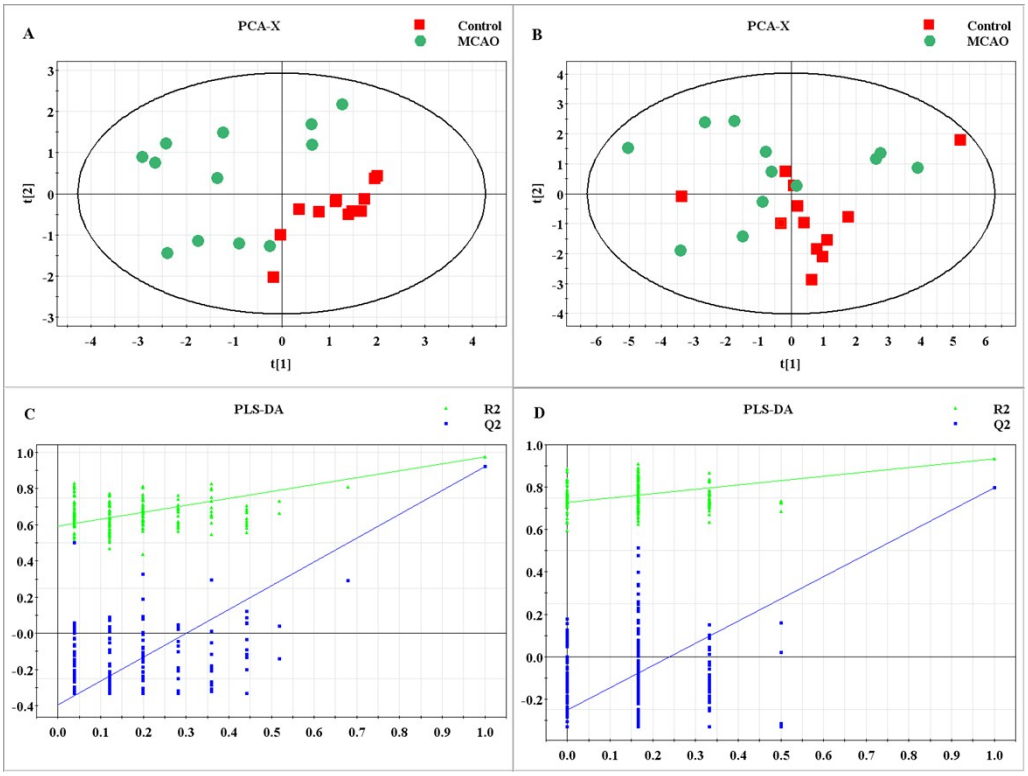

Figure S1 Plots of multivariate statistical analysis of the experimental group in ESI positive and negative ion mode **(A)** PCA scores plot of the MCAO group and Control group in ESI positive ion mode; **(B)** PCA scores plot of the MCAO group and Control group in ESI negative ion mode; **(C)** Permutation test plot of PLS-DA in ESI positive ion mode; **(D)** Permutation test plot of PLS-DA in ESI negative ion mode;

Table S1 Potential biomarkers related to ischemic strock based on lentivirus vectors overexpressing RKIP and their metabolic pathways.

No.	M/Z	RT(min)	VIP	Ion	Formula	Metabolite	Trend [a] $FC(\frac{MCAO}{Control})$	Trend [a] $FC(\frac{RKIP+MCAO}{MCAO})$	Pathway	FDR
1	248.962	0.552	1.2270	[M+Cl]-	$C_4H_7O_8P$	2-Oxo-3-hydroxy-4-phosphobutanoic acid[d]	1.21*	1.06	Vitamin B6 metabolism	0.026
2	118.083	0.646	1.5730	[M+H]+	$C_5H_{11}NO_2$	Betaine [c]	1.24**	0.97	Glycine, serine and threonine metabolism	0.012
3	167.022	0.787	1.2474	[M-H]-	$C_5H_4N_4O_3$	Uric acid [c]	1.31*	1.07	Purine metabolism	0.033
4	145.015	0.907	1.3153	[M-H]-	$C_5H_6O_5$	α-Ketoglutarate [c]	0.59**	2.62###	TCA cycle	0.004
5	228.098	0.910	1.1134	[M+H]+	$C_9H_{13}N_3O_4$	Deoxycytidine [c]	1.45***	0.84###	Pyrimidine metabolism	0.008
6	150.059	0.910	1.5117	[M+H]+	$C_5H_{11}NO_2S$	L-Methionine [b]	1.31**	1.07	Cysteine and methionine metabolism	0.004
7	112.051	0.910	1.4386	[M+H]+	$C_4H_5N_3O$	Cytosine [c]	1.47***	0.87##	Pyrimidine metabolism	0.008
8	132.103	1.164	2.6825	[M+H]+	$C_6H_{13}NO_2$	Isoleucine [c]	1.34**	1.14	Valine, leucine and isoleucine metabolism	0.006
	130.087	1.165	1.7233	[M-H]-	$C_6H_{13}NO_2$	Isoleucine [c]	1.59**	1.23#	Valine, leucine and isoleucine metabolism	0.006
9	166.087	1.940	2.1316	[M+H]+	$C_9H_{11}NO_2$	L-Phenylalanine [b]	1.45**	1.24	Phenylalanine metabolism	0.008
	164.072	1.936	1.7848	[M-H]-	$C_9H_{11}NO_2$	L-Phenylalanine [b]	1.33**	1.16#	Phenylalanine metabolism	0.008
10	218.104	2.397	1.2474	[M-H]-	$C_9H_{17}NO_5$	Pantothenic Acid [c]	1.40**	0.91	Alanine metabolism	0.063
11	205.099	3.796	1.7975	[M+H]+	$C_{11}H_{12}N_2O_2$	L-Tryptophan [b]	1.34*	1.11	Tryptophan metabolism	0.011
	203.083	3.789	1.6484	[M-H]-	$C_{11}H_{12}N_2O_2$	L-Tryptophan [b]	1.25*	0.93	Tryptophan metabolism	0.011
12	212.003	4.364	1.7278	[M-H]-	$C_8H_7NO_4S$	Indoxylsulfuric acid [c]	0.62*	1.89#	Tryptophan metabolism	0.011
13	666.323	5.227	2.6091	[M-H]-	$C_{29}H_{57}N_5O_{12}$	Gluten exorphin C[d]	3.66***	0.23###	Tryptophan metabolism	0.011

