

# **Pathway-based gene signatures predicting clinical outcome of lung adenocarcinoma**

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Table S1. Clinical characteristics of 443 lung adenocarcinoma in 4 institutes.

	CAN/DF	HLM	UM	MSK
Sample size	82	79	178	104
Age(mean, s.d.)	62(10)	67(10)	64(10)	65(10)
Gender(% male)	56%	51%	57%	36%
Stage I	68%	54%	65%	61%
Stage II	32%	26%	17%	19%
Stage III	0%	19%	18%	20%
Median follow-up(months)	51	39	53	43
Number of deaths	35	60	103	39

Table S2. Hazard ratios estimated from meta-analysis of genes in the HMGB1/RAGE signaling pathway.

Probesets	Gene	Uni gene	HR <sup>a</sup>	95% C.I. <sup>a</sup>	
204314_s_at	CREB1	Hs.584750	0.70	0.52	0.94
209190_s_at	DIAPH1	Hs.529451	0.61	0.46	0.82
213514_s_at	DIAPH1	Hs.529451	0.73	0.58	0.92
204363_at	F3	Hs.62192	1.25	1.10	1.42
214938_x_at	HMGB1	Hs.434102	0.58	0.37	0.89
216244_at	IL1RN	Hs.81134	1.15	1.03	1.27
205207_at	IL6	Hs.654458	1.18	1.02	1.35
202670_at	MAP2K1	Hs.145442	1.36	1.03	1.79
213490_s_at	MAP2K2	Hs.465627	1.33	1.03	1.71
205698_s_at	MAP2K6	Hs.463978	1.32	1.08	1.61
211500_at	MAPK11	Hs.57732	1.29	1.03	1.60
206106_at	MAPK12	Hs.432642	1.21	1.02	1.42
212535_at	MEF2A	Hs.268675	0.69	0.51	0.93
209199_s_at	MEF2C	Hs.699175	0.78	0.65	0.94
209200_at	MEF2C	Hs.699175	0.84	0.75	0.94
211524_at	NFKB2	Hs.73090	1.13	1.00	1.28
214062_x_at	NFKBIB	Hs.9731	0.86	0.76	0.97
212239_at	PIK3R1	Hs.132225	0.76	0.60	0.97
212240_s_at	PIK3R1	Hs.132225	0.77	0.61	0.97
207821_s_at	PTK2	Hs.395482	0.75	0.58	0.96
208820_at	PTK2	Hs.395482	0.73	0.57	0.92
201087_at	PXN	Hs.446336	1.50	1.05	2.14
206036_s_at	REL	Hs.631886	0.71	0.57	0.89
203843_at	RPS6KA3	Hs.445387	0.76	0.59	0.97
204035_at	SCG2	Hs.516726	1.13	1.02	1.26

**HR: hazard ratio; 95% C.I.: 95% confidence interval**

<sup>a</sup> Adjusted by age, sex, and stage

Table S3. Hazard ratios estimated from meta-analysis of genes in the Beta-adrenergic receptors regulation of ERK pathway.

Probesets	Gene	Uni gene	HR <sup>a</sup>	95% C.I. <sup>a</sup>	
209321_s_at	ADCY3	Hs.705457	1.43	1.12	1.84
204497_at	ADCY9	Hs.391860	0.77	0.68	0.88
204498_s_at	ADCY9	Hs.391860	0.69	0.55	0.87
206170_at	ADRB2	Hs.591251	0.84	0.70	1.00
217523_at	CD44	Hs.502328	0.86	0.75	0.98
201179_s_at	GNAI3	Hs.73799	1.64	1.20	2.25
211858_x_at	GNAS	Hs.125898	1.28	1.00	1.65
200852_x_at	GNB2	Hs.185172	1.50	1.11	2.03
211871_x_at	GNB5	Hs.155090	1.35	1.01	1.81
212294_at	GNG12	Hs.431101	0.77	0.61	0.96
205184_at	GNG4	Hs.159711	1.24	1.06	1.44
207157_s_at	GNG5	Hs.645427	1.70	1.16	2.49
206896_s_at	GNG7	Hs.515544	0.79	0.64	0.98
202670_at	MAP2K1	Hs.145442	1.36	1.03	1.79
213490_s_at	MAP2K2	Hs.465627	1.33	1.03	1.71
204524_at	PDPK1	Hs.459691	0.70	0.53	0.93
32029_at	PDPK1	Hs.459691	0.69	0.50	0.96
206370_at	PIK3CG	Hs.32942	0.86	0.78	0.96
205111_s_at	PLCE1	Hs.655033	0.85	0.72	1.00
208652_at	PPP2CA	Hs.483408	0.67	0.47	0.97
200605_s_at	PRKAR1A	Hs.280342	0.74	0.56	0.97
214487_s_at	RAP2A	Hs.508480	1.29	1.03	1.62
215992_s_at	RAPGEF2	Hs.113912	0.83	0.71	0.98
205590_at	RASGRP1	Hs.591127	0.84	0.73	0.97

