

Supplemental Information

Combining Native Mass Spectrometry and Lipidomics to Uncover Specific Membrane Protein-Lipid Interactions from Natural Lipid Sources

Yun Zhu,^{1,‡} Melanie T. Odenkirk,^{2,‡} Pei Qiao,^{1,‡} Tianqi Zhang,¹ Samantha Schrecke,¹ Ming Zhou,³ Michael T. Marty,⁴ Erin S. Baker,^{5,*} Arthur Laganowsky^{1,*}

¹ Department of Chemistry, Texas A&M University, College Station, TX 77843

² Department of Chemistry, North Carolina State University, Raleigh, NC 27695

³ Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, TX, 77030

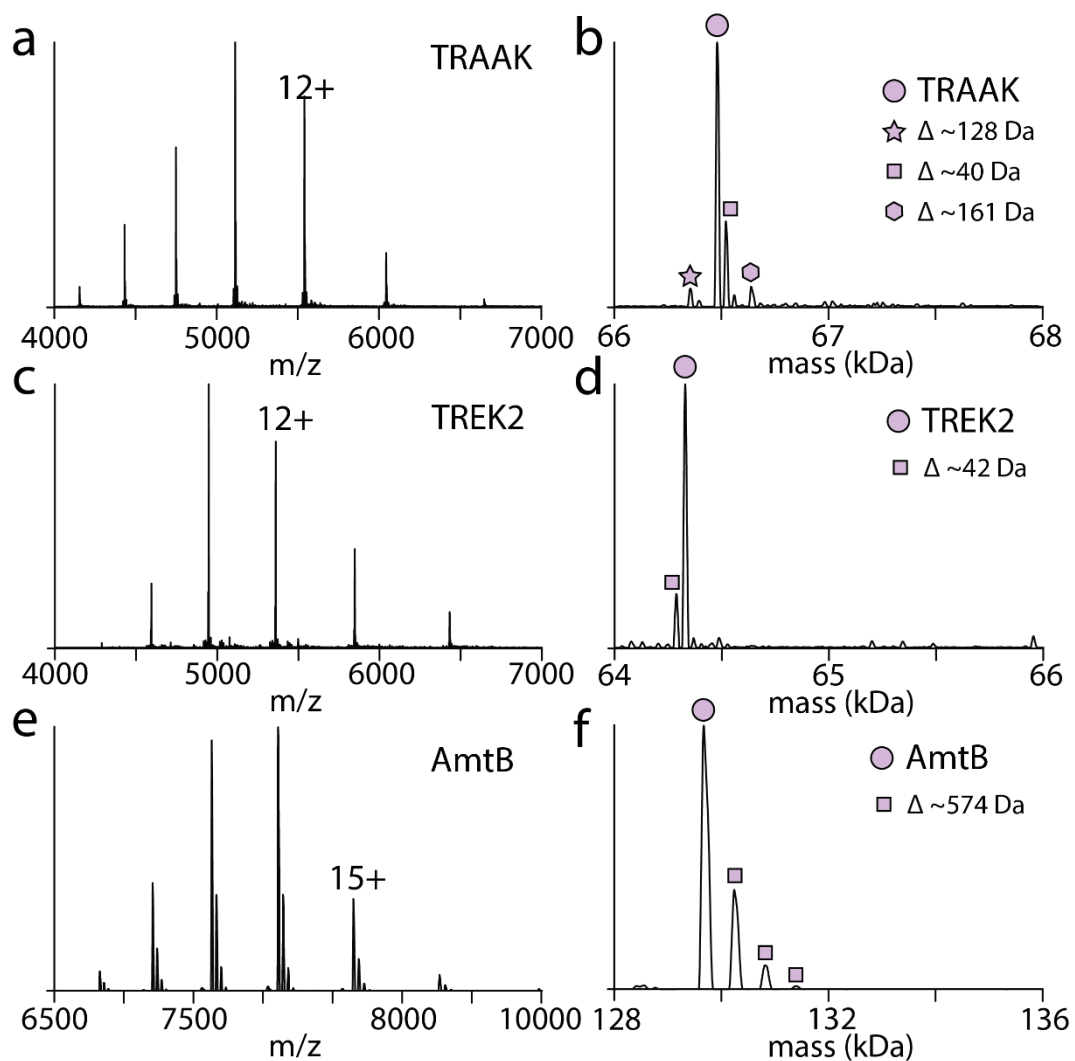
⁴ Department of Chemistry and Biochemistry, The University of Arizona, Tucson, AZ 85721

⁵ Department of Chemistry, University of North Carolina, Chapel Hill, NC 27514

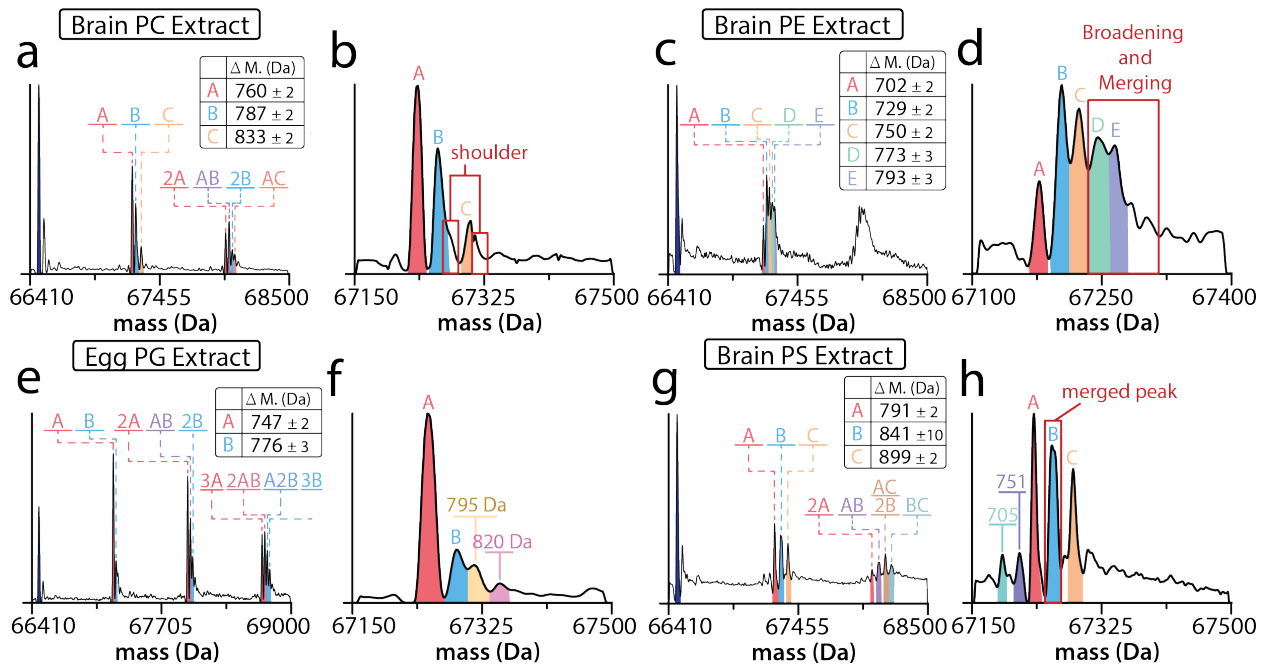
‡ These authors contributed equally to this work

