Supplementary materials

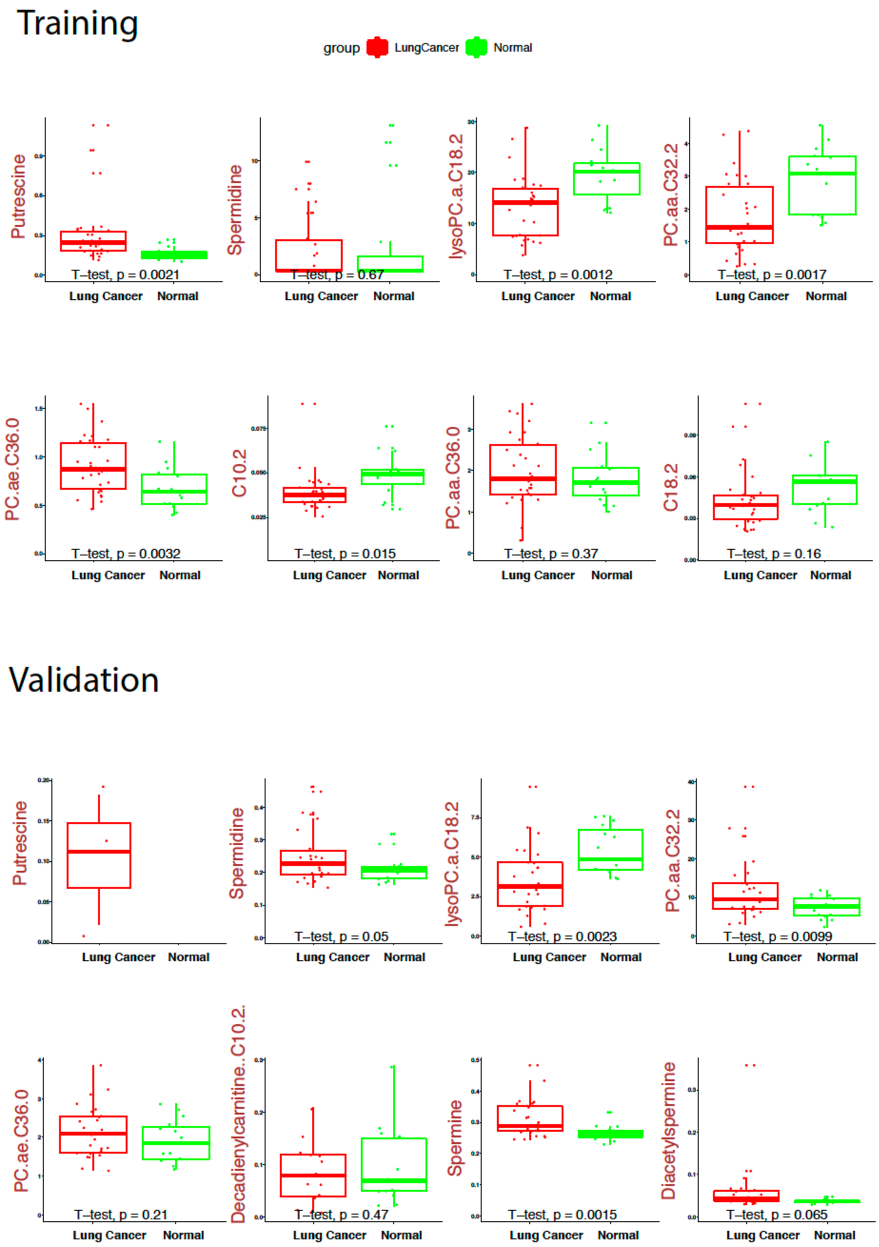

Figure 1. The full range of the Box Plots.

