

Table 1. The differentially changed mitochondrial associated proteins in in the brain samples of 139A- and ME7-infected mice collected at mid-early (80 dpi), mid-late (120 dpi) and terminal (180 dpi) stages

Protein	No. of identified peptide	No. of DEAP	Acetylated position (down)	Changed in sample (No. of DEAP)	Acetylated position (up)	Changed in sample (No. of DEAP)
1 28S ribosomal protein S9	1	1	aa. 28	ME7 80 dpi (1)	/	/
2 4-aminobutyrate aminotransferase	4	1	aa. 400	ME7 80 dpi (1)	/	/
3 60 kDa heat shock protein	2	1	aa. 130	ME7 80 dpi (1), 139A 80 dpi (1), ME7 180 dpi (1)	/	/
4 Aconitate hydratase	20	6	aa. 50, 168, 517, 736, 743	ME7 80 dpi (6), 139A 80 dpi (1)	/	/
5 Acyl-coenzyme A thioesterase 2	1	1	aa. 83	ME7 80 dpi (1)	aa. 83	ME7 120 dpi (1), 139A 120 dpi (1)
6 Acyl-coenzyme A thioesterase 9	4	3	aa. 102, 155	ME7 80 dpi (3), 139A 80 dpi (1)	aa. 102	ME7 120 dpi (1)
7 Aspartate aminotransferase	29	14	aa. 73, 82, 94, 122, 159, 363, 404	ME7 80 dpi (11), 139A 80 dpi (5), ME7 120 dpi (1), 139A 120 dpi (3), ME7 180 dpi (3)	aa 73, 404	ME7 120 dpi (4)
8 ATP synthase F(0) complex subunit B1	9	3	aa. 162, 225, 233	ME7 80 dpi (3), 139A 80 dpi (1), ME7 120 dpi (1), 139A 120 dpi (1), ME7 180 dpi (2)	/	/
9 ATP synthase subunit alpha	20	8	aa. 126, 261, 498, 539	ME7 80 dpi (4), 139A 80 dpi (1)	aa. 194, 230, 498, 541	ME7 80 dpi (2), 139A 80 dpi (1), ME7 120 dpi (2), ME7 180 (1)
10 ATP synthase subunit beta	11	5	aa. 212	ME7 120 dpi (2)	aa. 426, 259	ME7 (3)
11 ATP synthase subunit d	7	2	aa. 73, 117	ME7 80 dpi (2)	/	/

12	Calcium uniporter protein	2	1	aa. 331	ME7 80 dpi (1)	/	/
13	Citrate synthase	5	4	aa. 237, 366, 370	ME7 80 dpi (4), 139A 80 dpi (2)	/	/
14	Cytochrome b-c1 complex subunit 2	3	2	aa. 92, 250	ME7 80 dpi (2), 139A 80 dpi (1), ME7 180 dpi (1)	/	/
15	Cytochrome c1	1	1	/	ME7 80 dpi (1)	/	/
16	Dihydrolipoyl dehydrogenase	14	6	aa. 122, 401	ME7 80 dpi (5), 139A 80 dpi (1)	aa. 122, 420	ME7 120 dpi (2)
17	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex	3	3	aa. 268, 274	ME7 80 dpi (2), 139A 80 dpi (1), ME7 120 dpi (1)	aa. 268	ME7 120 dpi (1), 139A 120 dpi (1)
18	Electron transfer flavoprotein subunit alpha	5	2	aa. 69	ME7 80 dpi (2)	/	/
19	ES1 protein homolog	3	1	aa. 231	ME7 80 dpi (1), 139A 80 dpi (1), ME7 180 dpi (1)	/	/
20	Fumarate hydratase	8	4	aa. 77	ME 80 dpi (1)	aa. 63, 227	ME7 120 dpi (2), ME7 180 (1), 139A 180 dpi (1)
21	Glutamate dehydrogenase 1	12	4	aa. 84, 90, 527	ME7 80 dpi (3), 139A 80 dpi (2)	aa. 527	ME7 120 dpi (1)
22	Glutaminase kidney isoform	1	1	aa. 668	ME7 80 dpi (1)	/	/
23	Hydroxyacyl-coenzyme A dehydrogenase	3	1	aa. 157	ME7 80 dpi (1), 139A 80 dpi (1)	/	/
24	Isocitrate dehydrogenase [NAD] subunit alpha	9	8	aa. 200, 214, 326	ME7 80 dpi (5), 139A 80 dpi (1)	aa. 200, 214	ME7 120 dpi (5)
25	Isocitrate dehydrogenase [NAD] subunit	1	1	aa. 157	ME7 80 dpi (1)	/	/