* Corresponding Authors: erinmsb@unc.edu and alaganowsky@chem.tamu.edu

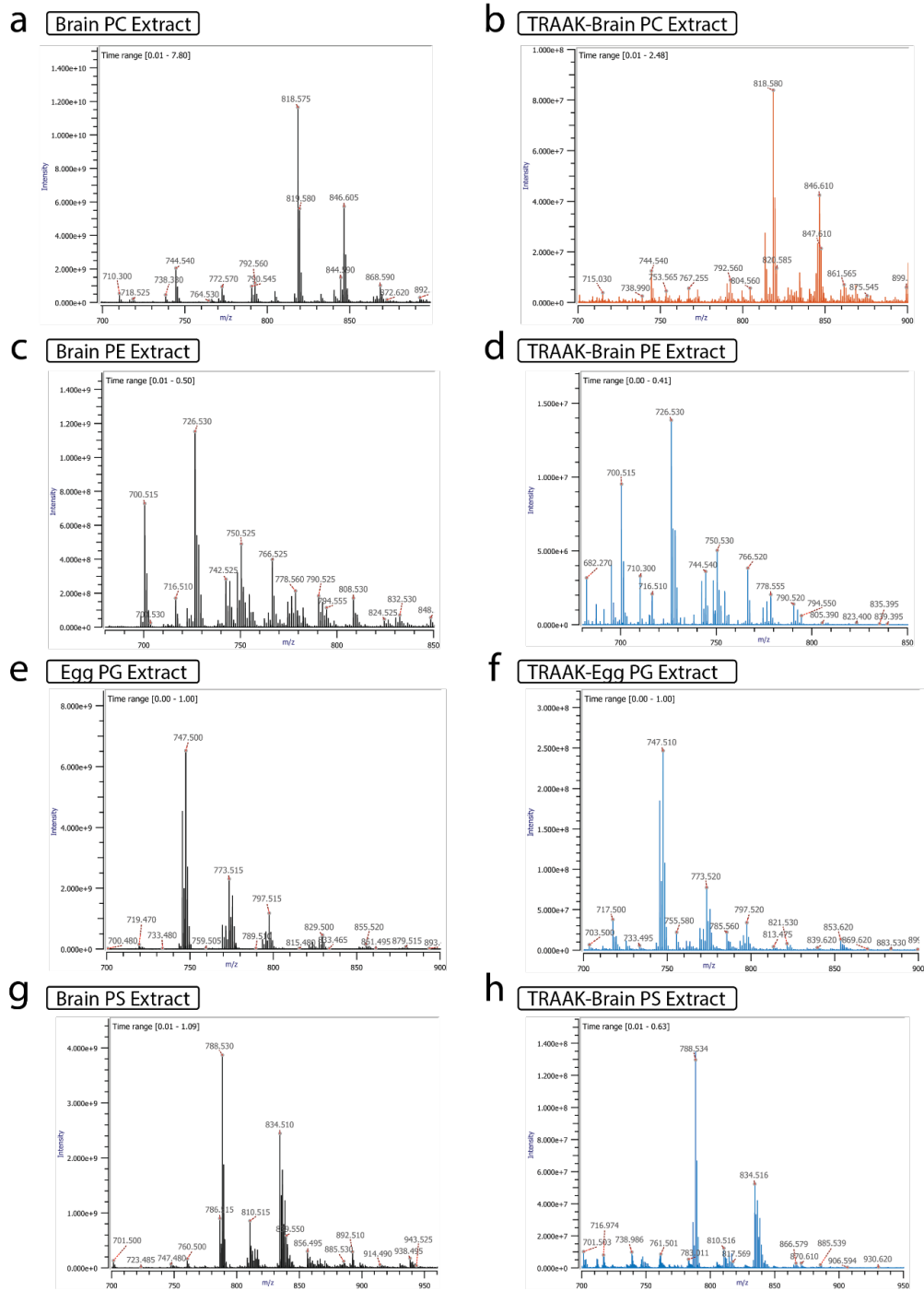
Supplemental Figures



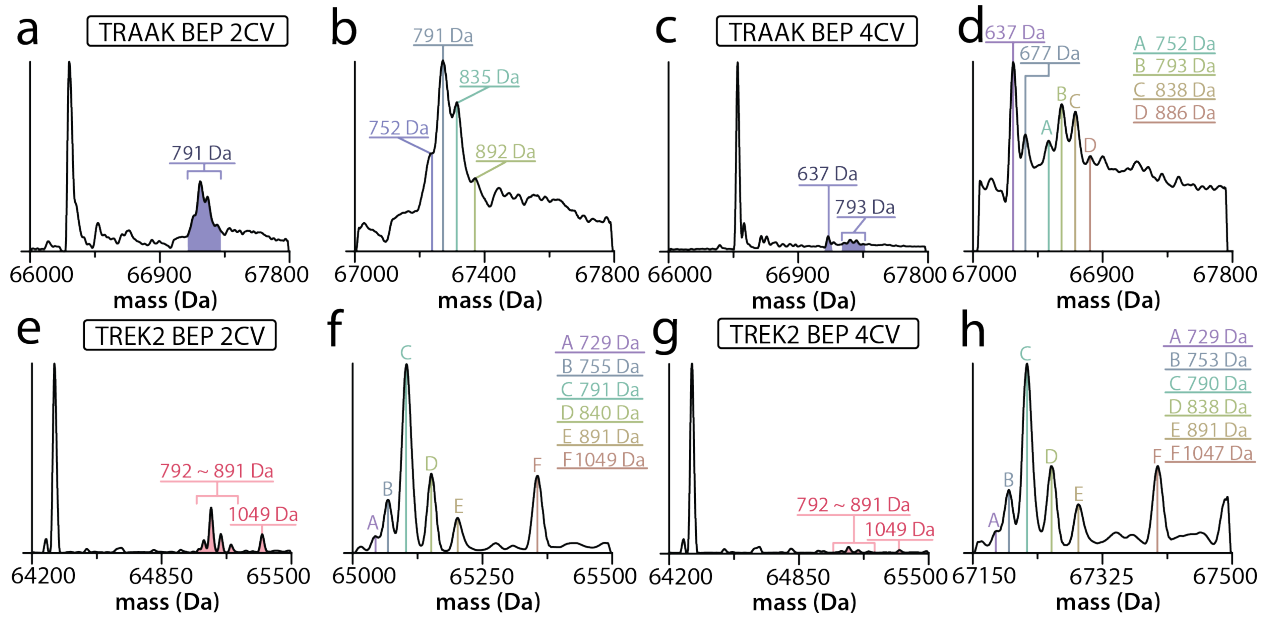
Supplemental Figure S1. Native mass spectra of optimized membrane proteins devoid of any major contaminants. Representative native mass spectra are shown (top to bottom) for TRAAK, TREK2, and AmtB. The deconvoluted mass spectra are shown to the right. For AmtB, a 574 Da mass addition is observed which corresponds to mis-cleavage of the pelB secretion sequence.



Supplemental Figure S2. TRAAK enriches specific lipids from a series of natural headgroup extracts. a) Deconvoluted spectrum of TRAAK mixed with a PC extract followed by a 2 CV wash. b) Zoom of the first ligand binding event. c) Deconvoluted spectrum of TRAAK mixed with a PE extract followed by a 2 CV wash. d) Zoom of the first ligand binding event. e) Deconvoluted spectrum of TRAAK mixed with a PG extract followed by a 2 CV wash. f) Zoom of the first ligand binding event. g) Deconvoluted spectrum of TRAAK mixed with a PS extract followed by a 2 CV wash. h) Zoom of the first ligand binding event.



Supplemental Figure S3. Negative mode mass spectra of natural headgroup extracts. The type of headgroup extract is labeled.



Supplemental Figure S4. TRAAK and TREK2 enrich specific lipids from a brain polar lipid extract (BEP). a) Deconvoluted spectrum of TRAAK mixed with a BEP extract followed by a 2 CV wash. b) Zoom of the first ligand binding event. c) Deconvoluted spectrum of TRAAK mixed with a BEP extract followed by a 4 CV wash. d) Zoom of the first ligand binding event. e) Deconvoluted spectrum of TREK2 mixed with a BEP extract followed by a 2 CV wash. f) Zoom of the first ligand binding event. g) Deconvoluted spectrum of TREK2 mixed with a BEP extract followed by a 4 CV wash. h) Zoom of the first ligand binding event.

Supplemental Table S1. Phospholipids and their abbreviations used in this work.

<i>Abbreviation</i>	<i>Lipid Name</i>
PA	Phosphatidic acid
LPA	Lyso phosphatidic acid
PC	Phosphatidylcholine
PC O/P	Phosphatidylcholine alkyl ether/plasmalogen
LPC	Lyso phosphatidylcholine
PE	Phosphatidylethanolamine
PE O/P	Phosphatidylethanolamine alkyl ether/plasmalogen
LPE	Lyso phosphatidylethanolamine
PG	Phosphatidylglycerol
LPG	Lyso phosphatidylglycerol
PI	Phosphatidylinositol
PS	Phosphatidylserine
CDL	Cardiolipin
EcPE	Phosphatidylethanolamine (<i>E. coli</i> Extract)
EcCDL	Cardiolipin (<i>E. coli</i> Extract)
BEP	Brain Extract Polar (from Porcine)
ANA	Anandamide
FFA	Free fatty acid
Cer	Ceramide
HexCer	Hexosyl Ceramide
SM	Sphingomyelin
AC	Acylcarnitine
TG	Triacylglycerol
DG	Diacylglycerol

Supplemental Table S2.

<i>Elution Gradient</i>			
<i>Time (min)</i>	<i>% MPA</i>	<i>% MPB</i>	<i>Flow rate (mL/min)</i>
0	60	40	0.25
2	50	50	0.25
3	40	60	0.25
12	30	70	0.25
15	25	75	0.25
17	22	78	0.25
19	15	85	0.25
22	8	92	0.25
25	1	99	0.25
34	1	99	0.25

Supplemental Table S3.

<i>Column wash</i>			
<i>Time (min)</i>	<i>% MPA</i>	<i>% MPB</i>	<i>Flow rate (mL/min)</i>
34.5	60	40	0.3
35	1	99	0.3
35.5	1	99	0.3
36	60	40	0.35
37	60	40	0.3
38	60	40	0.25

Supplemental Table S4. Lipidomic analysis of AmtB lipid washes with EcCDL and EcPE.

