Supplementary table S1. Top 50 mRNAs associated with GC death in the discovery stage

Genes	Cox *P*-value	Genes	Cox *P*-value
SIM1	1.13×10^{-6}	*PRKACG*	8.17×10^{-4}
RIMS1	3.58×10^{-5}	*ARRDC3*	8.63×10^{-4}
ANKRD30B	4.39×10^{-5}	*ISG20L2*	8.84×10^{-4}
WNT9B	4.75×10^{-5}	*MCC*	9.09×10^{-4}
PRICKLE1	5.69×10^{-5}	*SRMS*	9.22×10^{-4}
KCNS2	6.83×10^{-5}	*CATIP*	9.41×10^{-4}
PAMR1	7.62×10^{-5}	*IRPRIP*	9.47×10^{-4}
KCNT2	1.16×10^{-4}	*DCLK1*	9.61×10^{-4}
OR51G2	1.91×10^{-4}	*FLRT2*	9.78×10^{-4}
ZNF707	2.01×10^{-4}	*SLCO2A1*	9.94×10^{-4}
UPK1B	2.20×10^{-4}	*VWF*	1.03×10^{-3}
XG	2.48×10^{-4}	*LHX6*	1.09×10^{-3}
NT5E	2.70×10^{-4}	*THSD7A*	1.11×10^{-3}
IGFN1	2.74×10^{-4}	*PKIA*	1.12×10^{-3}
NEU2	4.21×10^{-4}	*TMEM120B*	1.14×10^{-3}
H2BFWT	4.23×10^{-4}	*ZNF536*	1.14×10^{-3}
OR51A4	4.63×10^{-4}	*SLC39A11*	1.19×10^{-3}
CNTN1	5.00×10^{-4}	*H2BFM*	1.20×10^{-3}
HOOK2	5.73×10^{-4}	*C8orf22*	1.23×10^{-3}
SLC25A15	6.19×10^{-4}	*FAHD2B*	1.33×10^{-3}
GDF6	6.22×10^{-4}	*OR4K15*	1.40×10^{-3}
ASPHD1	6.34×10^{-4}	*KCNJ8*	1.42×10^{-3}
OR5H2	6.63×10^{-4}	*SPRED1*	1.47×10^{-3}
PDE1B	7.29×10^{-4}	*LRRC8C*	1.48×10^{-3}
AJ239318	7.56×10^{-4}	*RPS6KA3*	1.50×10^{-3}

Cox *P*-value for each gene was obtained from the multivariate Cox regression adjusting for age and gender.

Genes with Cox *P*-value $< 5 \times 10^{-3}$ was considered to be associated with GC death.

Supplementary table S2. The correlation between mRNA expression values and corresponding methylation levels [a]

Genes	CpG loci	Chromosome	Start	End	Correlation coefficient [b]	*P*-value
ASPHD1	cg08515989	chr16	29901583	29901584	- 0.73	1.68×10^{-56}
	cg09328356	chr16	29901841	29901842	- 0.71	1.10×10^{-52}
	cg10093648	chr16	29901379	29901380	- 0.57	3.09×10^{-30}
	cg05192831	chr16	29901686	29901687	- 0.53	9.75×10^{-26}
	cg02488299	chr16	29901902	29901903	- 0.48	1.08×10^{-20}
PKIA	cg09043127	chr8	78516209	78516210	- 0.54	6.63×10^{-27}
	cg27140220	chr8	78516199	78516200	- 0.52	1.10×10^{-24}
NT5E	cg27297263	chr6	85450750	85450751	- 0.49	2.37×10^{-21}
	cg21730993	chr6	85449492	85449493	- 0.47	1.70×10^{-19}
	cg27039625	chr6	85449378	85449379	- 0.43	1.43×10^{-16}
	cg10663055	chr6	85449533	85449534	- 0.40	1.74×10^{-14}
	cg13315970	chr6	85449479	85449480	- 0.45	6.68×10^{-18}
GHR	cg07237214	chr5	42424502	42424503	- 0.44	5.95×10^{-17}
	cg18160072	chr5	42424323	42424324	- 0.41	7.25×10^{-15}
	cg03836184	chr5	42424736	42424737	- 0.41	2.70×10^{-15}
ERG	cg06032349	chr21	38660407	38660408	- 0.44	1.16×10^{-17}
CDO1	cg18520851	chr5	115813492	115813493	0.40	1.97×10^{-14}

[a] mRNAs were significantly associated with GC death at $P < 5\times 10^{-3}$ in TCGA. CpG loci were significantly associated with GC death at $P < 0.05$ in TCGA.