Table S1

Table 1A: Training cohort

Lung cancer subtypes						Age (yr)
	Adenocarcinoma (n)	Squamous (n)	Non Squamous (n)	Small cell (n)	Metastasis (n)	Mean±SD
Female (n=18)	13	5	-	-	-	47±2
Male (n=13)	9	3	-	1	-	56±2
Total (n= 31)	22	8	-	1	-	52±2

** Majority of patient at advanced stage 3+

Table 1B: Validation cohort

Lung cancer subtypes						Age (yr)
	Adenocarcinoma (n)	Squamous (n)	Non Squamous (n)	Small cell (n)	Metastasis (n)	Mean±SD
Female (n=9)	2	2	1	2	2	54±3
Male (n=17)	4	5	5	3	-	56±3
Total (n=26)	6	7	6	5	2	56±2

** Majority of patient at advanced stage 3+

Table 1C: Summary table of normal vs Lung cancer

	Tranining			Validation		
	Lung Cancer (n)	Normal (n)	Pvalue	Lung Cancer (n)	Normal (n)	Pvalue
Samples	31	15		26	15	
Age:	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Mean (Range) (yr)	50.7 (27 - 75)	43.7 (27 -56)	0.06	55.7 (27 - 70)	43.7 (27 -56)	0.000213
Sex:						
Male	13	6	0.75	17	6	0.12
Female	18	9		9	9	