26	Isocitrate dehydrogenase [NADP]	10	2	aa. 106,180	ME7 80 dpi (2)	/	/
27	Isovaleryl-CoA dehydrogenase	2	1	aa. 76	ME7 80 dpi (1)	/	/
28	Long-chain-specific acyl-CoA dehydrogenase	1	1	aa. 92	ME7 80 dpi (1)	/	/
29	Malate dehydrogenase	15	8	aa. 97, 297, 301, 307, 324, 338	ME7 80 dpi (8), 139A 80 dpi (1), ME7 180 dpi (1)	/	/
30	Methylglutaconyl-CoA hydratase	5	1	/	/	aa. 80	ME7 120 dpi (1)
31	Mitochondrial ATP synthase epsilon subunit	2	2	aa. 17, 26	ME7 80 dpi (2), ME7 180 (1)	/	/
32	Peptidyl-prolyl cis-trans isomerase F	1	1	/	/	aa. 85	ME7 120 dpi (1)
33	Persulfide dioxygenase ETHE1	1	1	aa. 66	ME7 80 dpi (1), 139A 80 dpi (1)	/	/
34	Presequence protease	4	2	/	/	aa. 305, 707	ME7 120 dpi (2), 139A 180 dpi (1)
35	Pyruvate dehydrogenase E1 component subunit alpha	10	8	aa. 85, 244, 313, 321	ME7 80 dpi (4), 139A 80 dpi (1)	aa. 63, 85, 244, 267, 313	ME7 120 dpi (6), 139A 120 dpi (1)
36	Pyruvate dehydrogenase E1 component subunit beta	2	1	aa. 354	ME7 80 dpi (1)	/	/
37	Pyruvate dehydrogenase protein X component	1	1	aa. 194	ME7 80 dpi (1)	/	/
38	Stress-70 protein	5	3	aa. 288, 612, 625	ME7 80 dpi (3), 139A 80 dpi (2)	/	/
39	Succinate dehydrogenase [ubiquinone] flavoprotein subunit	7	5	aa. 498, 550	ME7 80 dpi (4)	aa. 608	ME7 120 dpi (1), ME7 180 dpi (1)
40	Succinate--CoA ligase [ADP-forming] subunit beta	1	1	aa. 88	ME7 80 dpi (1)	aa. 88	ME7 120 dpi (1)

41	Succinate-semialdehyde dehydrogenase	2	1	aa. 128	ME7 80 dpi (1)	/	/
42	Superoxide dismutase [Mn]	9	6	aa. 68, 122	ME7 80 dpi (2), 139A 80 dpi (2), ME7 120 dpi (2), 130A 120 dpi (2), ME7 180 dpi (1)	aa. 68	ME7 120 dpi (1), 139A 120 dpi (2), 139A 180 dpi (1)
43	Trifunctional enzyme subunit alpha	8	4	aa. 60, 129, 353	ME7 80 dpi (3), 139A 80 dpi (1)	aa. 60	ME7 120 dpi (1), 139A 180 dpi (1)
44	Trifunctional enzyme subunit beta	1	1	/	/	aa. 333	ME7 120 dpi (1)

Table 2. The top 10 involved pathways in the brain samples of 139A- and ME7-infected mice collected at mid-early (80 dpi), mid-late (120 dpi) and terminal (180 dpi) stages

Brain sample	Involved pathway	P value	Acetylated Protein in Diff Exp
139A 180 dpi	Carbon metabolism - Mus musculus (mouse)	0.00019146	6
	Metabolic pathways - Mus musculus (mouse)	0.00110251	10
	Biosynthesis of amino acids - Mus musculus (mouse)	0.00190727	4
	HIF-1 signaling pathway - Mus musculus (mouse)	0.0035315	3
	Longevity regulating pathway - multiple species - Mus musculus (mouse)	0.00441966	2
	PPAR signaling pathway - Mus musculus (mouse)	0.00806604	2
	Glycolysis / Gluconeogenesis - Mus musculus (mouse)	0.00813558	3
	Glyoxylate and dicarboxylate metabolism - Mus musculus (mouse)	0.01025453	2
	Pyruvate metabolism - Mus musculus (mouse)	0.02450717	2
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	0.03940544	2
139A-120 dpi	Metabolic pathways - Mus musculus (mouse)	0.0000412	10
	Glycolysis / Gluconeogenesis - Mus musculus (mouse)	0.000172	4
	Carbon metabolism - Mus musculus (mouse)	0.000296	5
	HIF-1 signaling pathway - Mus musculus (mouse)	0.001244	3
	Cysteine and methionine metabolism - Mus musculus (mouse)	0.003018	2
	Biosynthesis of amino acids - Mus musculus (mouse)	0.006147	3
	Arginine and proline metabolism - Mus musculus (mouse)	0.00632	2
	Pyruvate metabolism - Mus musculus (mouse)	0.012394	2
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	0.020208	2
	Glucagon signaling pathway - Mus musculus (mouse)	0.024713	2
139A-80 dpi	Carbon metabolism - Mus musculus (mouse)	3.8998E-10	15
	Biosynthesis of amino acids - Mus musculus (mouse)	1.9413E-07	10
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	1.9661E-07	8
	Metabolic pathways - Mus musculus (mouse)	7.4289E-07	23