Class	Lipid	Adduct	Precursor Mz	EPE Extract		ECDL Extract		ECDL EPE Mixture	
				Retention Time (min.)	Log ₂ Area	Retention Time (min.)	Log ₂ Area	Retention Time (min.)	Log ₂ Area
PE	PE(16:0_17:1)	[M-H]	702.5079	21.87	20.164			21.79	19.832
PE	PE(16:1_18:1)	[M-H]	714.5079	20.83	17.896			20.74	17.567
PE	PE(16:0_18:1)	[M-H]	716.5236	22.25	20.619			22.16	20.163
PE	PE(16:0_18:0)	[M-H]	718.5392	22.04	16.192			21.91	17.590
PE	PE(17:1_18:1)	[M-H]	728.5236	21.87	17.967			21.79	17.400
PE	PE(16:0_19:1)	[M-H]	730.5392	23.08	16.597			23	16.907
PE	PE(18:1/18:1)	[M-H]	742.5392	22.25	19.995			22.16	19.607
PE	PE(16:0_20:1)	[M-H]	744.5549					21.95	16.121
PE	PE(18:0_18:1)	[M-H]	744.5549	23.42	16.683			23.37	17.916
PE	PE(18:0/18:0)	[M-H]	746.5705	23.29	15.899			23.25	16.952
PE	PE(18:1_19:1)	[M-H]	756.5549					23	14.639
PE	PE(18:0_20:4)	[M-H]	766.5392					22.33	16.873
PE	PE(16:0_22:4)	[M-H]	766.5392	22.37	15.301				
PE	PE(18:0_20:1)	[M-H]	772.5862					23.2	15.788
PE	PE(16:0_22:1)	[M-H]	772.5862					23.2	15.469
PE	PE(20:1_20:4)	[M-H]	792.5549					22.75	16.244
PE	PE(18:1_22:4)	[M-H]	792.5549					22.75	16.321
PE	PE(18:0_22:5)	[M-H]	792.5549					22.75	16.252
PE	PE(18:1_22:3)	[M-H]	794.5705					23.08	15.816
PE	PE(18:0_22:4)	[M-H]	794.5705					23.08	15.816
CDL	CDL(62:1)	[M-H]	1321.918					25.37	14.141
CDL	CDL(64:2)	[M-H]	1347.934			25.36	15.351	25.33	18.128
CDL	CDL(64:1)	[M-H]	1349.949					25.79	14.799
CDL	CDL(65:2)	[M-H]	1361.949			25.7	15.186	25.66	17.311
CDL	CDL(66:3)	[M-H]	1373.949			25.28	13.237	25.33	15.361
CDL	CDL(66:2)	[M-H]	1375.965			25.78	17.256	25.75	17.963
CDL	CDL(67:3)	[M-H]	1387.965					25.62	14.504
CDL	CDL(67:2)	[M-H]	1389.981			26.11	13.434	26.08	15.752

CDL	CDL(68:3)	[M-H]	1401.981					25.71	15.200
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Supplemental Table S5. Lipidomic analysis of TRAAK lipid enrichment with brain PC extracts.

Class	Lipid	m/z	Summed Area	Log₂Area	Normalized Log₂Area
LPC	LPC(0:0/16:0)	496.339766	13619	13.733	0
	LPC(0:0/18:0)	524.371066	16438	14.005	0.024
	LPC(18:1/0:0)	522.355416	26654	14.702	0.087
	LPC(16:0/0:0)	496.339766	31966	14.964	0.111
	LPC(0:0/18:1)	522.355416	46807	15.514	0.16
PC(P-)	PC(P-18:0/18:1)	772.621467	173891	17.408	0.33
	PC(P-18:0/18:2)	770.605817	432635	18.723	0.448
	PC(P-18:0/16:0)	746.605817	1892388	20.852	0.64
PC	PC(18:0_22:5)	836.616382	116319	16.828	0.278
	PC(14:0_16:0)	706.538132	190031	17.536	0.342
	PC(18:0_20:3)	812.616382	221070	17.754	0.361
	PC(16:0_18:3)	756.553782	248918	17.925	0.377
	PC(16:1_18:2)	756.553782	263722	18.009	0.384
	PC(18:1_18:2)	784.585082	290829	18.15	0.397
	PC(17:0_18:1)	774.600732	484196	18.885	0.463
	PC(16:0_22:5);PC(18:0_20:5)	808.585082	495758	18.919	0.466
	PC(18:0_22:4)	838.632032	604351	19.205	0.492
	PC(18:0_20:1)	816.647682	666547	19.346	0.504
	PC(14:0_18:1);PC(16:0_16:1)a	732.553782	848099	19.694	0.536
	PC(14:0_18:1);PC(16:0_16:1)b	732.553782	881951	19.75	0.541
	PC(16:0_18:2)	758.569432	909012	19.794	0.545
	PC(18:0_18:2)	786.600732	1018864	19.959	0.559
	PC(16:0_18:0)	762.600732	1143765	20.125	0.574
	PC(16:0_22:6)	806.569432	1149495	20.133	0.575
	PC(18:0_22:6)	834.600732	1265715	20.272	0.587
	PC(18:2/18:2)	782.569432	2374642	21.179	0.669
	PC(16:0/16:0)	734.569432	2700264	21.365	0.686
	PC(18:0/18:0)	790.632032	3026006	21.529	0.7
	PC(18:0_20:4)	810.600732	3560360	21.764	0.722
PC(18:1/18:1)	786.600732	4246839	22.018	0.744	
PC(18:0_18:1)	788.616382	20125430	24.263	0.946	

	PC(16:0_18:1)	760.585082	30510232	24.863	1
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Supplemental Table S6. Lipidomic analysis of TRAAK lipid enrichment with brain PE extracts.

<i>Class</i>	<i>Lipid</i>	<i>m/z</i>	<i>Summed Area</i>	<i>Log₂Area</i>	<i>Normalized Log₂Area</i>
LPE	LPE(0:0/18:1)	478.293914	18278	14.158	0.079
	LPE(18:1/0:0)	478.293914	36185	15.143	0.185
PE	PE(18:0_18:3)	740.52358	11018	13.428	0
	PE(18:1_18:2)	740.52358	33483	15.031	0.173
	PE(18:0_18:2)	742.53923	85518	16.384	0.319
	PE(18:0_20:3)	768.55488	95902	16.549	0.337
	PE(38:4)	766.53923	130725	16.996	0.386
	PE(16:0_22:5);PE(18:1_20:4)b	764.52358	139778	17.093	0.396
	PE(16:0_20:4);PE(18:2/18:2)	738.50793	140814	17.103	0.397
	PE(16:0_22:5);PE(18:1_20:4)a	764.52358	164629	17.329	0.422
	PE(18:0_20:1)	772.58618	166772	17.348	0.424
	PE(16:0_22:6)	762.50793	183927	17.489	0.439
	PE(18:0_20:2)	770.57053	357476	18.447	0.542
	PE(18:0_22:5)	792.55488	734053	19.486	0.655
	PE(16:0_18:1)	716.52358	984289	19.909	0.7
	PE(18:0_22:6)	790.53923	971234	19.889	0.698
	PE(18:1/18:1)	742.53923	1237393	20.239	0.736
	PE(18:0_20:4)	766.53923	1829531	20.803	0.797
PE(18:0_18:1)	744.55488	2381810	21.184	0.838	
PE(O/P-)	PE(P-16:0/20:3)	724.528665	62433	15.93	0.27
	PE(P-16:0/18:2)	698.513015	106565	16.701	0.354
	PE(P-18:0/22:5)a	776.559965	119352	16.865	0.371
	PE(P-18:0/20:3)	752.559965	180906	17.465	0.436
	PE(P-16:0/22:6)	746.513015	187111	17.514	0.441
	PE(O-18:0/22:5)	778.575615	403258	18.621	0.561
	PE(P-18:0/22:5)b	776.559965	495653	18.919	0.593
	PE(P-16:0/20:4)	722.513015	516461	18.978	0.6
	PE(O-18:0/22:6)	776.559965	802494	19.614	0.668
	PE(P-16:0/22:4)	750.544315	1034992	19.981	0.708

	PE(P-18:0/22:6)	774.544315	1064576	20.022	0.713
	PE(P-16:0/22:5)	748.528665	1476832	20.494	0.764
	PE(P-18:0/22:4)	778.575615	1612762	20.621	0.777
	PE(P-18:0/20:2)	754.575615	1884550	20.846	0.802
	PE(P-18:0/20:4)	750.544315	2036414	20.958	0.814
	PE(P-16:0/18:1)	700.528665	3183973	21.602	0.883
	PE(P-18:0/18:1)	728.559965	3729310	21.83	0.908
	PE(P-16:0/20:2)	726.544315	6731846	22.683	1

Supplemental Table S7. Lipidomic analysis of TRAAK lipid enrichment with egg PG extracts.