[b] The correlation coefficients between mRNA expression and encoding gene methylation were obtained with performing spearman correlation analysis. Correlation P values < 0.05 and the absolute value of coefficient > 0.4 were set as the cut-off criteria defining meaningful methylation-expression associations.

Supplementary table S3. Candidate mRNAs went for validation study (GSE84437)

Description	Genes
Genes which ranked among the most significant survival-associated genes in TCGA ($P < 1.00 \times 10^{-4}$)	*SIM1, RIMS1, ANKRD30B, WNT9B, PRICKLE1, KCNS2, PAMR1, KCNT2, OR51G2, ZNF707, UPK1B, XG, NT5E, IGFN1, NEU2, H2BFWT, OR51A4, CNTN1, HOOK2, SLC25A15, GDF6, ASPHD1, OR5H2, PDE1B, AJ239318, PRKACG, ARRDC3, ISG20L2, MCC, SRMS, CATIP, ITPRIP, DCLK1, FLRT2, SLCO2A1*
Genes whose both mRNA expression values and methylation levels were significantly associated with GC prognosis	*ASPHD1, CDO1, ERG, GHR, NT5E, PKIA*
Genes which were included in significant sub-networks [a]	*VMF, SELP, CD36, CD44, CD109*

[a] The plugin software ClusterOne was applied to detect significant models which may represent molecular complexes in PPI network associated with poor GC survival (Minimum size = 5, Minimum density = 0.6, Edge weights = unweight).

Supplementary table S4. The enriched GO terms of the 184 genes which encode mRNAs associated with GC death in TCGA at $P < 5\times 10^{-3}$

Category	ID	Description	P-value	Gene count
BP	GO:0001525	Angiogenesis	4.2×10^{-3}	8
	GO:0050731	Positive regulation of peptidyl-tyrosine phosphorylation	6.5×10^{-3}	5
	GO:0007165	Signal transduction	1.8×10^{-2}	19
	GO:0007159	Leukocyte cell-cell adhesion	2.1×10^{-2}	3
	GO:0035556	Intracellular signal transduction	3.0×10^{-2}	9
	GO:0007204	Positive regulation of cytosolic calcium ion concentration	3.4×10^{-2}	5
	GO:0050911	Detection of chemical stimulus involved in sensory perception of smell	4.0×10^{-2}	9
	GO:0007040	Lysosome organization	4.2×10^{-2}	3
CC	GO:0008076	Voltage-gated potassium channel complex	6.8×10^{-3}	5
	GO:0005886	Plasma membrane	9.9×10^{-3}	49
	GO:0005887	Integral component of plasma membrane	1.7×10^{-2}	21
	GO:0008282	ATP-sensitive potassium channel complex	2.5×10^{-2}	2
	GO:0045121	Membrane raft	3.2×10^{-2}	6
	GO:0070695	FHF complex	4.2×10^{-2}	2
MF	GO:0017046	Peptide hormone binding	2.4×10^{-2}	3
	GO:0004984	Olfactory receptor activity	4.0×10^{-2}	9

$P < 0.05$ was considered as threshold value of significant difference.

