Supplementary Table 1 Summary of studies reporting significant differences in blood composition of myalgic encephalomyelitis/chronic fatigue syndrome patients ($P \leq 0.1$)

Study/year	Population studied/study design	Diagnosis criteria	Technique	Metabolites with increased levels			Metabolites with decreased levels		
Germain et al., 2020[9]	26 ME/CFS (26 F & 0 M). Age range 22-72. Median age 52. Mean age 49.7. 26 HC (26 F & 0 M). Age range 22-66. Median age 43. Mean age 41.5.	CDC criteria	LC-MS	**Ceramides**	CER(18:1)	p = 0.004	Acyl choline	Palmitoylcholine	p = 0.01
					CER(20:0)	p = 0.03		Linoleoyl**choline**	p = 0.02
					CER(18:0)	p = 0.01		Arachidonoyl**choline**	p = 0.03
				Dipeptides	Gammaglutamyltyrosine	p =0.025 q= 1		Phenylalanylalanine	p< 0.05
					Hydroxyasparagine		Dipeptides	Etiocholanolone glucuronide	p< 0.05
					4-hydroxyglutamate			Cysteinylglycine	
				Sphingolipids		p = 0.03 q= 0.23		Valylleucine	
				Sphingomyelins		p = 0.035		3-hydroxylaurate	
				Acyl**carnitines**	arachidoyl**carnitine** (C20)	p = 0.057		Oleoylcholine	p = 0.06
					adipoyl**carnitine** (C6-DC)		Androgenic Steroids	DHEA	N/A
Zhang et al., 2019[10]	105 CFS (65 F & 40 M). 97 DD (56 F & 41 M). 190 HC (69 F & 121 M).	N.A	H-NMR	B: Isoleucine					p < 0.05
				B: Leucine					
				B: Glucose					
				B: Serine					
				B: Tyrosine					
				B: Valine					
				B: 1-methylhistidine					
				B: Alanine					
				F: Succinylacetone					
				F: Glutamate					
				F: Threonine					
				F: Lysine					
				F: Glutamine					
				F: Acetone					
				M: Proline					
				M: Glycerol					
				M: Glycine					
				M: Lactate					
				M: Pyruvate					
				M: Creatinine					
				M: N-Nitrosodimethylamine					
McGregor et al.,	11 ME/CFS (11F & 0 M) Mean age 30.9.	Canadian	H.NMR				Hypoxanthine		p < 0.001
							Lactate		p < 0.01

2019[11]	25 HC (24 F & 1 M). Mean age 33.6. Age range N/A.	criteria		Glucose		p < 0.01	Phenylalanine		N/A
Germain et al., 2018[12]	32 ME/CFS (32 F & 0 M). Age range 19-71. Median age 50. Mean 49.2. 19 HC (19 F & 0 M). Age range 20-66. Median age 50. Mean 48.5.	Fukuda criteria	LC-MS	Cofactors and Vitamins	Alpha-CEHC glucuronide	p = 0.018 q= 0.13	Nucleotides	Inosine 5'-monophosphate (IMP)	p = 0.003 q= 0.11
					Gamma-CEHC glucuronide	p = 0.019 q= 0.13			
					Heme	p = 0.02 q= 0.06		2'-O-methylcytidine	p = 0.009 q= 0.13
					Gamma-CEHC	p = 0.05 q= 0.08			
				Energy	Alpha-ketoglutarate	p = 0.03 q= 0.03		Adenosine 3'-5'-cyclic monophosphate (cAMP)	p = 0.012 q= 0.13
				Peptide	Gamma-glutamylthreonine	p = 0.03 q= 0.11			
Nagy-Szakal et al., 2018[13]	50 ME/CFS (41 F & 9 M). Age range 20-66. Median age 54. 50 HC (41 F & 9 M). Age range 21-67. Median age 53. Mean age 51.	Fukuda and Canadian consensus criteria	LC-MS/MS	**Lysine**		p < 0.05	Phosphatidyl**choline** (PC)		p = 0.017
				Phenylacetylglutamine			**Carnitine-choline**		
				Threonic acid					
				Hexaethylene glyco			Lysophosphatidyl**choline** (LPC)		p < 0.05
				α-N-phenylacetyl-glutamine					
				ε-caprolactam					
				Pantothenic acid (Vit. B5)					
				Urobilin					
				Mannitol					
				Tyrosine					
				Methionine			Betaine		
				Triglyceride (TG)		p = 0.580			
				Ceramide		p = 0.1			
Ruiz-Núñez et al., 2018[14]	98 CFS (77 F & 21 M). Age range 21-69. Median age 43. 99 HC (76 F & 23 M). Age range 19-65. Median age 39 years. Mean: N/A.	Fukuda criteria	LC-MS	Inflammation	TC/HDL-C ratio	p = 0.001	Thyroid function	TT3	p < 0.001
								TT4	
								HDL-C	
					Ferritin	p = 0.007		SPINA-GD	
								SPINA-GT	p = 0.010
								FT3	p = 0.047
				Vitamin D		N/A	Intestinal Permeability	Zonulin	p = 0.002
							Inflammation	Tryptophan	p = 0.003
								Kynurenine	p = 0.035
Germain et al.,	17 ME/CFS (17 F & 0	Fukuda	QE-MS	Palmitate		p = 0.033 q = 0.4	Ethanolamine phosphate		p = 0.002 q = 0.191
							ATP		p = 0.002 q = 0.129
							ADP		p = 0.003 q = 0.129

