

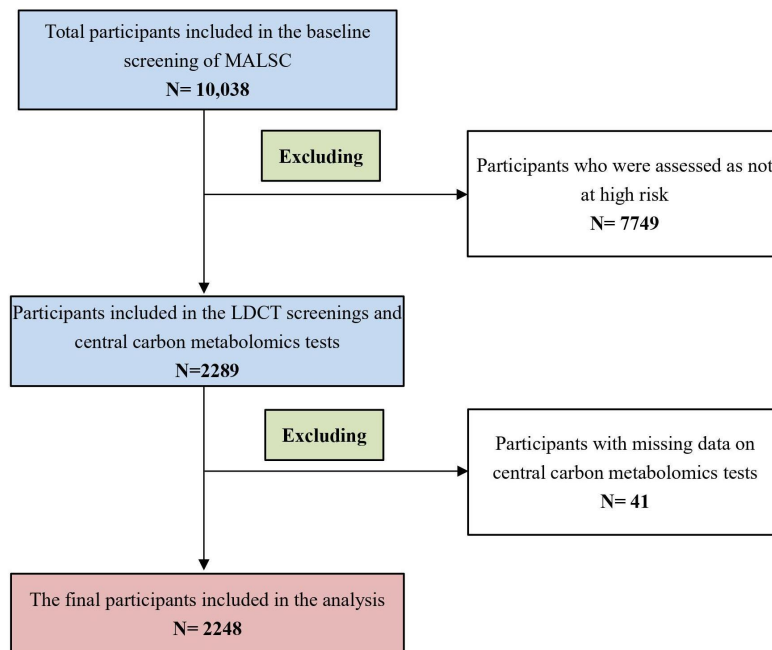


Fig. S1. Flow chart for the exclusion and inclusion of research participants.

Table S1 Distribution of basic clinical indicators in different PN groups

	Normal(n=1427)	Negative(n=537)	Positive (n=284)
RBC($10^{12}/L$, mean $\pm$ SD)	4.83 $\pm$ 0.5	4.85 $\pm$ 0.5	4.81 $\pm$ 0.4
WBC($10^9/L$)	6.51(5.50,7.60)	6.60(5.64,7.57)	6.70(5.72,7.67)
Hemoglobin(g/L)	146.00(136.00,156.00)	146.00(136.00,156.00)	145.00(137.00,154.00)
Average hemoglobin concentration(g/L)	319.00(313.00,324.00)	319.00(313.00,324.00)	319.00(314.00,325.00)
Platelet($10^9/L$)	180.00(147.00,214.00)	182.00(143.25,220.00)	183.00(146.00,215.00)
Platelet volume	0.18(0.15,0.20)	0.18(0.15,0.21)	0.18(0.16,0.21)
NEUT($10^9/L$)	3.69(3.02,4.46)	3.74(3.10,4.45)	3.82(3.12,4.66)
MNC($10^9/L$)	0.40(0.30,0.46)	0.40(0.30,0.50)	0.40(0.30,0.50)
Lcteric,n(%)			
-	1220(63.6)	454(23.7)	243(12.7)
+	207(62.7)	83(25.2)	40(12.1)
++	0(0.0)	0(0.0)	1(100.0)
Basophil count($10^9/L$)	0.30(0.20,0.40)	0.30(0.20,0.48)	0.30(0.20,0.50)
Eosinophil count($10^9/L$)	0.14(0.09,0.22)	0.14(0.09,0.22)	0.15(0.10,0.26)
Lymphocyte count($10^9/L$)	1.96(1.60,2.40)	1.97(1.60,2.40)	2.00(1.60,2.40)
Platelet distribution width(%)	63.30(58.00,68.43)	63.40(57.90,68.38)	64.55(58.10,69.20)
Lipoblood index,n(%)			
-	1371(63.3)	519(24.0)	275(12.7)
+	45(65.2)	15(21.7)	9(13.0)
++	7(77.8)	2(22.2)	0(0.0)
+++	3(75.0)	1(25.0)	0(0.0)
++++	1(100.0)	1(100.0)	0(0.0)
Mean platelet volume(fL)	9.70(8.78,10.90)	9.70(8.80,10.90)	9.80(8.90,11.28)
Average hemoglobin volume(pg)	30.30(29.30,31.20)	30.20(29.33,31.20)	30.20(29.40,31.10)
Mean corpuscular volume(fL)	94.70(91.90,97.50)	94.70(91.90,97.50)	94.50(92.00,97.50)
Hemolytic index,n(%)			
-	1417(63.6)	531(23.8)	280(12.6)
+	9(50.0)	5(27.8)	4(22.2)
++	0(0.0)	1(100.0)	0(0.0)
+++	1(100.0)	0(0.0)	0(0.0)
Neutrophil ratio(%, mean $\pm$ SD)	57.5 $\pm$ 8.0	57.9 $\pm$ 7.9	58.0 $\pm$ 8.0
Lymphocyte ratio(%, mean $\pm$ SD)	30.9 $\pm$ 7.5	30.6 $\pm$ 7.1	30.2 $\pm$ 7.3
Hematokrit(L/L)	0.46(0.43,0.49)	0.46(0.43,0.48)	0.45(0.43,0.48)
Basophil ratio(%)	0.50(0.40,0.60)	0.50(0.40,0.60)	0.50(0.40,0.70)
Eosinophilic ratio(%)	2.20(1.40,3.50)	2.20(1.40,3.50)	2.30(1.50,3.60)
Monocyte ratio(%)	5.60(4.70,6.60)	5.60(4.70,6.60)	5.60(4.80,6.70)
HDL(mmol/L)	1.34(1.14,1.58)	1.34(1.14,1.58)	1.30(1.11,1.51)
LDL(mmol/L)	2.84(2.34,3.41)	2.84(2.34,3.41)	2.79(2.27,3.41)
Total cholesterol(mmol/L)*	4.60(4.03,5.19)	4.60(4.03,5.19)	4.51(3.81,5.12)
Triglyceride(mmol/L)	1.47(1.06,2.10)	1.46(1.06,2.09)	1.43(1.02,1.97)
Blood glucose(mmol/L)	5.06(4.63,5.77)	5.06(4.63,5.77)	5.04(4.64,5.91)