**HR: hazard ratio; 95%C.I.: 95% confidence interval**

<sup>a</sup> **Adjusted by age, sex, and stage**

Table S4. Hazard ratios estimated from meta-analysis of genes in the Clathrin-coated vesicle cycle pathway.

Probesets	Gene	Uni gene	HR <sup>a</sup>	95% C.I. <sup>a</sup>	
215787_at	ACTA2	Hs.500483	0.77	0.62	0.95
205423_at	AP1B1	Hs.368794	1.33	1.01	1.75
205196_s_at	AP1S1	Hs.563509	1.22	1.02	1.44
211779_x_at	AP2A2	Hs.19121	0.67	0.48	0.93
212159_x_at	AP2A2	Hs.19121	0.67	0.48	0.92
212161_at	AP2A2	Hs.19121	0.68	0.47	0.97
202120_x_at	AP2S1	Hs.119591	1.66	1.18	2.33
211047_x_at	AP2S1	Hs.119591	1.39	1.04	1.86
208750_s_at	ARF1	Hs.286221	1.29	1.01	1.66
201358_s_at	COPB1	Hs.339278	0.57	0.37	0.88
201264_at	COPE	Hs.10326	1.46	1.12	1.89
217726_at	COPZ1	Hs.505652	1.48	1.06	2.05
201279_s_at	DAB2	Hs.481980	0.81	0.67	0.99
201280_s_at	DAB2	Hs.481980	0.82	0.70	0.95
210757_x_at	DAB2	Hs.481980	0.80	0.65	0.99
217886_at	EPS15	Hs.83722	0.67	0.48	0.95
217887_s_at	EPS15	Hs.83722	0.77	0.59	1.00
205425_at	HIP1	Hs.329266	0.79	0.66	0.95
215074_at	MYO1B	Hs.439620	0.73	0.65	0.82
212511_at	PICALM	Hs.163893	0.70	0.52	0.93
217861_s_at	PREB	Hs.279784	1.49	1.07	2.07
200863_s_at	RAB11A	Hs.321541	1.42	1.07	1.89
219681_s_at	RAB11FIP1	Hs.696035	0.79	0.67	0.94
211961_s_at	RAB7A	Hs.15738	0.62	0.41	0.93
203150_at	RABEPK	Hs.19012	1.34	1.01	1.80
201542_at	SAR1A	Hs.499960	0.72	0.52	0.98
218254_s_at	SAR1B	Hs.432984	0.72	0.57	0.90
201583_s_at	SEC23B	Hs.369373	1.36	1.07	1.72
212900_at	SEC24A	Hs.595540	0.68	0.51	0.91
212902_at	SEC24A	Hs.595540	0.72	0.56	0.93
215209_at	SEC24D	Hs.189641	0.76	0.66	0.88
215641_at	SEC24D	Hs.189641	0.73	0.63	0.85
209091_s_at	SH3GLB1	Hs.136309	1.44	1.11	1.89
210101_x_at	SH3GLB1	Hs.136309	1.42	1.06	1.91
212111_at	STX12	Hs.523855	0.66	0.49	0.89

