Figure S1. DEGs in HCC and non-cancerous tissues. Volcano plot of DEGs in (A) TCGA-LIHC and (B) ICGC LIRI-JP cohorts. (C) Venn diagram plot of DEGs in both cohorts. DEGs, differentially expressed genes; ICGC LIRI-JP, International Cancer Genome Consortium liver cancer-RIKEN, Japan; TCGA-LIHC, The Cancer Genome Atlas-liver hepatocellular carcinoma.



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Figure S2. Histogram of k and scale free topology plot.



Figure S3. Correlation between EPHX2 expression level and MSI in TCGA-LIHC cohort. EPHX2, epoxide hydrolase 2; MSI, microsatellite instability; TCGA-LIHC, The Cancer Genome Atlas-liver hepatocellular carcinoma.



Figure S4. Kaplan-Meier survival curves assessing the effect of high- or low-EPHX2 expression on OS in different types of cancer. OS in (A) BLCA, (B) BRCA, (C) CESC, (D) EAC, (E) ESCA, (F) HNSC and (G) KIRC. (H) OS and RFS in KIRP. OS in (I) LIHC, (J) LUAD, (K) LUSC, (L) OVC, (M) PDAC, (N) PCPG, (O) READ, (P) SARC, (Q) STAD, (R) THYM, (S) THCA and (T) UCEC. EPHX2, epoxide hydrolase 2; OS, overall survival; RFS, recurrence-free survival; BLCA, bladder carcinoma; BRCA, breast cancer; CESC, cervical squamous cell carcinoma; EAC, esophageal adenocarcinoma; ESCA, esophageal squamous cell carcinoma; HNSC, head-neck squamous cell carcinoma; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; LIHC, liver hepatocellular carcinoma; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; OVC, ovarian cancer; PDAC, pancreatic ductal adenocarcinoma; THYM, Thymoma; THCA, thyroid carcinoma; UCEC, uterine corpus endometrial carcinoma.



Figure S5. Kaplan-Meier survival curves assessing the effect of high- or low-EPHX2 expression on RFS in different types of cancer. RFS in (A) BLCA, (B) BRCA, (C) CESC, (D) EAC, (E) ESCA, (F) HNSC, (G) KIRC, (H) KIRP, (I) LIHC, (J) LUAD, (K) LUSC, (L) OVC, (M) PDAC, (N) PCPG, (O) READ, (P) SARC, (Q) STAD, (R) THYM, (S) THCA and (T) UCEC. EPHX2, epoxide hydrolase 2; RFS, recurrence-free survival; BLCA, bladder carcinoma; BRCA, breast cancer; CESC, cervical squamous cell carcinoma; EAC, esophageal adenocarcinoma; ESCA, esophageal squamous cell carcinoma; HNSC, head-neck squamous cell carcinoma; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; LIHC, liver hepatocellular carcinoma; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; OVC, ovarian cancer; PDAC, pancreatic ductal adenocarcinoma; PCPG, Pheochromocytoma and Paraganglioma; READ, rectum adenocarcinoma; SARC, sarcoma; STAD, stomach adenocarcinoma; THYM, Thymoma; THCA, thyroid carcinoma; UCEC, uterine corpus endometrial carcinoma.



Figure S6. EPHX2 expression in HCC tissue microarrays. The levels of EPHX2 in 90 paired HCC and normal samples were examined using immunohistochemistry. Representative images of EPHX2 staining in HCC tumor tissues (T) and corresponding adjacent tissues (A). EPHX2, epoxide hydrolase 2; HCC, hepatocellular carcinoma.



2000 µm

Figure S7. Univariate and multivariate analyses of factors associated with recurrence-free survival of patients with hepatocellular carcinoma in the tissue microarray cohort. AFP, α -fetoprotein; CI, confidence interval; EPHX2, epoxide hydrolase 2; HR, hazard ratio.

Characteristics	HR (95% CI)		P value
Univariate analysis			
Age (>50 vs. ≤50)	1.067 (0.558-2.038)	H I	0.845
Sex (female vs. male)	1.230 (0.378-4.007)	· ·	0.731
Cirrhosis (yes vs. no)	1.315 (0.688-2.512)	r <mark>i</mark> ∎i	0.407
HBV (positive vs. no)	2.073 (0.284-5.130)		0.472
Tumor multiplicity (multiple vs. single)	0.915 (0.432-1.936)	•	8.815
AFP (ng/ml) (≤20 vs. >20)	0.367 (0.253-0.879)	•	p<0.01
Tumor size (cm) (≤5 vs. >5)	0.766 (0.351-1.672)	÷	0.503
Tumor encapsulation (yes vs. no)	1.104 (0.562-2.172)	rin	0.773
Vascular invasion (yes vs. no)	1.538 (0.809-2.923)	Ļ∎—-	0.189
ΓΝΜ stage (III-IV vs. I-II)	2.941 (1.425-6.071)	¦⊷●	P<0.01
EPHX2 expression (low vs. high)	1.101 (1.042-1.365)	•	0.01
Multivariate analysis			
AFP (ng/ml) (≤20 vs. >20)	0.369 (0.151-0870)	•	0.023
TNM stage (III-IV vs. I-II)	3.234 (1.550-6.749)		➡ P<0.01
EPHX2 expression (low vs. high)	1.303 (0.820-2.071)	•	0.262