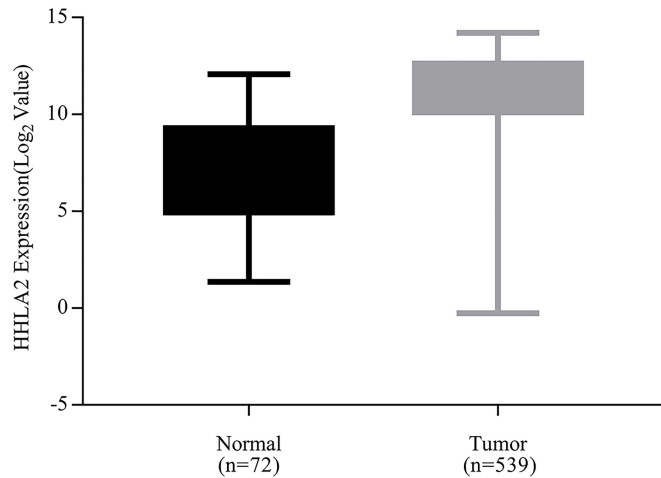
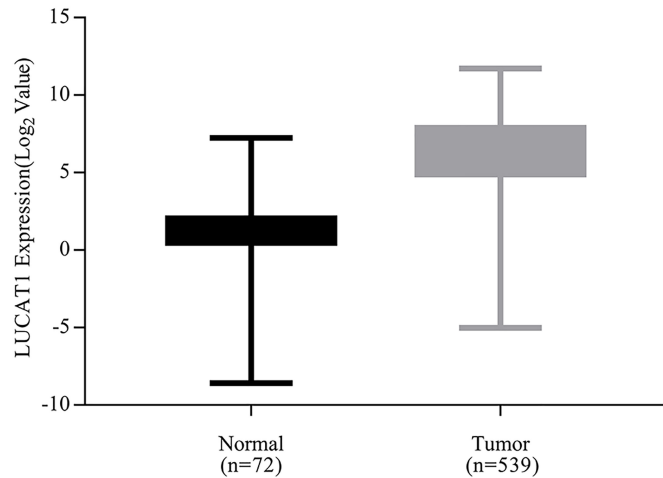