2017[15]	M). 15 HC (15 F & 0 M). Age range 42-68. Median and mean age: N/A.	criteria		Glycero-3-phosphate	p = 0.033 q = 0.24	Glyoxylate		p = 0.007 q = 0.129
						Taurine		p = 0.007 q = 0.13
						Choline phosphate(1-)		p = 0.008 q = 0.129
				Trans-vaccenate-elaidate-oleate	p = 0.037 q = 0.24	Glucose		p = 0.009 q = 0.129
						Glycocholate		p = 0.011 q = 0.137
						CDP-choline		p = 0.014 q = 0.164
				Stearate	p = 0.08 q= 0.342	5-amino-1-(5-phospho-D-ribosyl)imidazole-4-carboxamide		p = 0.037 q = 0.245
						Oxaloacetate		p = 0.039 q = 0.246
Yamano et al., 2016[16]	67 CFS (51 F & 16 M). 66 HC (51 F & 15 M). Age range 20-60. Median and mean age: N/A.	CDC criteria	CE-TOFMS	ratio of ornithine/citrulline	p < 0.001	Urea		p < 0.01
						Citrulline		
				ratio of pyruvate/isocitrate	p < 0.01	Citrate		p < 0.05
						Isocitrate		
				Ornithine	p < 0.05	Malate		
						Aconitate		p < 0.1
				Piruvate	p < 0.1	ATP		N/A
Naviaux et al., 2016[17]	45 CFS (23 F & 22 M). Age range 20-67. Mean age (52 F & 53 M). 39 HC (21 F & 18 M). Age range 23-69. Mean age (48 F & 53 M). Median age N/A.	Canadian, and Fukuda criteria	HILIC, ESI-MS, and MS/MS	Stress conditions	B: Pyrroline-5-Carboxylate (P5C)	p = 0.014	Vitamin	B: Riboflavin	p = 0.005
								B: Flavin Adenine Dinucleotide (FAD)	N/A
							Glycosphingolipids	B: Glucosylceramide (GC)	p = 0.03
								B: Dihexosylceramide (DHC)	
								B: Trihexosylceramide (THC)	
					B: Arginine		Purine	B: Purines	N/A
								F: Plasma adenosine	
								M: Plasma uric acid	
							Branch Chain Amino Acid	B: 2-Hydoxyisocaproic acid (HICA)	
					F: Hydroxyproline		Cholesterol	B: Lathosterol	
							Aromatic Amino Acid	M: 4-hydroxyphenyllactic acid (HPLA)	
								F: Phenyllactic acid (PLA)	
							Bile acid	F: Chenodeoxycholic acid (CDCA)	

B= both, F = female, M = male, HC = healthy control. N/A = not available.