Table S2 Distribution of plasma central carbon metabolites in different PNs groups (ng/mL)

	Normal(n=1427)	Negative(n=537)	Positive (n=284)	P-value*
2-Ketoglutaric acid	2187.5(1514.0,3570.4)	2199.6(1581.6,3627.4)	2520.3(1792.5,4700.6)	<0.001
2-Oxadipic acid	112.7(107.9,120.3)	112.4(106.9,120.8)	75.8(64.8,113.4)	<0.001
3-Hydroxybutyric acid	8090.7(4964.1,17194.6)	8830.1(5625.0,16705.0)	10833.3(5772.8,26674.2)	<0.001
Gluconic acid	978.1 (541.0,1397.6)	1032.7 (538.3,1497.4)	1093.0(773.5,1747.4)	<0.001
Phosphoenolpyruvic acid	141.8 (131.6,174.1)	143.4 (131.3,176.7)	175.6 (133.1,189.9)	<0.001
Fumaric acid	76.1(52.8,124.1)	82.0(53.9,125.9)	62.5 (51.3,123.2)	0.096
Glyceric acid	837.6 (627.3,1206.1)	860.2 (649.0,1192.0)	944.9(649.3,1247.1)	<0.001
Succinic acid	1081.2(828.6,1436.8)	1137.9(846.7,1508.2)	1444.2(914.1,1671.4)	<0.001
Hippuric acid	438.2(255.6,1244.9)	561.7(282.8,1656.2)	2353.0(334.7,3027.2)	<0.001
Homogentisic acid	19.8 (9.6,20.1)	19.7 (7.5,20.1)	4.2(3.4,9.1)	<0.001
Citric acid	15918.1(11645.3,19924.2)	16296.0(12481.5,20110.2)	20346.3 (16013.5,25906.8)	<0.001
Malic acid	781.0 (593.7,1099.0)	817.5 (621.4,1140.1)	1016.7 (762.6,1455.0)	<0.001
Glucaric acid	64.0(47.7,87.7)	64.3(46.7,91.1)	57.5(37.2,137.3)	0.215
Orotic acid	99.9(82.8,112.4)	99.7(82.1,113.3)	64.3(43.4,113.3)	<0.001
L-Lactic acid	348655.4(259263.6,654447.3)	382600.2(271296.0,635277.3)	493482.0 (362988.5,909554.6)	<0.001
Maleic acid	85.3(58.1,130.1)	91.7(59.9,139.4)	80.9(43.5,132.1)	0.011
cis-Aconite acid	350.9(250.0,470.5)	360.8(249.4,490.8)	469.5(330.7,720.3)	<0.001
Isocitric acid	3516.0(1981.5,4837.2)	3588.2(2072.5,5150.7)	4501.6(2801.4,6560.7)	<0.001

* P-value is derived from the Kruskal-Wallis H test.