	2-Oxocarboxylic acid metabolism - Mus musculus (mouse)	5.5069E-06	5
	Glyoxylate and dicarboxylate metabolism - Mus musculus (mouse)	1.1987E-05	5
	Glycolysis / Gluconeogenesis - Mus musculus (mouse)	3.2015E-05	7
	Pyruvate metabolism - Mus musculus (mouse)	0.00016141	5
	Glucagon signaling pathway - Mus musculus (mouse)	0.00102569	5
	Arginine biosynthesis - Mus musculus (mouse)	0.00124941	3
ME7-180 dpi	Cysteine and methionine metabolism - Mus musculus (mouse)	0.0000172	4
	Metabolic pathways - Mus musculus (mouse)	0.0000945	15
	Carbon metabolism - Mus musculus (mouse)	0.000337	7
	Pyruvate metabolism - Mus musculus (mouse)	0.000426	4
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	0.001198	4
	Glyoxylate and dicarboxylate metabolism - Mus musculus (mouse)	0.001488	3
	Oxidative phosphorylation - Mus musculus (mouse)	0.002029	5
	Parkinson's disease - Mus musculus (mouse)	0.005802	5
	Huntington's disease - Mus musculus (mouse)	0.005802	5
	Alzheimer's disease - Mus musculus (mouse)	0.008496	5
ME7-120 dpi	Carbon metabolism - Mus musculus (mouse)	4.6223E-15	23
	Biosynthesis of amino acids - Mus musculus (mouse)	1.511E-10	15
	Glycolysis / Gluconeogenesis - Mus musculus (mouse)	7.3068E-09	12
	Metabolic pathways - Mus musculus (mouse)	1.5321E-08	34
	Pentose phosphate pathway - Mus musculus (mouse)	6.5226E-06	7
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	8.4311E-06	8
	Arginine biosynthesis - Mus musculus (mouse)	0.00026325	4
	RNA degradation - Mus musculus (mouse)	0.00042343	5
	HIF-1 signaling pathway - Mus musculus (mouse)	0.000782	6
	Pyruvate metabolism - Mus musculus (mouse)	0.00155492	5

ME7-80 dpi	Carbon metabolism - Mus musculus (mouse)	1.1992E-16	28
	Metabolic pathways - Mus musculus (mouse)	2.9039E-13	51
	Biosynthesis of amino acids - Mus musculus (mouse)	2.0746E-11	18
	Citrate cycle (TCA cycle) - Mus musculus (mouse)	2.777E-10	13
	Glycolysis / Gluconeogenesis - Mus musculus (mouse)	3.7415E-09	14
	2-Oxocarboxylic acid metabolism - Mus musculus (mouse)	1.8879E-05	6
	Necroptosis - Mus musculus (mouse)	2.5058E-05	8
	Pentose phosphate pathway - Mus musculus (mouse)	7.7631E-05	7
	Central carbon metabolism in cancer - Mus musculus (mouse)	0.00014251	7
	Pyruvate metabolism - Mus musculus (mouse)	0.00014251	7

Table 3. The folds of the differentially expressed proteins within the pathway of citrate cycle (TCA cycle) in the brain samples of 139A- and ME7-infected mice collected at mid-early (80 dpi), mid-late (120 dpi) and terminal (180 dpi) stages