212112_s_at	STX12	Hs.523855	0.63	0.45	0.90
212799_at	STX6	Hs.518417	0.60	0.42	0.86
203457_at	STX7	Hs.593148	0.72	0.52	1.00
212631_at	STX7	Hs.593148	0.75	0.58	0.95
212632_at	STX7	Hs.593148	0.63	0.45	0.88
213480_at	VAMP4	Hs.6651	0.66	0.47	0.93
202546_at	VAMP8	Hs.534373	0.74	0.59	0.92
207967_at	VPS45	Hs.443750	0.78	0.63	0.96

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**HR: hazard ratio; 95% C.I.: 95% confidence interval**

<sup>a</sup> **Adjusted by age, sex, and stage**

Table S5. Results of multivariate Cox proportional hazards regression for 2418 genes, selected by the inverse-variance weighting method for four datasets.

Dataset	Number of significant hazard ratio	Minimum significant hazard ratio	Maximum significant hazard ratio
CAN/DF	820	0.05	8.35
HLM	574	0.11	4.65
UM	429	0.40	3.36
MSK	622	0.05	11.3

## **Figure legends**

Figure S1. The flowchart of data analysis.

Figure S2. Immune response\_HMGB1/RAGE signaling pathway.

Figure S3. Development\_Beta-adrenergic receptors regulation of ERK pathway.

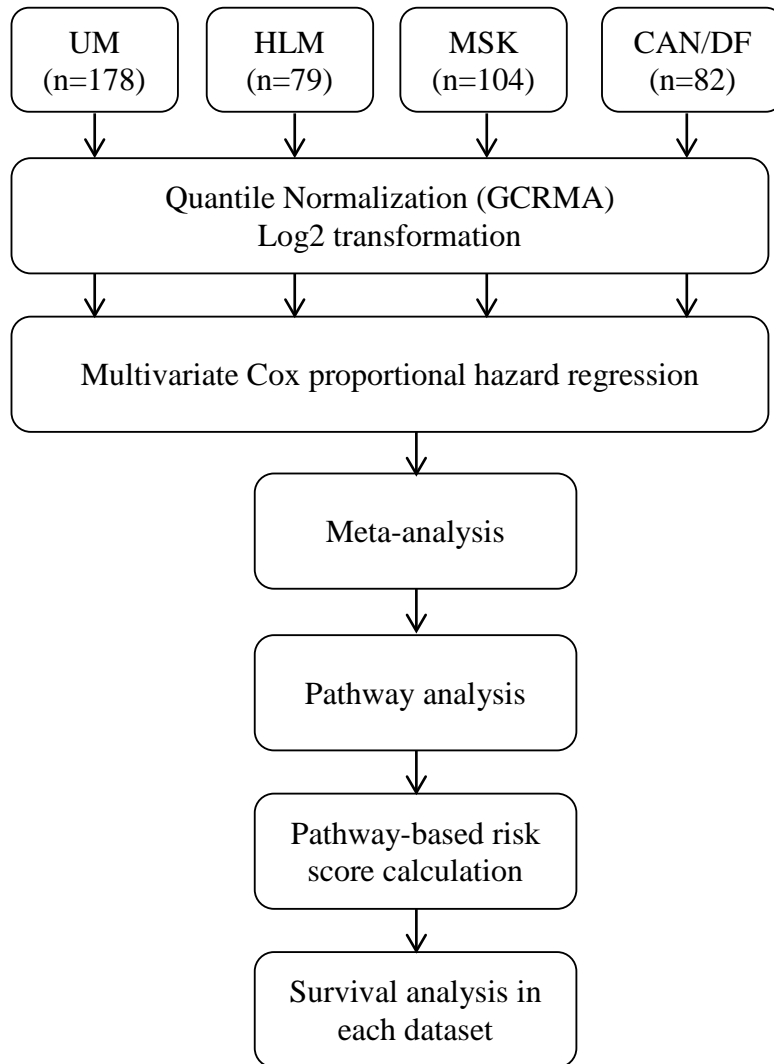
Figure S4. Transport\_Clatherin-coated vesicle cycle pathway.

