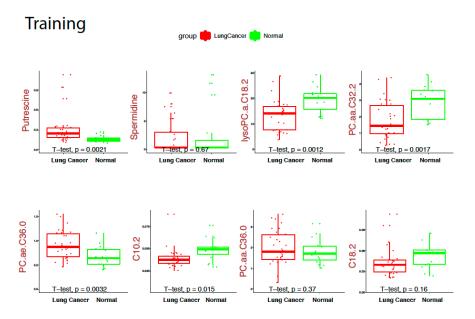
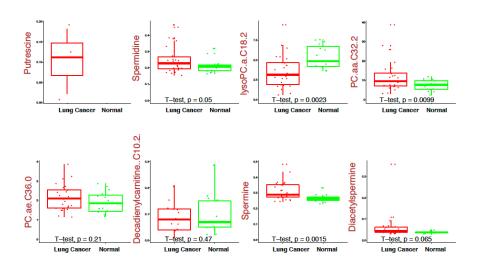
Supplementary materials



Validation



 $\textbf{Figure 1.} \ \textbf{The full range of the Box Plots}.$

Table S1

Table 1A: Training cohort

	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

	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

Turgered metabolites				Table 2: Statistical summ	ary of samples and metabo	lite measures				
Polyanie Metabolites	Targeted metabolites	Metabolites Classification	Patient Classification	Cohort	Number of samples	Number of missing samples	min value of metabolite	max value of metabolite	Median	Mean
Polyanie Metabolites	Valine	Amino Acids and Biogenic Amines	Normal	Training	15	0	198	376	263	267 0667
Molsteine						-				
Applies				-						
Description		-								
Spendine						*				
C12										
C12 Aysternitose Normal Transing 15 0 0.0238 0.0837 0.0522						•				
PostCaCR12		·								
PC ac C322 Grycerophospholipids Normal Training 15 0 1.5999 4.5478 3.9779 2.9107						0				
PC ac (3.6) Cycerophospholipids Nornal Training 15 0 1.001 3.1577 1.7144 1.80				0						
PC.as.C3A0										
Value										
Polyamine Metabolites Lang Caneer Training 31 0 0.115 1.13 0.2475 0.3999				0						
Methionine										
Anymine								-11		
Spermidine				_						
Spemidine										
CHO.2										
C18.2		-					111111			
hysoPC AC 18.2 Glycerophspholipids Lang Cancer Training 31 0 0.288 4.3774 1.1462 13.3284 PC AC 32.2 Glycerophspholipids Lang Cancer Training 31 0 0.2888 4.3774 1.442 1.78149 PC AC 35.0 Glycerophspholipids Lang Cancer Training 31 0 0.3143 3.6154 1.8023 2.0029 PC AC 35.0 Glycerophspholipids Lang Cancer Training 31 0 0.4613 1.5473 0.8711 0.9811 Valine Amino Acids and Biogenic Amines Normal Validation 15 0 2.33 442 2.90 2.945,333 Agrinic Polymnine Metabolite Normal Validation 15 0 75.1 2.37 116 1.988 Gundhine Polymnine Metabolite Normal Validation 15 0 2.7 99 47.3 59.7353 Methienine Polymnine Metabolite Normal Validation 15 0 2.7 99 47.3 59.7353 Methienine Polymnine Metabolite Normal Validation 15 0 2.7 59 47.3 59.7353 Spermine Polymnine Metabolite Normal Validation 15 0 2.7 59 47.3 59.7353 Spermine Polymnine Metabolite Normal Validation 15 0 0.164 0.319 0.208 0.2118 Spermine Polymnine Metabolites Normal Validation 15 0 0.23 0.333 0.256 0.208 0.2118 Spermine Acylearnine Acylearnine Normal Validation 15 0 0.0237 0.0343 0.0265 Decadesylvamine Acylearnine Normal Validation 15 0 0.0237 0.0473 0.0564 0.0269 PC ac 52.2 Glycerophspholipids Normal Validation 15 0 0.237 11.49 7.99 7.2373 PC ac C50.0 Glycerophspholipids Normal Validation 15 0 0.237 11.49 7.99 7.2373 PC ac C50.0 Glycerophspholipids Normal Validation 15 0 0.257 11.49 7.99 7.2373 PC ac C50.0 Glycerophspholipids Normal Validation 15 0 0.257 11.49 7.99 7.2373 PC ac C50.0 Glycerophspholipids Normal Validation 15 0 0.257 0.054 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269 0.0269										
PCast G32.2 Glycerophospholipids Lung Cancer Training 31 0 0.2588 4.3734 1.4442 1.78149 PCast G36.0 Glycerophospholipids Lung Cancer Training 31 0 0.3143 3.6154 1.8023 2.0092 PCast G36.0 Glycerophospholipids Lung Cancer Training 31 0 0.4613 1.5473 0.8711 0.9188 Valine Amino Acids and Biogenic Amines Normal Validation 15 0 2.233 442 229 294-5333 Anginic Polyamine Metabolites Normal Validation 15 0 7.51 2.27 111.6 139.88 Ontabline Polyamine Metabolites Normal Validation 15 0 275 631 38.4 39.02 Spermidine Polyamine Metabolites Normal