Table S2

Table 2: Statistical summary of samples and metabolite measures

Targeted metabolites	Metabolites Classification	Patient Classification	Cohort	Number of samples	Number of missing samples	min value of metabolite	max value of metabolite	Median	Mean
Valine	**Amino Acids and Biogenic Amines**	Normal	Training	15	0	198	376	263	267.0667
Putrescine	**Polyamine Metabolites**	Normal	Training	15	0	0.104	0.269	0.154	0.1637
Methionine	**Polyamine Metabolites**	Normal	Training	15	0	17.7	35.9	25.8	26.5133
Arginine	**Polyamine Metabolites**	Normal	Training	15	0	72.4	234	120	137.3933
Ornithine	**Polyamine Metabolites**	Normal	Training	15	0	56.6	142	72.5	79.14
Spermidine	**Polyamine Metabolites**	Normal	Training	15	0	0.256	13.1	0.335	2.7091
C10.2	**Acylcarnitines**	Normal	Training	15	0	0.0297	0.076	0.0493	0.0489
C18.2	**Acylcarnitines**	Normal	Training	15	0	0.0238	0.0853	0.0567	0.0522
lysoPC.a.C18.2	**Glycerophospholipids**	Normal	Training	15	0	12.1476	29.259	20.1631	19.521
PC.aa.C32.2	**Glycerophospholipids**	Normal	Training	15	0	1.5099	4.5478	3.0779	2.9107
PC.aa.C36.0	**Glycerophospholipids**	Normal	Training	15	0	1.008	3.1557	1.7134	1.803
PC.ae.C36.0	**Glycerophospholipids**	Normal	Training	15	0	0.4003	1.157	0.6427	0.6749
Valine	**Amino Acids and Biogenic Amines**	Lung Cancer	Training	31	0	135	369	193	208
Putrescine	**Polyamine Metabolites**	Lung Cancer	Training	31	0	0.115	1.13	0.2475	0.3099
Methionine	**Polyamine Metabolites**	Lung Cancer	Training	31	0	11.6	63.6	22.25	24.0533
Arginine	**Polyamine Metabolites**	Lung Cancer	Training	31	0	37.7	262	95.6	112.2867
Ornithine	**Polyamine Metabolites**	Lung Cancer	Training	31	0	47.1	167	69.35	76.13
Spermidine	**Polyamine Metabolites**	Lung Cancer	Training	31	0	0.333	9.9	0.335	2.14
C10.2	**Acylcarnitines**	Lung Cancer	Training	31	0	0.0255	0.0889	0.0376	0.039
C18.2	**Acylcarnitines**	Lung Cancer	Training	31	0	0.0208	0.1127	0.0398	0.0438
lysoPC.a.C18.2	**Glycerophospholipids**	Lung Cancer	Training	31	0	3.815	28.7725	14.1162	13.3528
PC.aa.C32.2	**Glycerophospholipids**	Lung Cancer	Training	31	0	0.2588	4.3734	1.4442	1.78149
PC.aa.C36.0	**Glycerophospholipids**	Lung Cancer	Training	31	0	0.3143	3.6154	1.8023	2.0029
PC.ae.C36.0	**Glycerophospholipids**	Lung Cancer	Training	31	0	0.4613	1.5473	0.8711	0.9148
Valine	**Amino Acids and Biogenic Amines**	Normal	Validation	15	0	233	442	280	294.5333
Arginine	**Polyamine Metabolites**	Normal	Validation	15	0	75.1	237	116	139.88
Ornithine	**Polyamine Metabolites**	Normal	Validation	15	0	27	90	47.3	50.7533
Methionine	**Polyamine Metabolites**	Normal	Validation	15	0	27.5	63.1	38.4	39.02
Spermidine	**Polyamine Metabolites**	Normal	Validation	15	0	0.164	0.319	0.208	0.2118
Spermine	**Polyamine Metabolites**	Normal	Validation	15	0	0.23	0.332	0.263	0.2655
Diacetylspermine	**Acylcarnitines**	Normal	Validation	15	0	0.0287	0.0473	0.0364	0.0369
Decadienylcarnitine (C10.2)	**Acylcarnitines**	Normal	Validation	13	2	0.02	0.29	0.07	0.1008
PC.aa.C32.2	**Glycerophospholipids**	Normal	Validation	15	0	2.37	11.89	7.69	7.3293
PC.ae.C36.0	**Glycerophospholipids**	Normal	Validation	15	0	1.17	2.86	1.85	1.9033
lysoPC.a.C18.2	**Glycerophospholipids**	Normal	Validation	15	0	3.63	7.59	4.87	5.4073
MTA	**Polyamine Metabolites**	Lung Cancer	Validation	9	17	0.0041	0.267	0.0945	0.1067
Valine	**Amino Acids and Biogenic Amines**	Lung Cancer	Validation	26	0	120	316	192	204.6154
Arginine	**Polyamine Metabolites**	Lung Cancer	Validation	26	0	51.6	252	89.8	116.8347
Ornithine	**Polyamine Metabolites**	Lung Cancer	Validation	26	0	17.4	93.7	47.15	45.9423
Methionine	**Polyamine Metabolites**	Lung Cancer	Validation	26	0	14.5	50.8	31.8	31.4423
Putrescine	**Polyamine Metabolites**	Lung Cancer	Validation	3	23	0.0219	0.182	0.112	0.1053
Spermidine	**Polyamine Metabolites**	Lung Cancer	Validation	26	0	0.154	0.464	0.2285	0.2531
Spermine	**Polyamine Metabolites**	Lung Cancer	Validation	26	0	0.245	0.482	0.2885	0.3108
Diacetylspermine	**Acylcarnitines**	Lung Cancer	Validation	26	0	0.0297	0.358	0.0423	0.0611
Decadienylcarnitine (C10.2)	**Acylcarnitines**	Lung Cancer	Validation	15	11	0.01	0.21	0.08	0.0813
PC.aa.C32.2	**Glycerophospholipids**	Lung Cancer	Validation	26	0	3.08	38.67	9.48	12.1392
PC.ae.C36.0	**Glycerophospholipids**	Lung Cancer	Validation	26	0	1.14	3.86	2.095	2.1485
lysoPC.a.C18.2	**Glycerophospholipids**	Lung Cancer	Validation	26	0	0.6	9.44	3.13	3.5692