Figure S5. Distributions of hazard ratios and p values, estimated from multivariate Cox proportional hazards regression. Black dots denoted 2418 genes and red dots denoted three pathway-based signatures and CPBR score

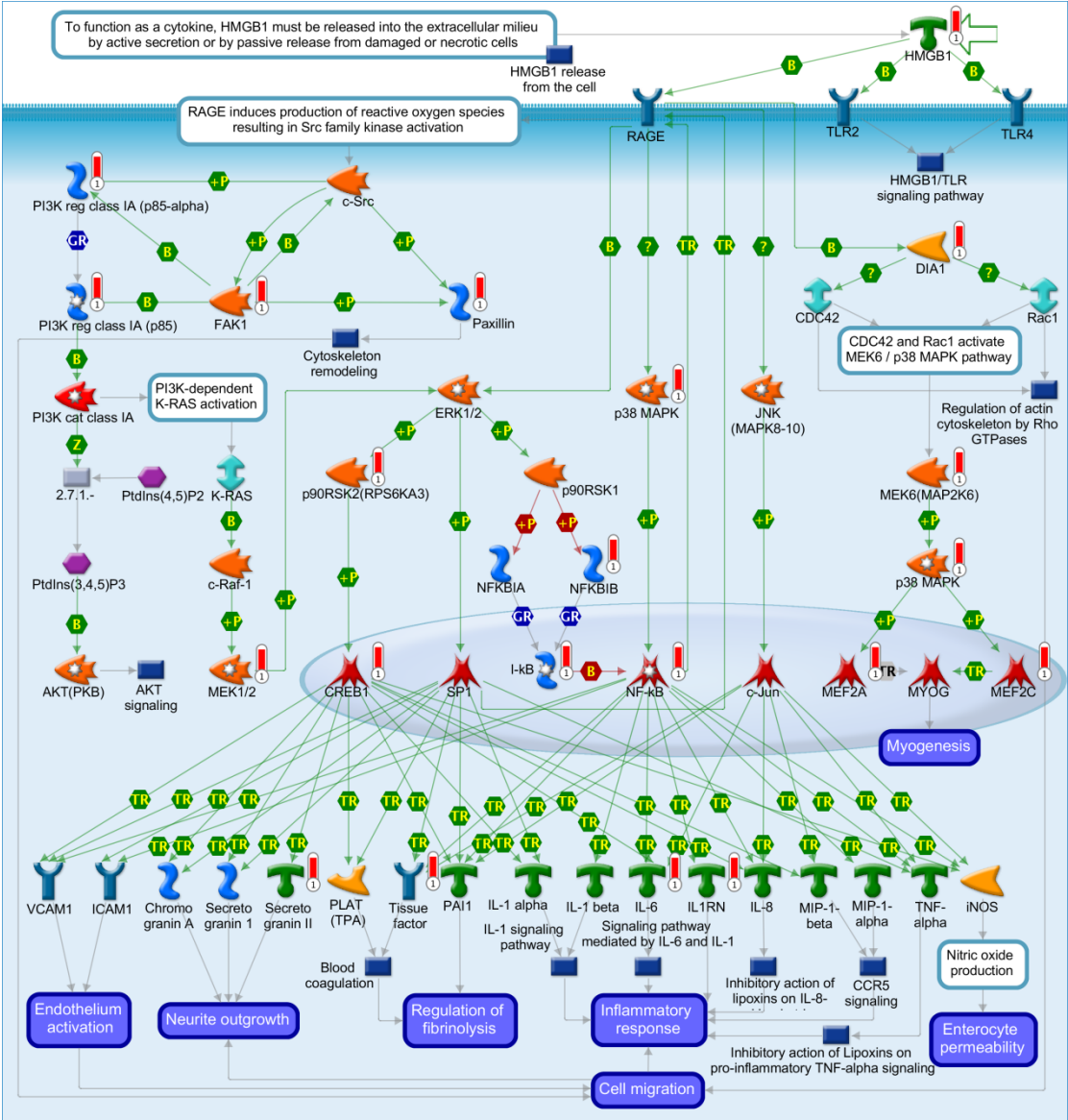


**Figure S1**

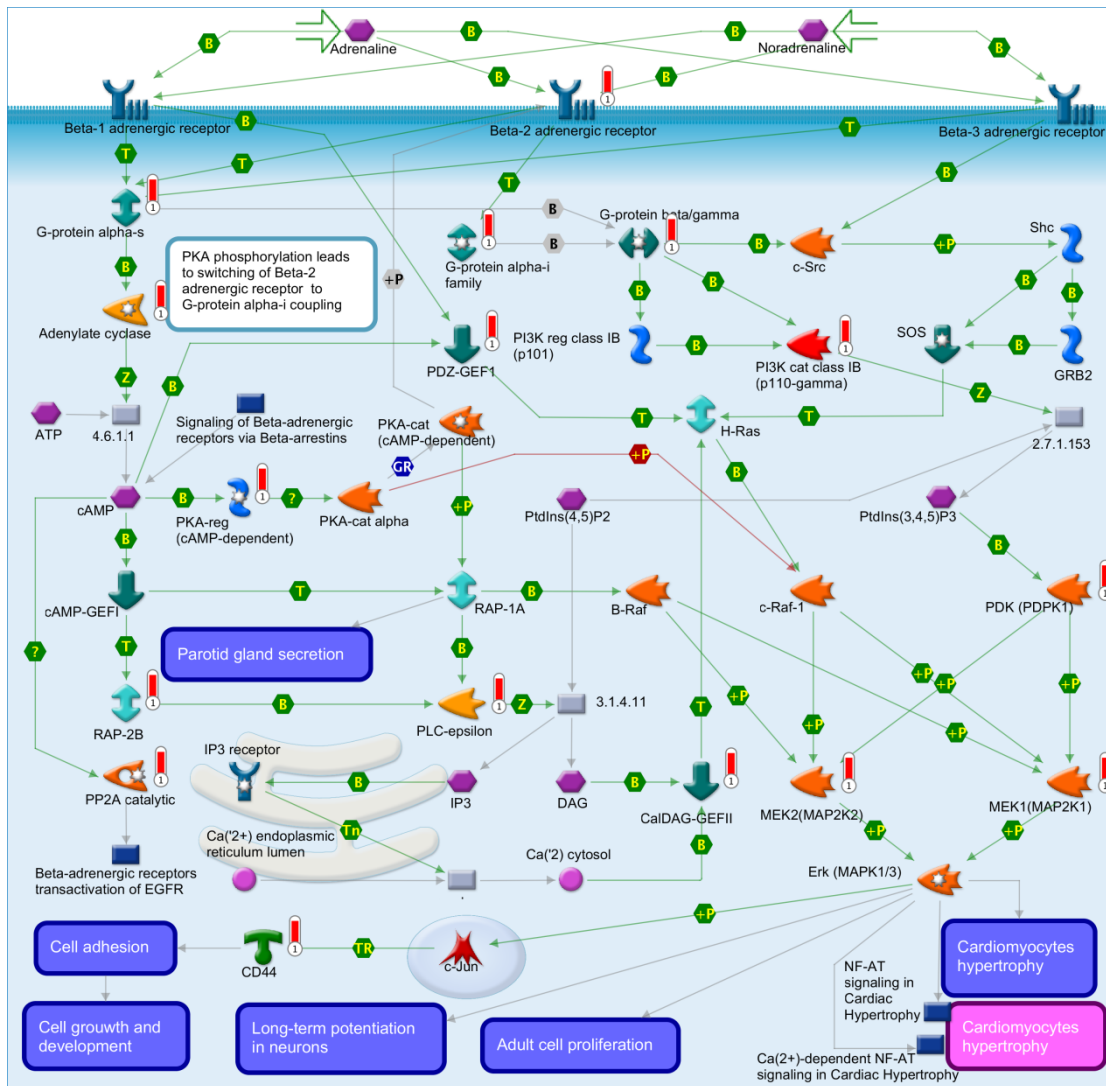
Affymetrix HG-U133A  
Microarray raw data