<i>Class</i>	<i>Lipid</i>	<i>m/z</i>	<i>Summed Area</i>	<i>Log₂Area</i>	<i>Normalized Log₂Area</i>
PG	PG(16:1_20:4)	767.48686	9673	13.24	0
	PG(14:0_18:2)	717.47121	11869	13.535	0.0297
	PG(16:0_18:0)	749.53381	35596	15.119	0.1893
	PG(15:0_18:1)	733.50251	39948	15.286	0.206
	PG(17:0_18:2)	759.51816	41189	15.33	0.2105
	PG(16:1_18:2)b	743.48686	41730	15.349	0.2124
	PG(18:0_18:3);PG(16:0_20:3)	771.51816	45574	15.476	0.2252
	PG(18:0_20:2)	801.56511	56559	15.787	0.2566
	PG(18:0_22:4)	825.56511	58588	15.838	0.2617
	PG(16:0_19:1);PG(17:0_18:1)	761.53381	72815	16.152	0.2933
	PG(16:0_22:4)	797.53381	74123	16.178	0.2959
	PG(16:0/16:0)	721.50251	77837	16.248	0.303
	PG(16:1_18:2)a	743.48686	101964	16.638	0.3422
	PG(16:0_20:3)	771.51816	136247	17.056	0.3843
	PG(18:0_20:3)	799.54946	138054	17.075	0.3862
	PG(18:0_22:6)	821.53381	153922	17.232	0.402
	PG(16:0_16:1)	719.48686	166759	17.347	0.4137
	PG(18:1_20:4)	795.51816	172497	17.396	0.4186
	PG(16:1_18:1)	745.50251	261601	17.997	0.4791
	PG(18:0_22:5)	823.54946	324421	18.308	0.5103
	PG(16:0_22:6)	793.50251	472866	18.851	0.5651
	PG(16:0_22:5)	795.51816	788285	19.588	0.6393
	PG(18:1_18:2)	771.51816	907989	19.792	0.6599
	PG(18:1/18:1)	773.53381	1129183	20.107	0.6915
	PG(16:0_20:4)	769.50251	1188622	20.181	0.699
	PG(18:0_20:4)	797.53381	2284311	21.123	0.7939
	PG(18:0_18:2)	773.53381	3810375	21.862	0.8682
	PG(16:0_20:1)	775.54946	4146948	21.984	0.8805
	PG(16:0_18:2)	745.50251	6443933	22.62	0.9446
	PG(16:0_18:1)	747.51816	9437611	23.17	1

Supplemental Table S8. Lipidomic analysis of TRAAK lipid enrichment with brain PS extracts.

<i>Class</i>	<i>Lipid</i>	<i>m/z</i>	<i>Summed Area</i>	<i>Log₂Area</i>	<i>Normalized Log₂Area</i>
PS	PS(18:1_20:4)	808.513409	58992	15.848	0
	PS(18:0_20:2)	814.560359	71395	16.124	0.0626
	PS(18:0_20:5)	808.513409	86776	16.405	0.1266
	PS(18:1_20:3)	810.529059	106455	16.7	0.1936
	PS(18:0_18:2)	786.529059	186815	17.511	0.3781
	PS(18:1/18:1)	786.529059	196825	17.587	0.3953
	PS(18:0_22:4)	838.560359	321963	18.297	0.5567
	PS(18:0_22:5)	836.544709	357221	18.446	0.5908
	PS(18:0_20:4)	810.529059	589944	19.17	0.7553
	PS(18:0_22:6)	834.529059	697948	19.413	0.8105
PS(18:0_18:1)	788.544709	1243734	20.246	1	

Supplemental Table S9. Lipidomic analysis of TRAAK with a brain polar lipid extract (BEP).

<i>Class</i>	<i>Lipid</i>	<i>Ionization Mode</i>	<i>Adduct</i>	<i>Precursor m/z</i>	<i>CV1 Log₂ Area</i>	<i>CV2 Log₂ Area</i>	<i>CV3 Log₂ Area</i>	<i>CV4 Log₂ Area</i>
AC (Acyl carnitine)	AC(14:1)	Positive	[M+H]	370.2952	14.4405	14.0288		
	AC(16:0)	Positive	[M+H]	400.3421				17.8181
	AC(18:1)	Positive	[M+H]	426.3578				15.9522
	AC(18:2)	Positive	[M+H]	424.3421		14.2208	15.7394	15.4206
ANA (Anandamide)	ANA(16:0)	Positive	[M+H]	300.2897				20.6858
	ANA(18:3)	Positive	[M+H]	322.2741				18.5419
	ANA(20:2)	Positive	[M+H]	352.3210	18.6755	18.7338		
Cer (Ceramide)	Cer(d18:1/24:0)	Positive	[M+H]	650.6446	15.9596	15.5212	14.8540	16.2490
DG (Diacylglycerol)	DG(16:0_18:1)	Positive	[M+NH4]	612.5562	12.7758			
	DG(18:1/18:1)	Positive	[M+NH4]	638.5718	15.2322			
	DG(18:1_18:2)	Positive	[M+NH4]	636.5562	13.2348			
FFA (Free fatty acid)	FA 12:0	Negative	[M-H]	199.1704	12.3853			17.2926
	FA 13:0	Negative	[M-H]	213.1860				18.1935
	FA 14:0	Negative	[M-H]	227.2017	13.8325	17.8484	14.0310	21.0465
	FA 14:1	Negative	[M-H]	225.1860				20.3719
	FA 14:2	Negative	[M-H]	223.1704				13.9668
	FA 15:0	Negative	[M-H]	241.2173	14.9128	15.1758		21.9754
	FA 15:1	Negative	[M-H]	239.2017				20.7873
	FA 16:0	Negative	[M-H]	255.2330	24.7484	28.1187	20.6917	23.6624
	FA 16:1	Negative	[M-H]	253.2173	14.7382			22.3333
	FA 16:2	Negative	[M-H]	251.2017				17.3911
	FA 17:0	Negative	[M-H]	269.2486	17.2774	17.9181	15.0163	20.2748
	FA 17:1	Negative	[M-H]	267.2330				21.1060
	FA 17:2	Negative	[M-H]	265.2173	10.3966			16.0919
	FA 18:0	Negative	[M-H]	283.2643	24.8561	27.3515	21.7479	25.0837
FA 18:1	Negative	[M-H]	281.2486	21.2938	24.8818	17.9234	23.4707	
FA 18:2	Negative	[M-H]	279.2330	13.5206			20.4726	

	FA 18:3	Negative	[M-H]	277.2173				16.7627
	FA 19:0	Negative	[M-H]	297.2799	13.7699		11.2761	16.5201
	FA 19:1	Negative	[M-H]	295.2643	11.2544			18.0003
	FA 20:0	Negative	[M-H]	311.2956	19.0459	18.9910	18.4472	19.0821
	FA 20:1	Negative	[M-H]	309.2799	14.4809			20.3013
	FA 20:2	Negative	[M-H]	307.2643				19.5762
	FA 20:3	Negative	[M-H]	305.2486				17.0642
	FA 20:4	Negative	[M-H]	303.2330	12.2932	12.6223		17.9277
	FA 21:0a	Negative	[M-H]	325.3112	13.0262		12.6303	14.9721
	FA 21:0b	Negative	[M-H]	325.3112	14.5167		14.2545	14.9358
	FA 22:0	Negative	[M-H]	339.3269	17.1873	17.2643	16.4546	17.1362
	FA 22:1	Negative	[M-H]	337.3112	15.6732	15.6375	15.7953	18.4238
	FA 22:2	Negative	[M-H]	335.2956				17.2862
	FA 22:3a	Negative	[M-H]	333.2799				16.2082
	FA 22:3b	Negative	[M-H]	333.2799				16.2719
	FA 22:4	Negative	[M-H]	331.2643				16.9995
	FA 22:5	Negative	[M-H]	329.2486				14.1189
	FA 22:6	Negative	[M-H]	327.2330				14.9018
	FA 23:0	Negative	[M-H]	353.3425	15.2516	15.0890	15.2427	15.7388
	FA 24:0a	Negative	[M-H]	367.3582	13.6607	17.4340	13.5918	17.5754
	FA 24:0b	Negative	[M-H]	367.3582	17.2956		17.4448	
	FA 24:1	Negative	[M-H]	365.3425				16.6828
	FA 25:0	Negative	[M-H]	381.3738	15.8300	16.1034	15.5053	16.0189
	FA 26:0a	Negative	[M-H]	395.3895	13.9758	17.1553	13.9493	17.6558
FA 26:0b	Negative	[M-H]	395.3895	16.7029		16.9913	17.6301	
HexCer (Hexosyl Ceramide)	HexCer(d18:2/2 4:0)	Negative	[M-H]	808.6672		11.6917		
LPC (Lyso phosphatidyl choline)	LPC(0:0/16:0)	Positive	[M+H]	496.3398				16.8408
	LPC(0:0/18:0)	Positive	[M+H]	524.3711				14.2323
	LPC(0:0/18:1)	Positive	[M+H]	522.3554				14.7109
	LPC(16:0/0:0)	Positive	[M+H]	496.3398				20.8733
	LPC(18:0/0:0)	Positive	[M+H]	524.3711				17.4716