Table S3

Table 3A: Univariate Summary Measure of each Metabolite

	Training			Validation		
	AUC	**P value**	**FC**	**AUC**	**P value**	**FC**
Arginine	6.61E-01	1.30E-01	-3.25E-01	6.64E-01	1.33E-01	-3.26E-01
C10.2	7.71E-01	9.44E-03	-1.28E-01	NA	NA	NA
C18.2	6.73E-01	1.85E-01	-1.11E-01	NA	NA	NA
Diacetylspermi	NA	NA	NA	7.60E-01	2.59E-02	2.12E-01
lysoPC.a.C18.2	7.73E-01	1.86E-03	-6.60E-01	7.65E-01	3.16E-03	-8.15E-01
Methionine	6.67E-01	4.01E-01	-2.19E-01	6.85E-01	2.08E-02	-3.44E-01
Ornithine	5.46E-01	6.97E-01	-6.91E-02	5.69E-01	3.21E-01	-1.70E-01
PC.aa.C32.2	7.96E-01	2.12E-03	-9.63E-01	6.94E-01	2.75E-02	5.91E-01
PC.aa.C36.0	5.71E-01	4.13E-01	7.44E-02	NA	NA	NA
PC.ae.C36.0	7.51E-01	6.69E-03	4.28E-01	6.12E-01	2.53E-01	1.64E-01
Putrescine	8.33E-01	2.03E-02	6.64E-01	NA	NA	NA
Spermidine	5.89E-01	6.12E-01	2.46E-01	6.29E-01	1.11E-01	1.90E-01
Spermine	NA	NA	NA	7.67E-01	5.20E-03	1.95E-01
Valine	8.04E-01	2.19E-03	-3.83E-01	9.09E-01	2.58E-06	-5.33E-01

AUC – Area Under the Curve; FC – Fold Change, NA - Not available

Table 3B: t-tests for key Metabolites using training data (A) and validation data (B)

Training Data A				
Metabolites	**t-statistic**	**P value**	**-log10 (p)**	**FDR**
Putrescine	3.54E+00	9.88E-04	3.01E+00	6.44E-03
Valine	-3.51E+00	1.07E-03	2.97E+00	6.44E-03
lysoPC.a.C18.2	3.30E+00	1.97E-03	2.70E+00	7.89E-03
PC.aa.C32.2	-3.18E+00	2.72E-03	2.57E+00	8.15E-03
PC.ae.C36.0	3.02E+00	4.27E-03	2.37E+00	9.32E-03
C10.2	-2.99E+00	4.66E-03	2.33E+00	9.32E-03
Validation Data B				
Metabolites	**t-statistic**	**P value**	**-log10 (p)**	**FDR**
Valine	-5.50E+00	2.58E-06	5.59E+00	2.58E-05
lysoPC.a.C18.2	-3.15E+00	3.16E-03	2.50E+00	1.58E-02
Spermine	2.96E+00	5.20E-03	2.28E+00	1.73E-02
Methionine	-2.41E+00	2.08E-02	1.68E+00	4.59E-02
Diacetylspermine	2.32E+00	2.59E-02	1.59E+00	4.59E-02
PC aa. C32:2	2.29E+00	2.75E-02	1.56E+00	4.59E-02

-log10 (p), FDR False Discovery Rate; t-statistic,

Table 3C: Training data, generalized linear regression multivariate model statistics – key metabolites

	Estimate	S.E.	P value
(Intercept)	0.9438	0.2969	0.0029
Valine	0.0012	0.0011	0.2724
Putrescine	-0.6203	0.2991	0.0447
PC.aa.C32.2	0.1294	0.0563	0.027
PC.aa.C36.0	-0.2273	0.08	0.0071
C10.2	10.3848	5.2603	0.0555

Table 3D: Validation data, generalized linear regression multivariate model statistics – key metabolites

	Estimate	S. E.	P Value
(Intercept)	1.3407	0.4139	0.0025
Valine	0.0051	0.0009	1.84E-06
Spermine	-2.8954	1.0274	0.0077
Ornithine	-0.007	0.0036	0.0633

S.E., Standard Error