diet therapy

Metabolites	Univariate test FDR	Multivariate test VIP score	Fold change
Increased			
3-Aminobutyric acid	0.063	**3.79**	**22.4**
C5:1-DC	0.419	**1.74**	**2.1**
HexCer(d18:1/20:0)	0.453	**1.68**	1.2
HexCer(d18:1/14:0)	0.453	**1.60**	1.3
Decreased			
3-Indoleacetic acid	0.448	**1.62**	**0.40**

C5:1-DC, glutaconylcarnitine; FDR, false discovery rate; HexCer, hexosylceramide; LC/MS/MS, liquid chromatography-tandem mass spectrometry; VIP, variable importance for prediction.

FDRs <0.05, VIP scores ≥1.5, and fold changes ≤0.5 or ≥2.0 are indicated in bold.

Supplementary Figure 1. Sample handling protocols.



EDTA-2Na, ethylenediaminetetraacetic acid disodium salt.