		Positive	[M+H]	522.3554				17.0966
	LPC(18:1/0:0)							
LPE (Lyso phosphatidyl ethanolamine)	LPE(0:0/18:0)	Negative	[M-H]	480.3096	13.0828			10.7723
	LPE(0:0/18:1)	Negative	[M-H]	480.3085	12.8323			
	LPE(18:0/0:0)	Negative	[M-H]	480.3096	9.4305			12.6159
	LPE(18:1/0:0)	Negative	[M-H]	480.3085	12.8891			
PC (Phosphatidylcholine)	PC(15:0_18:2)	Positive	[M+H]	744.5538		16.2311	16.3327	
	PC(15:0_20:4);PC(17:2_18:2)	Positive	[M+H]	768.5538		18.2055	18.1109	
	PC(16:0/16:0)	Positive	[M+H]	734.5694		15.1437	14.2813	
	PC(16:0_18:1)	Positive	[M+H]	760.5851	16.4143	19.3224	19.6746	16.2302
	PC(16:0_20:4);PC(18:1_18:3)	Positive	[M+H]	782.5694	18.8873	18.0576	18.6225	
	PC(16:0_22:4)	Positive	[M+H]	810.6007			15.4891	
	PC(16:0_22:5);PC(18:0_20:5)	Positive	[M+H]	808.5851	14.7602			
	PC(16:0_22:6)	Positive	[M+H]	806.5694	15.6497			
	PC(17:0_20:4)	Positive	[M+H]	796.5851	16.9231	16.2434	15.3767	
	PC(17:0_22:5)	Positive	[M+H]	822.6007	13.5553			
	PC(18:0_18:1)	Positive	[M+H]	788.6164	18.9711	18.9775	18.2437	
	PC(18:0_18:1)-	Negative	[M-H]	846.6230	12.9642			
	PC(18:0_18:2)	Positive	[M+H]	786.6007	16.3416	13.4996	15.6961	
	PC(18:0_20:4)	Positive	[M+H]	810.6007	16.1985		15.5613	
	PC(18:0_20:4)-	Negative	[M-H]	868.6073	11.2720			
	PC(18:0_22:6)	Positive	[M+H]	892.6073	10.8258			
	PC(18:1/18:1)	Positive	[M+H]	786.6007	16.3228		15.4562	
	PC(18:1_20:3)	Positive	[M+H]	810.6007			15.9957	
	PC(18:1_20:4)	Positive	[M+H]	808.5851	15.1779			
	PC(18:1_22:5)	Positive	[M+H]	834.6007	14.4809			
PC(18:2/18:2)	Positive	[M+H]	782.5694	14.5002				
PC(37:4)	Positive	[M+H]	796.5851	17.1627	16.9330			
PC(37:5)	Positive	[M+H]	794.5694	19.0792			18.2140	

	PC(37:6)	Positive	[M+H]	792.5538	19.1709	18.3582	18.4888	
PC(O/P-) (Alyl/alkenyl ether phosphatidyl choline)	PC(O- 16:0/20:4);PC(P- 18:0/18:3)	Positive	[M+H]	768.5902		17.1619		
	PC(P-16:0/16:0)	Positive	[M+H]	718.5745		14.7869		
	PC(P-18:0/16:0)	Positive	[M+H]	746.6058		14.8993	13.8476	
PE (Phosphatidy lethanolamin e)	PE(16:0_18:0)	Negative	[M-H]	718.5392	13.0773		11.6312	
	PE(16:0_18:1)	Negative	[M-H]	716.5236	12.1507	9.2691	13.8451	
	PE(16:0_20:4);P E(18:2/18:2)	Negative	[M-H]	738.5079		12.2219	8.9396	13.4427
	PE(16:0_22:5);P E(18:1_20:4)	Negative	[M-H]	764.5236		13.8662	11.8498	13.9994
	PE(16:0_22:6)	Negative	[M-H]	762.5079	15.0853	14.7149	13.9857	
	PE(18:0_18:1)	Negative	[M-H]	744.5549	12.1267	10.3955	15.6545	
	PE(18:0_18:2)	Positive	[M+H]	744.5538	15.4453		16.3985	
	PE(18:0_18:2);P E(18:1/18:1)	Negative	[M-H]	742.5392		8.1137	15.8023	
	PE(18:0_20:1)	Negative	[M-H]	772.5862	13.6666	15.7404	14.0860	
	PE(18:0_20:2)	Negative	[M-H]	770.5705	13.0526	13.2636		
	PE(18:0_20:3)	Negative	[M-H]	768.5549	13.7825			
	PE(18:0_20:4)	Negative	[M-H]	766.5392	16.6604	12.8465	17.4380	14.2404
	PE(18:0_20:5)	Negative	[M-H]	764.5236			13.7432	
	PE(18:0_22:5)	Negative	[M-H]	792.5549	15.1295	11.4263	14.9829	
	PE(18:0_22:6)	Negative	[M-H]	790.5392	16.8137	18.4464	17.5025	13.8812
	PE(18:1_20:5)	Positive	[M+H]	764.5225	17.2850		16.1146	
	PE(36:1)	Negative	[M-H]	744.5549	17.2412	7.8329	14.4784	
	PE(38:4)	Negative	[M-H]	766.5392		12.7495	13.2519	6.4429
	PE(40:7)	Negative	[M-H]	788.5236	12.4959			
	PE(O/P-) (Allyl/alkenyl ether phosphatidyl)	PE(O-16:0/22:6)	Negative	[M-H]	748.5287	16.4791		
PE(O- 16:0/22:6);PE(P- 16:0/22:5);PE(P- 18:0/20:5)		Negative	[M-H]	748.5287		13.3807	11.9267	

ethanolamine)	PE(O-18:0/20:3);PE(P-18:0/20:2)	Negative	[M-H]	754.5756		8.0928		
	PE(O-18:0/22:6)	Negative	[M-H]	776.5600	15.4182	16.4213	15.3782	
	PE(O-40:5);PE(P-40:4)	Negative	[M-H]	778.5756			14.7181	
	PE(P-16:0/18:1)	Negative	[M-H]	700.5287	15.1061	17.6444	16.2746	
	PE(P-16:0/18:2);PE(P-20:0/18:2)	Negative	[M-H]	726.5443			17.3665	
	PE(P-16:0/20:2)	Negative	[M-H]	726.5443	15.5800			
	PE(P-16:0/20:2);PE(P-18:0/18:2)	Negative	[M-H]	726.5443				13.7922
	PE(P-16:0/20:4)	Negative	[M-H]	722.5130	13.6484	14.9172	13.9904	
	PE(P-16:0/22:4)	Negative	[M-H]	750.5443	14.6122	15.5057	14.7772	
	PE(P-16:0/22:5)	Negative	[M-H]	748.5287	16.4791			
	PE(P-16:0/22:6)	Negative	[M-H]	746.5130	14.5867	9.0224	14.3341	
	PE(P-18:0/18:1)	Negative	[M-H]	728.5600	12.2393	14.1704	14.1264	
	PE(P-18:0/18:2)	Negative	[M-H]	726.5443		18.0953		
	PE(P-18:0/20:3)	Negative	[M-H]	752.5600		15.1015		
	PE(P-18:0/20:4)	Negative	[M-H]	750.5443	15.5772	17.4709	15.8737	
	PE(P-18:0/20:5)	Negative	[M-H]	748.5287	17.3129			
	PE(P-18:0/22:4)	Negative	[M-H]	778.5756	13.7159	12.9207	14.7454	
	PE(P-18:0/22:5)	Negative	[M-H]	776.5600	12.3894	16.4633	13.4633	
	PE(P-18:0/22:6)	Negative	[M-H]	774.5443	15.7331	17.4279	16.0072	
PI (Phosphatidylinositol)	PI(16:0_18:1)	Negative	[M-H]	835.5342			12.4165	
	PI(16:0_18:2)	Negative	[M-H]	833.5186			12.7659	
	PI(16:0_20:4)	Negative	[M-H]	857.5186	12.0885	13.5906	13.1759	
	PI(16:0_22:5);PI(18:1_20:4)	Negative	[M-H]	883.5342	13.2949	7.5622	13.5619	
	PI(18:0_20:3)	Negative	[M-H]	887.5655	15.4724		11.4089	
PI(18:0_20:4)	Negative	[M-H]	885.5499	17.9154	18.0033	17.0958	13.6347	

	PI(18:0_22:3)	Negative	[M-H]	915.5968				13.5093
PS (Phosphatidylserine)	PS 15:0-18:0	Negative	[M-H]	748.5134	17.2990		16.1439	
	PS 16:0-17:1	Negative	[M-H]	746.4978	14.6305			
	PS 16:0-18:0	Negative	[M-H]	762.5291		13.1362		
	PS 16:0-19:0	Negative	[M-H]	776.5447	13.3740	15.8990		
	PS 16:0-19:1	Negative	[M-H]	774.5291	17.1198	16.9216	15.6096	
	PS 16:0-22:0	Negative	[M-H]	818.5917		17.4990	16.7019	
	PS 17:0-18:0	Negative	[M-H]	776.5447		13.8437		
	PS 18:0-18:0	Negative	[M-H]	790.5604		17.8081	16.8846	
	PS(40:0)	Negative	[M-H]	818.5917	15.8115	17.4990	16.7019	
SM (Sphingomyelin)	SM(d17:0/18:1)	Positive	[M+H]	717.5905				16.9351
	SM(d17:1/16:0)	Positive	[M+H]	689.5592			16.8824	
	SM(d17:1/18:0)	Positive	[M+H]	717.5905	16.6237		16.9694	
	SM(d35:2)	Positive	[M+H]	715.5749				16.4905
TG (Triacylglycerol)	TG(12:0_16:0_18:1);TG(14:0_14:0_18:1);TG(14:0_16:0_16:1)	Positive	[M+NH4]	794.7232	18.3617	18.0075	18.3879	
	TG(16:0_18:0_19:1)	Positive	[M+NH4]	892.8328	14.7183			
	TG(12:0_12:0_18:1);TG(12:0_14:0_16:1);TG(12:0_14:1_16:0)	Positive	[M+NH4]	738.6606	16.6518	17.1273	17.2584	17.6946
	TG(12:0_14:0_18:1);TG(12:0_16:0_16:1)	Positive	[M+NH4]	766.6919	17.5404	17.6050	17.5726	17.8273
	TG(12:0_14:0_18:2);TG(12:0_16:1_16:1)	Positive	[M+NH4]	764.6763	16.1674	15.9412	16.1972	16.5485