14	283.084	5.345	1.5256	[M+Cl]-	$C_{13}H_{16}N_2O_3$	6-Hydroxymelatonin[d]	0.54*	2.20##	Tryptophan metabolism	0.011
15	321.045	6.513	1.4852	[M-H]-	$C_{10}H_{15}N_2O_8P$	5-Thymidylic acid[d]	0.35**	1.17	Pyrimidine metabolism	0.008
16	380.257	11.350	1.2757	[M+H]+	$C_{18}H_{38}NO_5P$	Sphingosine-1-phosphate [c]	1.32***	1.17	Phospholipid metabolism	0.011
	378.244	11.343	1.5173	[M-H]-	$C_{18}H_{38}NO_5P$	Sphingosine-1-phosphate [c]	1.35*	1.17	Phospholipid metabolism	0.011
17	586.317	11.957	1.4818	[M+FA-H]-	$C_{28}H_{48}NO_7P$	PC(20:5/0:0) [d]	2.46*	0.93	Phospholipid metabolism	0.011
18	619.291	12.323	1.3220	[M+Cl]-	$C_{30}H_{48}O_{11}$	Cholic acid glucuronide[d]	1.34*	1.51##	sucrose metabolism	0.033
19	544.345	12.959	1.7226	[M+H]+	$C_{28}H_{50}NO_7P$	PC(20:4/0:0) [d]	0.85*	0.68###	Phospholipid metabolism	0.011
20	496.344	13.147	2.5269	[M+H]+	$C_{24}H_{50}NO_7P$	PC(16:0/0:0) [c]	0.86***	1.08##	Phospholipid metabolism	0.011
	530.304	13.142	1.5233	[M+Cl]-	$C_{24}H_{50}NO_7P$	PC(16:0/0:0) [c]	0.83*	1.17	Phospholipid metabolism	0.011
21	522.359	14.066	1.7145	[M+H]+	$C_{26}H_{52}NO_7P$	PC(0:0/18:1) [d]	0.85*	0.86#	Phospholipid metabolism	0.011
22	433.238	14.111	1.5997	[M-H]-	$C_{21}H_{39}O_7P$	LPA(0:0/18:2) [d]	0.71**	0.77##	Glycerolipid metabolism	0.024
23	457.238	14.160	2.2095	[M+FA-H]-	$C_{18}H_{39}NO_7P$	LysoPC(10:0) [d]	0.65***	0.63###	Phospholipid metabolism	0.011
24	400.343	14.351	1.0367	[M+H]+	$C_{23}H_{45}NO_4$	L-Palmitoylcarnitine [c]	0.76*	1.32##	Fatty acid metabolism	0.009
25	282.282	16.992	1.4505	[M+H]+	$C_{18}H_{35}NO$	Oleamide [c]	0.47**	1.66	Fatty acid metabolism	0.009
26	255.234	17.712	1.8568	[M-H]-	$C_{16}H_{32}O_2$	Palmitic acid [d]	1.11**	1.17#	Fatty acid metabolism	0.009
27	281.249	17.883	1.6319	[M-H]-	$C_{18}H_{34}O_2$	Vaccenic acid [d]	0.52*	1.52	Fatty acid metabolism	0.009

[a](**FC>1**): up-regulate and (**FC<1**): down-regulate; (* $p < 0.05$, ** $p < 0.01$, ***$p < 0.001$ versus control group; # $p < 0.05$, ## $p < 0.01$, ###$p < 0.001$ versus MCAO group)

[b]:The metabolites were verified by standard compound.

[c]: Metabolites analyzed based on MS/MS chromatograms.

[d]: Metabolites putatively annotation.