Validation 15 0 275 631 38.4 39.02 Spermidine Polyamine Metabolites Normal Validation 15 0 0.275 631 38.4 39.02 Spermidine Polyamine Metabolites Normal Validation 15 0 0.275 631 38.4 39.02 Spermidine Polyamine Metabolites Normal Validation 15 0 0.664 0.319 0.208 0.2118 Spermidine Polyamine Metabolites Normal Validation 15 0 0.623 0.332 0.265 Diaccyl-pleprimire Acyl-carnitines Normal Validation 15 0 0.0237 0.0473 0.0364 0.0369 Poladine-pleprimire Acyl-carnitines Normal Validation 15 0 0.0227 0.0473 0.0364 0.0369 PCast G32.2 Glycerophospholipids Normal Validation 15 0 0.277 11.89 7.69 7.3293 PCast G36.0 Glycerophospholipids Normal Validation 15 0 0.277 11.89 7.69 7.3293 PCast G36.0 Glycerophospholipids Normal Validation 15 0 0.3.63 7.79 4.87 5.4073 MTA Polyamine Metabolites Lung Cancer Validation 9 17 0.0041 0.267 0.0945 0.0167 Valine Amino Acids and Biogenic Amines Lung Cancer Validation 26 0 0.174 9.97 4.715 4.59423 Platesties Polyamine Metabolites Lung Cancer Validation 26 0 0.154 0.0464 0.2285 0.2531 Spermidine Polyamine Metabolites Lung Cancer Validation 26 0 0.						-	******			
PCas C36.0 Glycerophospholipids Lang Cancer Training 31 0 0.3143 3.6154 1.8023 2.0079										
PCac C5.0 Clycerophospholipids Lang Cancer Training 31 0 0.4613 1.5473 0.5711 0.948						0				
Valine										
Arginine Polyamine Metabolites Normal Validation 15 0 75.1 237 116 139.88						0				
Orathine										
Methionine Polyamine Metabolites Normal Validation 15 0 27.5 63.1 38.4 39.02	-	-								
Spermitine Polyamine Metabolites Normal Validation 15 0 0.164 0.319 0.208 0.2118										
Spemine Polyamine Metabolites Normal Validation 15 0 0.23 0.332 0.263 0.2655										
Diacetylspermine Acylearnitines Normal Validation 15 0 0.0287 0.0473 0.0364 0.0369										
Decadienylearnitine (Cl0.2) Acylearnitines Normal Validation 13 2 0.02 0.29 0.07 0.1008	<u> </u>	-								
PC.aa.C32.2 Glycerophospholipids Normal Validation 15 0 2.37 11.89 7.69 7.3293 PC.ac.C36.0 Glycerophospholipids Normal Validation 15 0 1.17 2.86 1.85 1.9033 JysoPC.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 Anginine Polyamine Metabolites Lung Cancer Validation 26 0 51.6 252 89.8 118,8347 Omithine Polyamine Metabolites Lung Cancer Validation 26 0 17.4 93.7 47.15 45.9423 Putrescine Polyamine Metabolites Lung Cancer Validation 26 </td <td></td> <td>-</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>		-								
PCae C36.0 Glycerophospholipids Normal Validation 15 0 1.17 2.86 1.85 1.9033	, , , , , , , , , , , , , , , , , , , ,									
Normal Validation 15 0 3.63 7.59 4.87 5.4073						0				
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 Anginine Polyamine Metabolites Lung Cancer Validation 26 0 51.6 252 89.8 118,8347 Omthine Polyamine Metabolites Lung Cancer Validation 26 0 17.4 93.7 47.15 45.9423 Methionine Polyamine Metabolites Lung Cancer Validation 26 0 17.4 93.7 47.15 45.9423 Putrescine Polyamine Metabolites Lung Cancer Validation 3 23 0.0219 0.182 0.112 0.1053 Spermidine Polyamine Metabolites Lung Cancer Validation 26 0 0.134 0.464 0.2285 0.2318 Spermine Polyamine Metabolites Lung Cancer Validation <td></td>										