TG(12:0_16:1_18:1);TG(14:0_14:0_18:2);TG(14:0_16:1_16:1)	Positive	[M+NH4]	792.7076	17.3864	17.1474	17.1434	
TG(14:0_14:0_16:0);TG(12:0_16:0_16:0)	Positive	[M+NH4]	768.7076	17.3928	17.6320	17.8065	17.4027
TG(14:0_16:0_16:0)	Positive	[M+NH4]	796.7389	18.9837	18.6314	19.0080	19.0569
TG(14:0_16:0_17:0)	Positive	[M+NH4]	810.7545	17.6223	17.0372	17.7237	17.5282
TG(14:0_16:0_17:1)	Positive	[M+NH4]	808.7389	18.2666	17.0341	17.4432	17.8793
TG(14:0_16:0_18:1);TG(16:0_16:0_16:1)	Positive	[M+NH4]	822.7545	19.2475	18.7055	19.2912	19.4108
TG(14:0_16:0_18:2);TG(14:0_16:1_18:1);TG(16:0_16:1_16:1)	Positive	[M+NH4]	820.7389	18.8136	18.1633	18.6565	19.0961
TG(14:0_16:1_18:2)	Positive	[M+NH4]	818.7232	16.8378		17.2093	17.5279
TG(14:0_18:1_18:1)	Positive	[M+NH4]	848.7702	18.8388	19.1140	19.6340	19.9772
TG(14:0_18:1_18:2);TG(16:1_16:1_18:1)	Positive	[M+NH4]	846.7545	18.0003	18.2932	18.8986	18.8142
TG(15:0_16:0_18:1);TG(15:0_17:0_17:1)	Positive	[M+NH4]	836.7702	16.8109	16.1672	17.2222	16.7705
TG(15:0_16:0_18:2);TG(15:0_16:1_18:1)	Positive	[M+NH4]	834.7545	17.3939		16.5785	17.2967

TG(15:0_16:0_20:3);TG(16:0_17:1_18:2)	Positive	[M+NH4]	860.7702	15.0955			
TG(16:0_16:0_18:0)	Positive	[M+NH4]	852.8015	17.4048	17.5513	17.5032	17.9631
TG(16:0_16:0_18:1)	Positive	[M+NH4]	850.7858	19.2377	19.3924	19.8409	20.1243
TG(16:0_16:0_18:2)	Positive	[M+NH4]	848.7702		19.1140	19.6340	19.9671
TG(16:0_16:1_20:4);TG(16:0_18:2_18:3)	Positive	[M+NH4]	870.7545	12.3520			
TG(16:0_17:0_18:1)	Positive	[M+NH4]	864.8015	16.9079	16.3788	16.7133	17.0208
TG(16:0_17:0_18:2)	Positive	[M+NH4]	862.7858	16.3377	16.1552	16.5909	16.9674
TG(16:0_17:1_18:1)	Positive	[M+NH4]	862.7858		16.3374	16.5795	16.9674
TG(16:0_18:0_18:0)	Positive	[M+NH4]	880.8328	15.9227	16.1681	16.7381	16.6320
TG(16:0_18:0_18:1)	Positive	[M+NH4]	878.8171	18.6606	18.8709	19.3817	19.6014
TG(16:0_18:0_18:2);TG(16:0_18:1_18:1)	Positive	[M+NH4]	876.8015	20.4848	20.7774	21.3056	21.5805
TG(16:0_18:1_18:2)	Positive	[M+NH4]	874.7858	20.1524	20.6275	20.9206	21.0661
TG(16:0_18:1_18:3);TG(16:0_18:2_18:2)	Positive	[M+NH4]	872.7702	18.5978	19.1232	19.4470	19.7265
TG(16:0_18:1_20:4)	Positive	[M+NH4]	898.7858	19.6658		20.1304	20.1668
TG(16:0_18:2_19:0)	Positive	[M+NH4]	890.8171	15.5553			

TG(16:1_16:1_18:2)	Positive	[M+NH4]	844.7389	14.8142		15.4268	
TG(16:1_18:1_20:4);TG(18:2/18:2/18:2)	Positive	[M+NH4]	896.7702	18.9126	19.2190	19.3493	19.6251
TG(16:1_18:2_18:3)	Positive	[M+NH4]	868.7389	14.9013	15.5807		
TG(18:0/18:0/18:0)	Positive	[M+NH4]	908.8641	14.9625	15.3194	15.9164	16.8269
TG(18:0_18:0_18:1)	Positive	[M+NH4]	906.8484	17.7671	18.2071	18.4909	18.9411
TG(18:0_18:1_18:1)	Positive	[M+NH4]	904.8328	19.2782	19.8134	20.4932	20.6431
TG(18:0_18:1_18:2);TG(18:1/18:1/18:1)	Positive	[M+NH4]	902.8171	22.3211	22.4374	22.8249	22.9645
TG(18:0_18:1_20:1)	Positive	[M+NH4]	932.8641			18.5196	15.1533
TG(18:1_18:2_18:2)	Positive	[M+NH4]	898.7858	19.3813	19.7188	19.9184	20.0657
TG(18:1_20:1_20:1)	Positive	[M+NH4]	958.8797	13.9166	18.5778	18.8574	18.9987
TG(18:2_18:3_18:3)	Positive	[M+NH4]	892.7389		16.1048	15.9678	
TG(46:3)	Positive	[M+NH4]	790.6919	16.9396			
TG(48:0)	Positive	[M+NH4]	824.7702	19.7340	19.6445	19.5960	19.8613
TG(49:0)	Positive	[M+NH4]	838.7858	18.5139	18.1030	18.2391	18.3790
TG(49:3)	Positive	[M+NH4]	832.7389	17.0321			16.6639
TG(52:6)	Positive	[M+NH4]	868.7389		15.6155	15.3432	
TG(54:4)	Positive	[M+NH4]	900.8015	20.9515	21.3765	21.1352	21.4119
TG(54:6)	Positive	[M+NH4]	896.7702	19.2079			19.4845
TG(54:7)	Positive	[M+NH4]	894.7545	17.4287	17.8175		
TG(58:2)	Positive	[M+NH4]	960.8954	17.3593	19.9223	19.9517	19.6495
TG(58:4)	Positive	[M+NH4]	956.8641	15.3659			

	TG(58:5)	Positive	[M+NH4]	954.8484	17.5618	18.1009	18.2945	
	TG(60:10)	Positive	[M+NH4]	972.8015		17.0425		
	TG(60:13)	Positive	[M+NH4]	966.7545				16.1705

Supplemental Table S10. Lipidomic analysis of TREK2 with a brain polar lipid extract (BEP).

<i>Class</i>	<i>Lipid</i>	<i>Ionization Mode</i>	<i>Adduct</i>	<i>Precursor m/z</i>	<i>CV1 Log₂ Area</i>	<i>CV2 Log₂ Area</i>	<i>CV3 Log₂ Area</i>	<i>CV4 Log₂ Area</i>
FFA (Free fatty acid)	FA 12:0	Negative	[M-H]	199.1704				14.68
	FA 14:0	Negative	[M-H]	227.2017	16.02	16.02	15.98	15.96
	FA 15:0	Negative	[M-H]	241.2173	14.38	14.38		
	FA 16:0	Negative	[M-H]	255.2330	20.62	20.62	20.67	19.91
	FA 17:0a	Negative	[M-H]	269.2486	13.70	13.70	13.04	13.96
	FA 17:0b	Negative	[M-H]	269.2486			14.46	
	FA 18:1	Negative	[M-H]	281.2486	16.68	16.68	16.94	
	FA 18:0	Negative	[M-H]	283.2643	21.77	21.77	22.22	22.10
	FA 20:4	Negative	[M-H]	303.2330	13.71	13.71		
	FA 20:0a	Negative	[M-H]	311.2956			15.16	16.91
	FA 20:0b	Negative	[M-H]	311.2956	17.54	17.54	15.15	
	FA 21:0	Negative	[M-H]	325.3112	15.16	15.16		13.63
	FA 22:6	Negative	[M-H]	327.2330	12.90	12.90		
	FA 22:1	Negative	[M-H]	337.3112	16.72	16.72	16.52	16.92