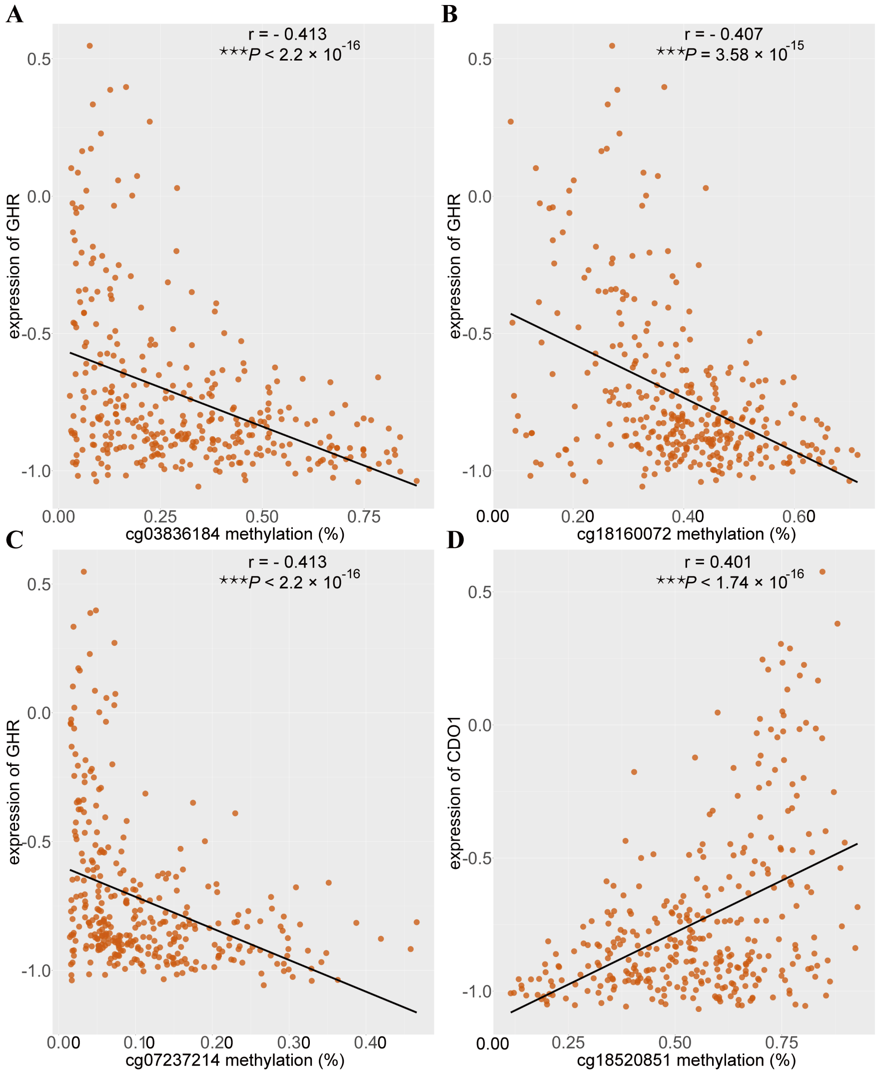
Abbreviations: GO, gene ontology; BP, biological process; MF, molecular function; CC, cellular component.

Supplementary table S5. Top 20 enriched pathways of the 184 genes which encode mRNAs associated with GC death in TCGA at $P < \mathbf{5} \times 10^{-3}$

Pathway ID	Description	*P*-value	Gene count
R-HSA-162582	Signal Transduction	1.4×10^{-6}	29
R-HSA-372790	Signaling by GPCR	3.7×10^{-6}	19
hsa04740	Olfactory transduction	3.8×10^{-6}	11
R-HSA-112316	Neuronal System	1.6×10^{-4}	8
R-HSA-212676	Dopamine Neurotransmitter Release Cycle	1.8×10^{-4}	3
hsa04924	Renin secretion	2.4×10^{-4}	4
R-HSA-381753	Olfactory Signaling Pathway	3.1×10^{-4}	8
R-HSA-388396	GPCR downstream signaling	3.4×10^{-4}	13
R-HSA-447043	Neurofascin interactions	6.8×10^{-4}	2
hsa04916	Melanogenesis	1.2×10^{-3}	4
P02771	Pyrimidine Metabolism	1.2×10^{-3}	2
hsa05034	Alcoholism	1.4×10^{-3}	5
hsa04340	Hedgehog signaling pathway	1.4×10^{-3}	3
R-HSA-112310	Neurotransmitter Release Cycle	1.7×10^{-3}	3
R-HSA-109582	Hemostasis	1.7×10^{-3}	9
R-HSA-373760	L1CAM interactions	2.0×10^{-3}	4
hsa05217	Basal cell carcinoma	2.2×10^{-3}	3
hsa05203	Viral carcinogenesis	2.5×10^{-3}	5
R-HSA-112315	Transmission across Chemical Synapses	2.6×10^{-3}	5
R-HSA-264642	Acetylcholine Neurotransmitter Release Cycle	2.8×10^{-3}	2

The online tool KOBAS was applied to perform pathway enrichment analysis.

$P < 0.05$ was considered as threshold value of significant difference.



Supplementary Figure S1. Spearman correlation between mRNA expression values and corresponding methylation levels in the discovery stage. Correlation $P < 0.05$ and the absolute value of coefficient > 0.4 were set as the cut-off criteria defining meaningful methylation-expression associations. (A-C) The correlations of *GHR*. (D) The correlation of *CDO1*.