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 Omithine 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 31.423 Putrescine Polyamine Metabolites Lung Cancer Validation 3 23 0.0219 0.182 0.112 0.053 Spermide Polyamine Metabolites Lung Cancer Validation 26 0 0.154 0.464 0.2285 0.2511 Spermine Polyamine Metabolites Lung Cancer Validation 26 0 0.245 0.482 0.2885 0.3108 Diacetylspermine Acylearnitines Lung Cancer Validation <td></td> <td></td> <td>Lung Cancer</td> <td>Validation</td> <td>9</td> <td>17</td> <td>0.0041</td> <td>0.267</td> <td>0.0945</td> <td>0.1067</td>			Lung Cancer	Validation	9	17	0.0041	0.267	0.0945	0.1067
Arginine Polyamine Metabolites Lung Cancer Validation 26 0 51.6 252 89.8 116.8347 Omthine 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 31.423 Putrescine Polyamine Metabolites Lung Cancer Validation 3 23 0.0219 0.182 0.112 0.1053 Spermine Polyamine Metabolites Lung Cancer Validation 26 0 0.154 0.464 0.2285 0.2531 Spermine 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 Acylcaraitines Lung Cancer Validation	Valine		Lung Cancer	Validation	26	0	120	316	192	204.6154
Methionine Polyamine Metabolites Lung Cancer Validation 26 0 14.5 50.8 31.8 31.4423	Arginine	Polyamine Metabolites	Lung Cancer	Validation	26	0	51,6	252	89,8	116,8347
Putrescine Polyamine Metabolites Lung Cancer Validation 3 23 0.0219 0.182 0.112 0.1053	Ornithine	Polyamine Metabolites	Lung Cancer	Validation	26	0	17.4	93.7	47.15	45.9423
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 Diacctylspermine Acylcarnitines Lung Cancer Validation 26 0 0.0297 0.358 0.0423 0.0611 Decadionylcarnitine (C10.2) Acylcarnitines Lung Cancer Validation 15 11 0.01 0.21 0.08 0.0813 PC.ac C32.2 Glycerophospholipids Lung Cancer Validation 26 0 3.08 38.67 9.48 12.1992 PC.ac C36.0 Glycerophospholipids Lung Cancer Validation 26 0 1.14 3.86 2.095 2.1485	Methionine	Polyamine Metabolites	Lung Cancer	Validation	26	0	14,5	50,8	31,8	31,4423
Spermine Polyamine Metabolites Lung Cancer Validation 26 0 0.245 0.482 0.2885 0.3108	Putrescine	Polyamine Metabolites	Lung Cancer	Validation	3	23	0.0219	0.182	0.112	0.1053
Diacetylspermine Acylearnitines Lung Cancer Validation 26 0 0.0297 0.358 0.0423 0.0611	Spermidine	Polyamine Metabolites	Lung Cancer	Validation	26	0	0.154	0,464	0,2285	0,2531
Decedient/learnitine (Cl0.2) Aeylearnities Lung Cancer Validation 15 11 0.01 0.21 0.08 0.0813 PC ac C32.2 Glycerophospholipids Lung Cancer Validation 26 0 3.08 38.67 9.48 12.1392 PC ac C36.0 Glycerophospholipids Lung Cancer Validation 26 0 1.14 3.86 2.095 2.1485	Spermine	Polyamine Metabolites	Lung Cancer	Validation	26	0	0.245	0.482	0.2885	0.3108
PC ac C32.2 Glycerophospholipids Lung Cancer Validation 26 0 3.08 38.67 9.48 12.1392 PC ac C36.0 Glycerophospholipids Lung Cancer Validation 26 0 1.14 3.86 2.095 2.1485	Diacetylspermine	Acylcarnitines	Lung Cancer	Validation	26	0	0.0297	0.358	0.0423	0.0611
PC ac C32.2 Glycerophospholipids Lung Cancer Validation 26 0 3.08 38.67 9.48 12.1392 PC ac C36.0 Glycerophospholipids Lung Cancer Validation 26 0 1.14 3.86 2.095 2.1485	Decadienylearnitine (C10.2)	Acylcarnitines	Lung Cancer	Validation	15	11	0,01	0,21	0,08	0,0813
PC.ac.C36.0 Glycerophospholipids Lung Cancer Validation 26 0 1.14 3.86 2.095 2.1485			Lung Cancer	Validation	26	0	3.08	38.67	9.48	12.1392
VsoPC a C182 Giverantes platinids Lune Cancer Validation 26 0 0.6 9.44 3.13 3.5602	PC.ac.C36,0		Lung Cancer	Validation	26	0	1.14	3.86	2,095	2,1485
1,000 to the color 0.00 7.77 3.10 3.10 3.10 3.10 1.77 3.10 3.	lysoPC.a.C18.2	Glycerophospholipids	Lung Cancer	Validation	26	0	0.6	9.44	3.13	3.5692

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.ac.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
Diacetylsperm ine	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