	FA 22:0	Negative	[M-H]	339.3269	16.90	16.90	16.75	16.93
	FA 23:0	Negative	[M-H]	353.3425	15.76	15.76	16.13	16.34
	FA 24:0a	Negative	[M-H]	367.3582			18.24	14.32
	FA 24:0b	Negative	[M-H]	367.3582	18.30	18.30	18.81	18.28
	FA 25:0	Negative	[M-H]	381.3738	17.35	17.35	16.52	17.22
	FA 26:0a	Negative	[M-H]	395.3895	13.98	13.98	13.64	14.08
	FA 26:0b	Negative	[M-H]	395.3895	16.75	16.75	17.03	17.74
LPA (Lysophosphatidic acid)	LPA 17:3	Negative	[M-H]	417.2048	17.07	17.07	17.04	16.73
LPG (Lysophosphatidylglycerol)	LPG 18:1	Negative	[M-H]	509.2885	16.54	16.54	17.21	13.24
PC (Phosphatidylcholine)	PC(16:0/16:0)	Negative	[M-H]	792.5760	13.62	13.62	12.64	12.62
	PC(16:0_18:1)	Negative	[M-H]	818.5917	18.39	18.39	16.80	15.86
	PC(16:0_20:4)	Negative	[M-H]	840.5760	14.88	14.88		
	PC(18:0_18:2)	Negative	[M-H]	844.6073	14.88	14.88		
	PC(18:0_18:1)	Negative	[M-H]	846.6230	15.86	15.86	15.18	14.12
	PC(18:0_20:4)	Negative	[M-H]	868.6073	14.73	14.73		
PE (Phosphatidylethanolamine)	PE(16:0_18:1)	Negative	[M-H]	716.5236			12.78	
	PE(16:0_20:4); PE(18:2/18:2)	Negative	[M-H]	738.5079	14.28	14.28		
	PE(18:1/18:1)	Negative	[M-H]	742.5392	16.08	16.08	14.24	13.73
	PE(18:0_18:1)	Negative	[M-H]	744.5549	14.27	14.27	13.72	13.74
	PE(36:1)	Negative	[M-H]	744.5549				13.74
	PE(16:0_22:6)	Negative	[M-H]	762.5079	15.28	15.28		

	PE(16:0_22:5); PE(18:1_20:4)	Negative	[M-H]	764.5236	15.00	15.00		
	PE(18:0_20:4)	Negative	[M-H]	766.5392	16.74	16.74	14.84	14.10
	PE(18:0_22:6)	Negative	[M-H]	790.5392	16.86	16.86	14.50	13.70
	PE(18:0_22:5)	Negative	[M-H]	792.5549	14.84	14.84	12.55	12.64
PE(O/P-) (Alkyl/alkenyl ether phosphatidylethanolamine)	PE(P-16:0/18:1)	Negative	[M-H]	700.5287	16.39	16.39	15.45	14.75
	PE(P-16:0/20:4)	Negative	[M-H]	722.5130	15.17	15.17	13.13	
	PE(P-16:0/20:2)	Negative	[M-H]	726.5443				15.09
	PE(P-18:0/18:2)	Negative	[M-H]	726.5443	17.75	17.75	15.80	
	PE(P-18:0/18:1)	Negative	[M-H]	728.5600	14.44	14.44	13.76	13.49
	PE(P-16:0/22:5)	Negative	[M-H]	748.5287			14.79	
	PE(P-16:0/22:4)	Negative	[M-H]	750.5443	15.91	15.91	13.54	13.10
	PE(P-18:0/20:4)	Negative	[M-H]	750.5443	16.68	16.68	14.76	14.23
	PE(P-18:0/22:6)	Negative	[M-H]	774.5443	16.80	16.80		13.96
	PE(O-18:0/22:6)	Negative	[M-H]	776.5600	16.26	16.26		
	PE(P-18:0/22:4)	Negative	[M-H]	778.5756	15.24	15.24	13.95	
	PI (Phosphatidylinositol)	PI(16:0_20:4)	Negative	[M-H]	857.5186	13.33	13.33	
PI(18:0_20:4)		Negative	[M-H]	885.5499	16.56	16.56	13.58	12.57
PS (Phosphatidylserine)	PS 16:0-17:1	Negative	[M-H]	746.4978	14.58	14.58		
	PS 15:0-18:0	Negative	[M-H]	748.5134	17.31	17.31		
	PS 16:0-19:1	Negative	[M-H]	774.5291	16.46	16.46	14.12	13.76

	PS 16:0-19:0	Negative	[M-H]	776.5447	15.53	15.53		13.13
	PS 17:0-18:0	Negative	[M-H]	776.5447	13.81	13.81		
	PS(40:0)	Negative	[M-H]	846.6230	15.89	15.89	15.29	14.41
AC (Acyl carnitine)	AC(18:2)	Positive	[M+H]	424.3421				18.79
ANA (Anandamide)	ANA(20:1)	Positive	[M+H]	354.3367				13.58
Cer (Ceramide)	Cer(d18:1/24:0)	Positive	[M+H]	650.6446	15.41			
DG (Diacylglycerol)	DG(16:0_18:1)	Positive	[M+NH4]	612.5562	16.29			
	DG(18:0_18:1)	Positive	[M+NH4]	640.5875	16.21	14.74	15.36	
LPC (Lyso phosphatidyl choline)	LPC(0:0/16:0)	Positive	[M+H]	496.3398	14.04	15.09		
	LPC(16:0/0:0)	Positive	[M+H]	496.3398	17.90			
	LPC(0:0/18:1)	Positive	[M+H]	522.3554	15.56			
	LPC(18:1/0:0)	Positive	[M+H]	522.3554	17.28			
	LPC(0:0/18:0)	Positive	[M+H]	524.3711	11.94			
	LPC(18:0/0:0)	Positive	[M+H]	524.3711	17.09			
LPE (Lyso phosphatidyl ethanolamine)	LPE(0:0/18:1)	Positive	[M+H]	480.3085	16.48			
	LPE(18:1/0:0)	Positive	[M+H]	480.3085	16.61			
	LPE(0:0/22:6)	Positive	[M+H]	526.2928	14.64	12.32		
	LPE(22:6/0:0)	Positive	[M+H]	526.2928	15.45	11.87		
PC (Phosphatidyl choline)	PC(14:0_16:0)	Positive	[M+H]	706.5381	18.47	14.69		
	PC(14:0_18:1);PC(16:0_16:1)	Positive	[M+H]	732.5538	20.23	15.62		
	PC(16:0/16:0)	Positive	[M+H]	734.5694	21.83	17.74	15.39	14.89
	PC(15:0_18:2)	Positive	[M+H]	744.5538	21.46	17.52		
	PC(16:0_18:3)	Positive	[M+H]	756.5538	16.89	14.16		
	PC(16:0_18:2)	Positive	[M+H]	758.5694	18.85		13.39	
	PC(16:0_18:1)	Positive	[M+H]	760.5851	24.23	20.75	18.95	18.49

	PC(16:0_18:0)	Positive	[M+H]	762.6007	20.33	16.16		
	PC(15:0_20:4) ;PC(17:2_18:2)	Positive	[M+H]	768.5538	18.29	18.91	16.79	15.83
	PC(17:0_18:3) a	Positive	[M+H]	770.5694	17.72			
	PC(17:0_18:3) b	Positive	[M+H]	770.5694	17.87			
	PC(17:0_18:2) a	Positive	[M+H]	772.5851	18.78			
	PC(16:0_20:4) ;PC(18:1_18:3)	Positive	[M+H]	782.5694	19.88	16.76	15.29	14.94
	PC(18:2/18:2)	Positive	[M+H]	782.5694		16.94		14.66
	PC(18:0_18:2)	Positive	[M+H]	786.6007		11.20		
	PC(18:1/18:1)	Positive	[M+H]	786.6007	20.97	8.11	15.29	15.20
	PC(18:0_18:1)	Positive	[M+H]	788.6164	23.47	19.07	17.32	16.88
	PC(37:6)a	Positive	[M+H]	792.5538	22.21	18.69		15.80
	PC(37:6)b	Positive	[M+H]	792.5538			16.45	
	PC(15:0_22:5)	Positive	[M+H]	794.5694	21.46		14.84	
	PC(37:5)a	Positive	[M+H]	794.5694		17.29		13.89
	PC(17:0_20:4)	Positive	[M+H]	796.5851		16.99		
	PC(37:4)	Positive	[M+H]	796.5851	21.25	16.99	14.76	14.32
	PC(16:0_20:4) ;PC(18:1_18:3)	Positive	[M+H]	804.5514	19.88	16.76	15.29	14.94
	PC(16:0_22:6)	Positive	[M+H]	806.5694	18.83			
	PC(18:2_20:4)	Positive	[M+H]	806.5694		15.64		
	PC(18:1/18:1)	Positive	[M+H]	808.5827	20.97	8.11	15.29	15.20
PC(18:1_20:4)	Positive	[M+H]	808.5851	18.14	14.68			
PC(18:0_18:1)	Positive	[M+H]	810.5983	23.47	19.07	17.32	16.88	
PC(16:0_22:4)	Positive	[M+H]	810.6007	20.61	16.49		14.20	