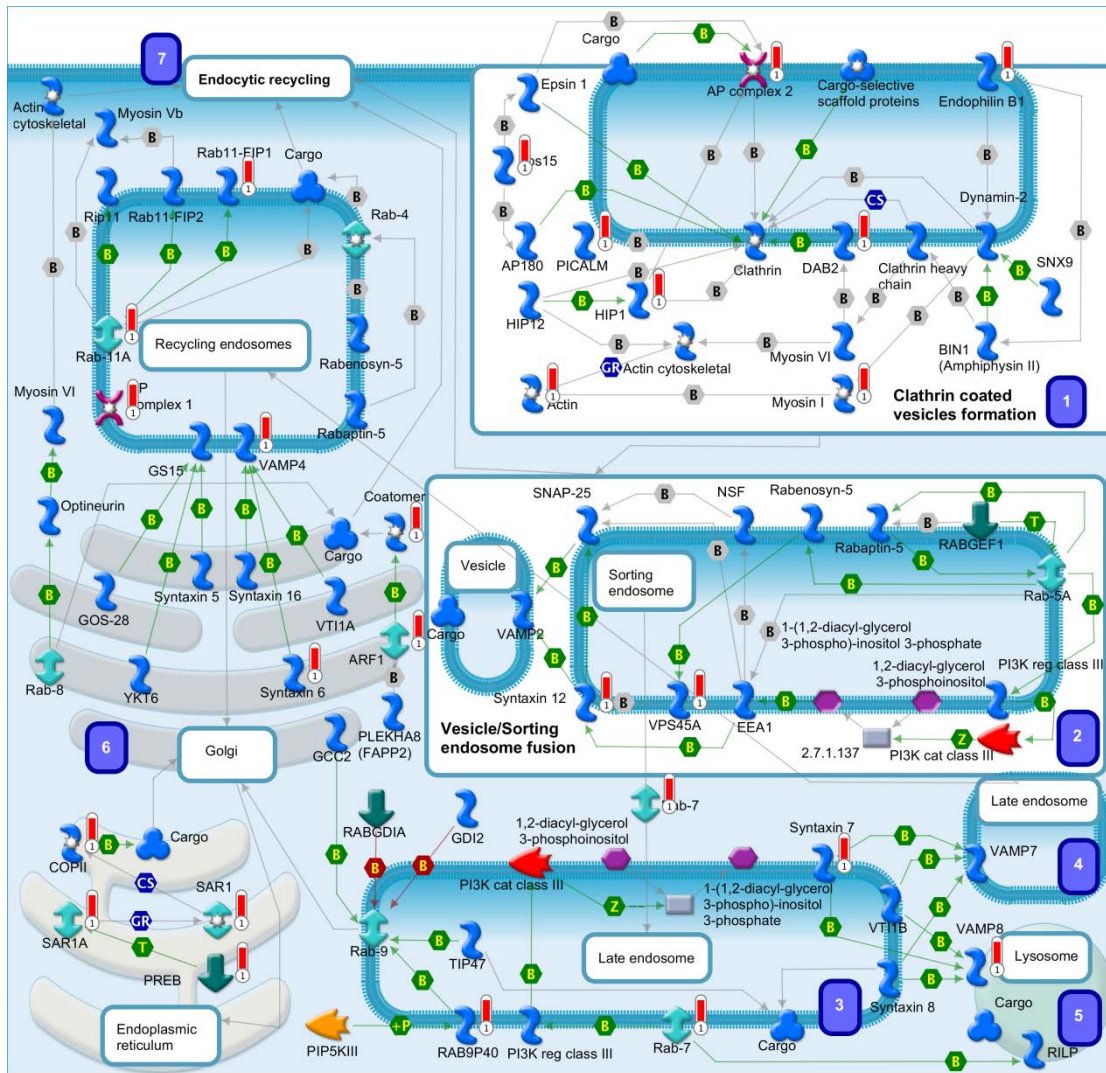
**Figure S2.**



**Figure S3.**



**Figure S4.**



**Figure S5.**