Diff Exp Proteins	Modification	ME7-80 dpi	139A-80 dpi	ME7-120 dpi	139A-120 dpi	ME7-180 dpi	139A-180 dpi
In 180 dpi							
Fumarate hydratase	N-Term (TMT6plex); K5 (Acetyl); Q10 (Deamidated)	1.032	1.326	2.307	1.298	1.17	1.546
Malate dehydrogenase	N-Term (Acetyl); N-Term (TMT6plex); Q2 (Deamidated); K11 (TMT6plex)	0.919	1.139	2.411	1.498	1.507	2.075
Fumarate hydratase	N-Term (TMT6plex); K7 (Acetyl)	0.925	1.039	1.252	1.106	1.702	1.278
Succinate dehydrogenase flavoprotein subunit	[ubiquinone] N-Term (TMT6plex); K8 (Acetyl); K15 (TMT6plex)	0.701	0.832	1.919	1.102	1.775	1.12
In 120 dpi							
Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex	N-Term (TMT6plex); K2 (TMT6plex); K7 (TMT6plex); K8 (Acetyl)	0.57	0.542	1.978	1.926	0.776	1.161
Pyruvate dehydrogenase E1 component subunit alpha	N-Term (TMT6plex); K2 (TMT6plex); K10 (Acetyl)	0.699	0.659	2.044	1.981	0.8505	1.2335
Fumarate hydratase	N-Term (TMT6plex); K5 (Acetyl); Q10 (Deamidated)	1.032	1.326	2.307	1.298	1.17	1.546
Malate dehydrogenase	N-Term (Acetyl); N-Term (TMT6plex); Q2 (Deamidated); K11 (TMT6plex)	0.919	1.139	2.411	1.498	1.507	2.075
Succinate--CoA ligase [ADP-forming] subunit beta	N-Term (TMT6plex); K10 (Acetyl); K11 (TMT6plex)	0.586	0.795	1.694	1.244	1.047	1.273
Isocitrate dehydrogenase [NAD] subunit alpha	N-Term (TMT6plex); K8 (Acetyl); N10	0.8175	0.954	1.867	1.4855	1.047	1.346

Dihydrolipoyl dehydrogenase	(Deamidated); M12 (Oxidation)							
	N-Term (TMT6plex); K5 (Acetyl); M6 (Oxidation); M7 (Oxidation); K10 (TMT6plex)	0.424	0.56	1.6	0.916	0.824	0.842	
Succinate dehydrogenase flavoprotein subunit	[ubiquinone] N-Term (TMT6plex); K8(Acetyl); K15 (TMT6plex)	0.701	0.832	1.919	1.102	1.775	1.12	
In 80 dpi								
Dihydrolipoyl dehydrogenase	N-Term (TMT6plex); K5 (Acetyl); M6 (Oxidation); M7 (Oxidation); K10 (TMT6plex)	0.424	0.56	1.6	0.916	0.824	0.842	
Citrate synthase	N-Term (TMT6plex); K4 (TMT6plex); K10 (Acetyl)	0.362	0.515	1.09	0.944	0.675	0.814	
Malate dehydrogenase	N-Term (TMT6plex); N1 (Deamidated); K6 (Acetyl); K13 (TMT6plex)	0.5	0.664	0.809	0.856	0.706	1.106	
Pyruvate dehydrogenase E1 component subunit alpha	N-Term (TMT6plex); K2 (TMT6plex); K10 (Acetyl)	0.699	0.659	2.044	1.981	0.8505	1.2335	
Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex	N-Term (TMT6plex); K2 (TMT6plex); K7 (TMT6plex); K8 (Acetyl)	0.57	0.542	1.978	1.926	0.776	1.161	
Isocitrate dehydrogenase	N-Term (TMT6plex); C5 (Carbamidomethyl); K6 (Acetyl); N7 (Deamidated)	0.484	0.607	1.088	0.846	0.804	0.812	
Aconitate hydratase	N-Term (TMT6plex); K6 (Acetyl); N7 (Deamidated); N9 (Deamidated)	0.452	0.56	1.201	1.061	0.794	0.786	
Isocitrate dehydrogenase [NAD] subunit alpha	N-Term (TMT6plex); K10 (Acetyl);	0.627	0.583	0.707	0.917	0.838	0.674	

	C15 (Carbamidomethyl); K20 (TMT6plex)							
Pyruvate dehydrogenase E1 component subunit beta	N-Term (TMT6plex); K7 (Acetyl); K8 (TMT6plex)	0.643	0.701	0.996	0.88	0.8255	1.0335	
Succinate--CoA ligase [ADP-forming] subunit beta	N-Term (TMT6plex); K10 (Acetyl); K11 (TMT6plex)	0.586	0.795	1.694	1.244	1.047	1.273	
Isocitrate dehydrogenase [NADP]	N-Term (TMT6plex); K8 (Acetyl)	0.597	0.7445	1.261	1.1625	0.9805	1.023	
Fumarate hydratase	N-Term (TMT6plex); M3 (Oxidation); K6 (Acetyl)	0.5255	0.707	1.3715	1.027	0.7775	1.176	
Succinate dehydrogenase [ubiquinone] flavoprotein subunit	N-Term (TMT6plex); N-Term (Acetyl)	0.578	0.818	1.204	1.01	0.706	1.006	