	PC(18:0_20:4)	Positive	[M+H]	810.6007	19.50			
	PC(18:0_20:2)	Positive	[M+H]	814.6320	17.49			
	PC(18:1_22:6)	Positive	[M+H]	832.5851	16.37	12.86		
	PC(18:0_22:6)	Positive	[M+H]	834.6007		15.37		
	PC(18:0_22:4)	Positive	[M+H]	838.6320	17.84			
PC(O/P-) (Akyl/alkenyl ether phosphatidyl choline)	PC(P-32:0);PC(O-32:1)	Positive	[M+H]	718.5745	16.95			
	PC(P-18:0/16:0)	Positive	[M+H]	746.6058	20.26	15.59		
	PC(O-16:0/20:3)	Positive	[M+H]	770.6058	17.69			
	PC(P-18:0/18:1)	Positive	[M+H]	772.6215	15.81			
	PC(O-40:6);PC(P-40:5)	Positive	[M+H]	820.6215	16.70			
	PC(O-18:0/22:5);PC(P-18:0/22:4)	Positive	[M+H]	822.6371		13.96		
PE (Phosphatidyl ethanolamin e)	PE(16:0_18:1)	Positive	[M+H]	718.5381	20.79	16.78		
	PE(18:1_18:2) a	Positive	[M+H]	742.5381	16.87			
	PE(18:1_18:2) b	Positive	[M+H]	742.5381	15.87			
	PE(18:0_18:2)	Positive	[M+H]	744.5538	21.33	17.52		15.35
	PE(18:0_18:1)	Positive	[M+H]	746.5694	22.10	18.04	15.66	15.17
	PE(16:0_22:6)	Positive	[M+H]	764.5225	20.13	16.59		
	PE(18:0_20:5)	Positive	[M+H]	766.5381	18.87	16.23		
	PE(18:1_20:4)	Positive	[M+H]	766.5381	19.86			
SM (Sphingomye lin)	SM(d34:1)	Positive	[M+H]	703.5749	16.43			
	SM(d18:2/18:0)	Positive	[M+H]	729.5905	17.09			

14:0_16:0_16:1)								
TG(14:0_16:0_16:0)	Positive	[M+NH4]	796.7389	17.32	16.74	17.02	17.15	
TG(14:0_16:0_17:1)	Positive	[M+NH4]	808.7389	15.86	15.92	15.86		
TG(14:0_16:0_17:0)	Positive	[M+NH4]	810.7545	16.86	16.98	16.68	16.83	
TG(14:0_16:0_18:2);TG(14:0_16:1_18:1);TG(16:0_16:1_16:1)	Positive	[M+NH4]	820.7389	15.56	15.71	15.45	15.68	
TG(14:0_16:0_18:1);TG(16:0_16:0_16:1)	Positive	[M+NH4]	822.7545	16.39	16.19	16.46	16.22	
TG(48:0)	Positive	[M+NH4]	824.7702	17.47	17.33	17.36	17.62	
TG(15:0_16:0_18:2);TG(15:0_16:1_18:1)	Positive	[M+NH4]	834.7545	15.10	14.66	14.70		
TG(15:0_16:0_18:1);TG(15:0_17:0_17:1)	Positive	[M+NH4]	836.7702	15.54				
TG(49:0)	Positive	[M+NH4]	838.7858	16.07	16.21	16.19	15.88	
TG(14:0_18:3_18:3)	Positive	[M+NH4]	840.7076	17.14				
TG(16:1_16:1_18:3)	Positive	[M+NH4]	842.7232	17.33				
TG(14:0_18:1_18:2);TG(16:1_16:1_18:1)	Positive	[M+NH4]	846.7545	14.82	14.33	13.97		
TG(14:0_18:1_18:1)	Positive	[M+NH4]	848.7702	16.80	16.35		16.49	

	TG(16:0_16:0_18:2)	Positive	[M+NH4]	848.7702	16.80	15.98	16.14	
	TG(16:0_16:0_18:1)	Positive	[M+NH4]	850.7858	17.12	16.18	16.34	16.07
	TG(16:0_16:0_18:0)	Positive	[M+NH4]	852.8015	17.48	17.28	17.24	17.26
	TG(16:0_17:0_18:2)	Positive	[M+NH4]	862.7858	14.96			
	TG(16:0_18:1_18:3);TG(16:0_18:2_18:2)	Positive	[M+NH4]	872.7702	16.12	14.72	15.12	15.22
	TG(16:0_18:1_18:2)	Positive	[M+NH4]	874.7858	17.42	15.50	14.80	15.36
	TG(16:0_18:0_18:2);TG(16:0_18:1_18:1)	Positive	[M+NH4]	876.8015	18.54	16.40	16.31	16.50
	TG(16:0_18:0_18:1)	Positive	[M+NH4]	878.8171	17.19	15.39	15.27	14.55
	TG(16:0_18:0_18:0)	Positive	[M+NH4]	880.8328	16.61	16.30	16.47	16.39
	TG(18:1_18:2_18:2)	Positive	[M+NH4]	898.7858	15.20	14.69	14.58	15.05
	TG(54:4)	Positive	[M+NH4]	900.8015	15.83			
	TG(18:0_18:1_18:2);TG(18:1/18:1/18:1)	Positive	[M+NH4]	902.8171	16.64	15.75	15.49	15.37
	TG(18:0_18:1_18:1)	Positive	[M+NH4]	904.8328	15.78	14.50	13.96	
	TG(18:0/18:0/18:0)	Positive	[M+NH4]	908.8641	14.49	14.87	14.46	14.63

Supplemental Table S11. Enriched structural motifs for both TRAAK and TREK2 with a BEP.

<i>Protein-Lipid Wash Sample</i>	<i>Test performed</i>	<i>Classifier</i>	<i>Count</i>	<i>Library Count</i>	<i>% Present</i>	<i>% Present in Library</i>	<i>p-value</i>	<i>Fold change</i>
TREK2 CV1	Specific chain	(18:1)	13/136	29/623	9.56	4.65	0.0358	2.05
	Specific chain	(16:0_20:4)	4/136	4/623	2.94	0.64	0.0383	4.58
	Main class	PS	6/137	9/582	4.38	1.55	0.0478	2.83
TREK2 CV2	Specific chain	(16:0_20:4)	4/104	4/623	3.85	0.64	0.0175	5.99
	Main class	PS	6/106	9/582	5.66	1.55	0.0179	3.66
	Specific chain	(18:0_20:4)	3/104	3/623	2.88	0.48	0.0411	5.99
TREK2 CV3	Main class	TG	24/71	93/582	33.8	15.98	0.0008	2.12
	Main class	FFA	16/71	59/582	22.54	10.14	0.0047	2.22
	Main class	SM	1/71	61/582	1.41	10.48	0.0090	0.13
	Main class	PC	10/71	164/582	14.08	28.18	0.0103	0.5
	Subclass	PE P-	8/71	22/582	11.27	3.78	0.0107	2.98
	Specific chain	(18:1)	8/61	29/623	13.11	4.65	0.0122	2.82
	Specific chain	(18:0_18:1)	3/61	4/623	4.92	0.64	0.0182	7.66
	Chain characteristics	saturated (SFA)	28/61	194/623	45.9	31.14	0.022	1.47
TREK2 CV4	Main class	FFA	15/66	59/582	22.73	10.14	0.0064	2.24
	Main class	TG	19/66	93/582	28.79	15.98	0.0150	1.80
	Specific chain	(18:1)	7/60	29/623	11.67	4.65	0.0308	2.51
	Chain characteristics	saturated (SFA)	27/60	194/623	45	31.14	0.031	1.45
TRAAK CV1	Main class	PC	17/146	164/582	11.64	28.18	0	0.41
	Main class	TG	49/146	93/582	33.56	15.98	0	2.10
	Main class	SM	1/146	61/582	0.68	10.48	0	0.07
	Main class	FFA	25/146	59/582	17.12	10.14	0.0287	1.69
TRAAK CV2	Main class	TG	42/110	93/582	38.18	15.98	0	2.39
	Main class	PC	13/110	164/582	11.82	28.18	0.0002	0.42
	Chain characteristics	saturated (SFA)	42/90	194/623	46.67	31.14	0.0056	1.50
	Main class	PS	7/110	9/582	6.36		0.0070	4.12

	Sub-class	PE P-	11/110	22/582	10.00	3.78	0.0116	2.65
	Specific chain	16:0_20:4	3/90	4/623	3.33	0.64	0.0466	5.19
TRAAC CV3	Main class	PC	14/119	164/582	11.76	28.18	0.0001	0.42
	Main class	TG	44/119	93/582	36.97	15.98	0	2.31
	Main class	SM	2/119	61/582	1.68	10.48	0.0012	0.16
	Chain characteristics	saturated (SFA)	42/96	194/623	43.75	31.14	0.0191	1.40
	Specific chain	18:0_20:4	3/96	3/623	3.13	0.48	0.0341	6.49
	Sub-class	PE P-	10/119	22/582	8.40	3.78	0.0490	2.22
	TRAAC CV4	Main class	PC	2/105	164/582	1.90	28.18	0
Main class		FFA	40/105	59/582	38.10	10.14	0	3.76
Main class		TG	41/105	93/582	39.05	15.98	0	2.44
Main class		PE	4/105	102/582	3.81	17.53	0.0001	0.22
Main class		SM	2/105	61/582	1.90	10.48	0.0043	0.18
Specific chain		(18:0)	8/70	21/623	11.43	3.37	0.0055	3.39
Chain characteristics		polyunsaturated (PUFA)	15/70	219/623	21.43	35.15	0.0231	0.61
Chain characteristics		saturated (SFA)	31/70	194/623	44.29	31.14	0.0311	1.42