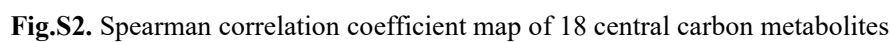


Fig.S2. Spearman correlation coefficient map of 18 central carbon metabolites

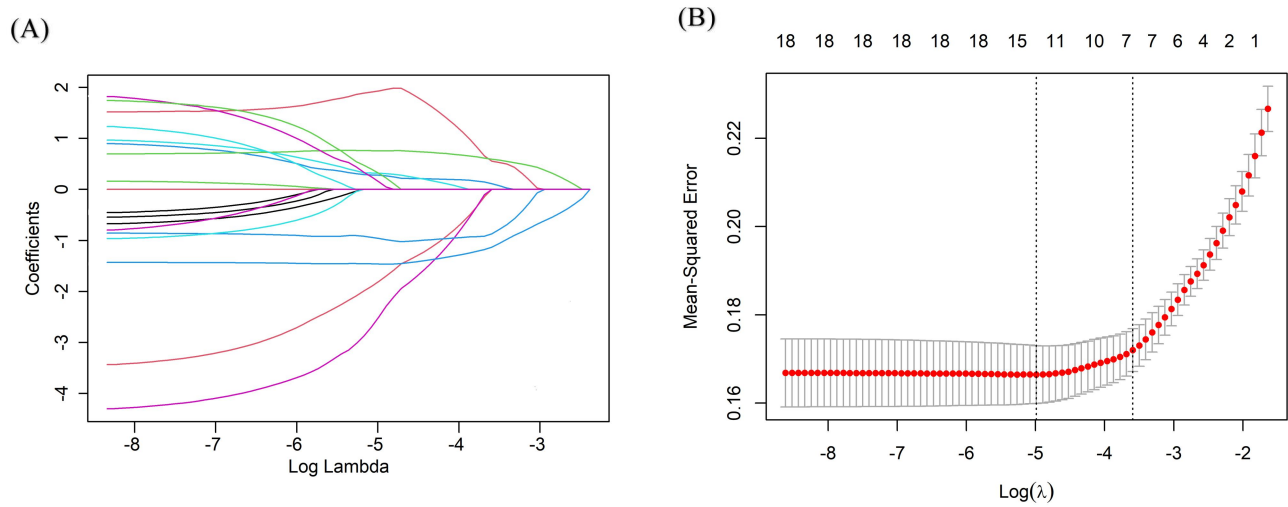


Fig.S3. LASSO regression selects metabolites of model PPNs risk prediction model in high-risk lung cancer population. (A) The change trajectory of each variable coefficient (λ). (B) Cross-validation plot for the penalty term

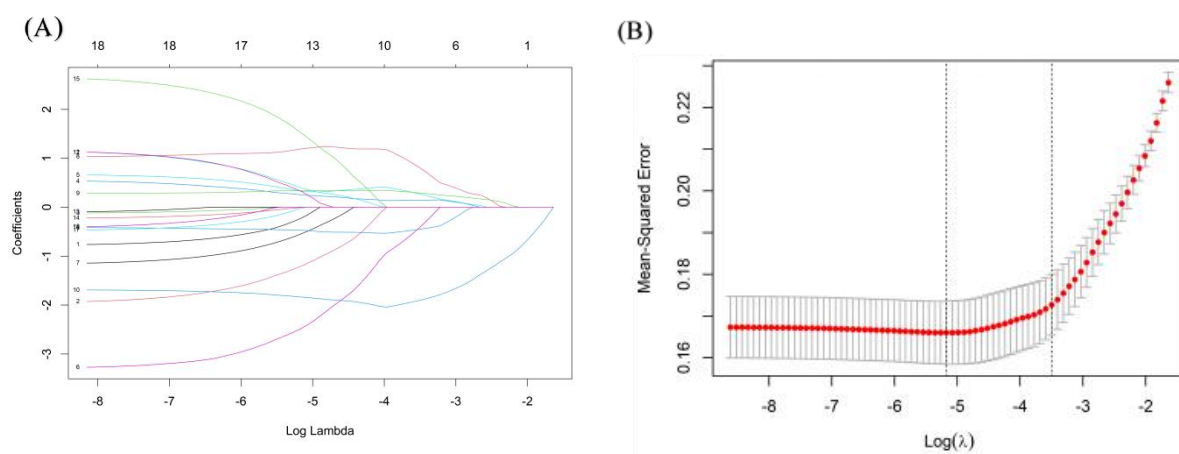


Fig.S4. LASSO regression selects metabolites of PPNs versus NPNs. (A) The change trajectory of each variable coefficient (λ). (B) Cross-validation plot for the penalty term

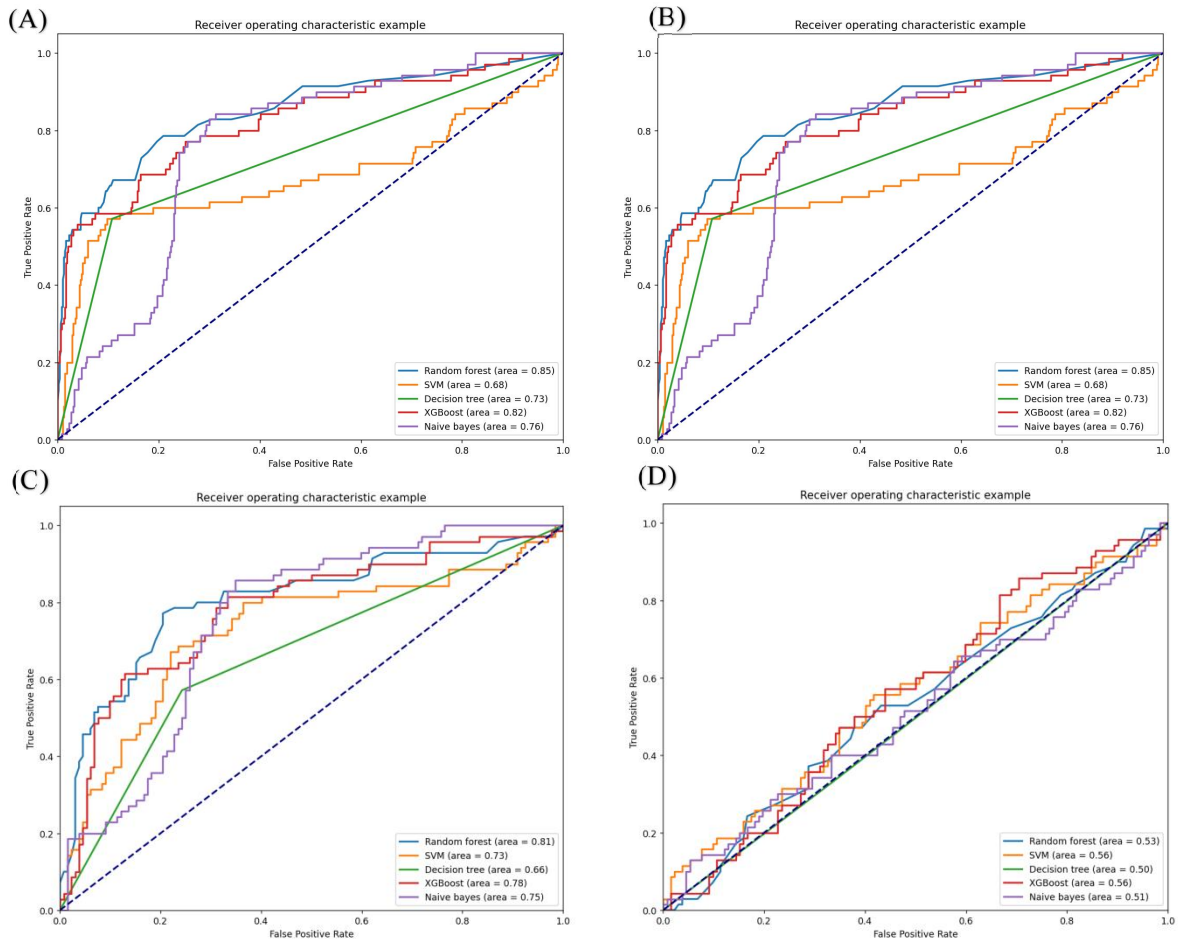


Fig. S5. ROC curves of prediction models in different data sets. (A) PPNs risk prediction model in high-risk lung cancer population (metabolite-only) (B) PPNs risk prediction model in high-risk lung cancer population (demographic characteristics and clinical general detection indicators) (C) PPNs versus NPNs (metabolite-only) (D) PPNs versus NPNs (demographic characteristics and clinical general detection indicators). XGBoost: Extreme Gradient Boosting; SVM: support vector machine