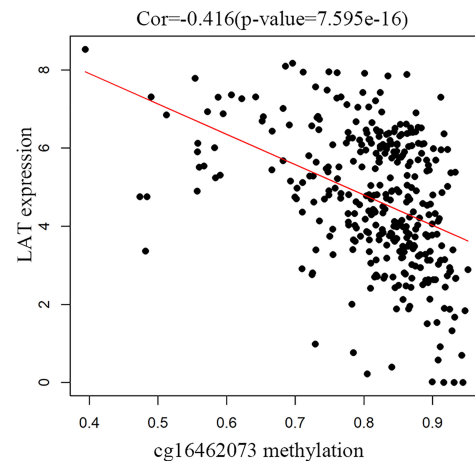
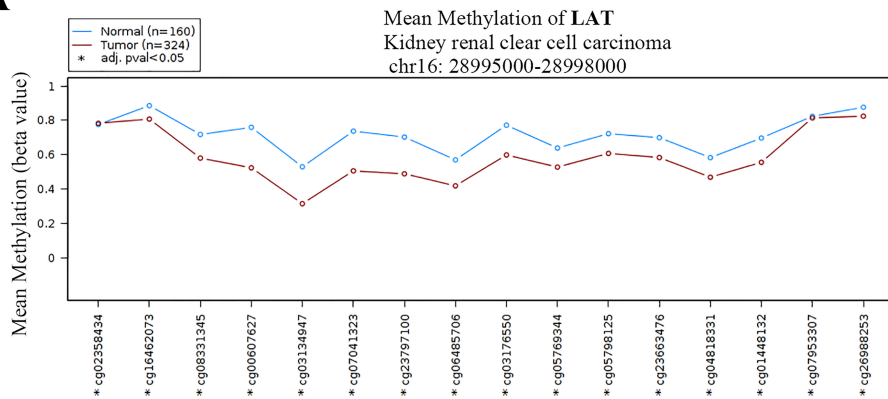
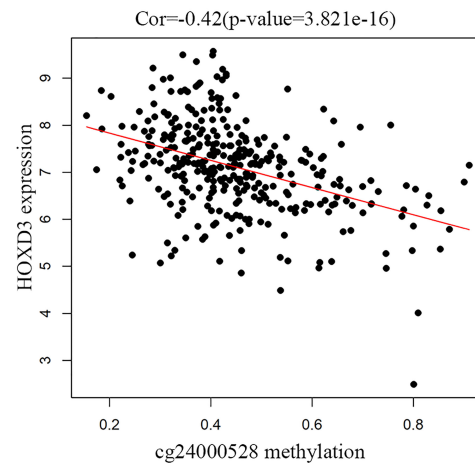
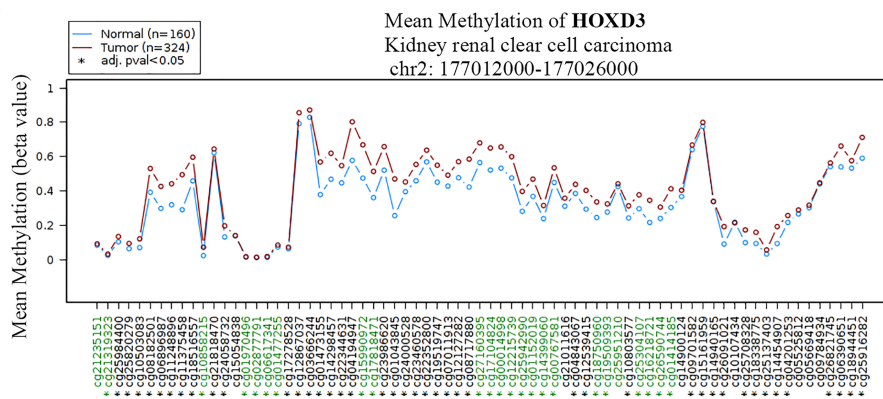
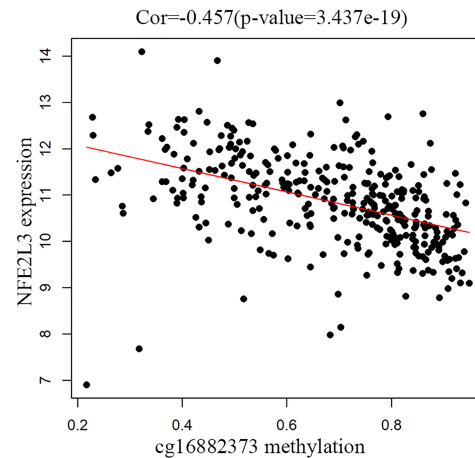
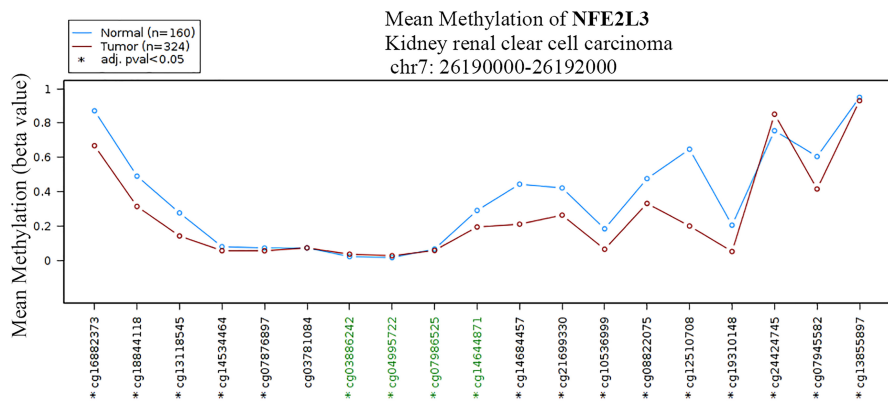
**Figure S1**

**A**



**B**



**Figure S2****A****B****C**

**Table S2.** The KEGG pathway annotation of candidate DNA methylation-driven gene with the use of GSEA

Gene	Gene sets	NES	FDR q-val	
LAT	KEGG_UBIQUITIN_MEDIATED_PROTEOLYSIS	-2.19593	0.0024342	
	KEGG_RENAL_CELL_CARCINOMA	-2.17908	0.0012171	
	KEGG_ERBB_SIGNALING_PATHWAY	-2.16282	8.11E-04	
	KEGG_VASOPRESSIN_REGULATED_WATER_REABSORPTION	-2.14901	6.09E-04	
	KEGG_PROSTATE_CANCER	-2.13281	9.18E-04	
	KEGG_ENDOCYTOSIS	-2.11924	0.0014711	
	KEGG_COLORECTAL_CANCER	-2.11616	0.0012609	
	KEGG_ENDOMETRIAL_CANCER	-2.10814	0.0015524	
	KEGG_TIGHT_JUNCTION	-2.10151	0.0020144	
	KEGG_INSULIN_SIGNALING_PATHWAY	-2.09393	0.0021298	
	KEGG_AMINOACYL_TRNA_BIOSYNTHESIS	-2.08709	0.0021191	
	KEGG_NEUROTROPHIN_SIGNALING_PATHWAY	-2.07291	0.0027774	
	KEGG_REGULATION_OF_ACTIN_CYTOSKELETON	-2.07252	0.0025638	
	KEGG_SPHINGOLIPID_METABOLISM	-2.05628	0.0029849	
	KEGG_AMYOTROPHIC_LATERAL_SCLEROSIS_ALS	-2.04616	0.0032518	
	KEGG_WNT_SIGNALING_PATHWAY	-2.04282	0.0032742	
	KEGG_ADHERENS_JUNCTION	-2.04241	0.0032086	
	KEGG_THYROID_CANCER	-2.03697	0.0034674	
	KEGG_PANCREATIC_CANCER	-2.03547	0.0034144	
	KEGG_AXON_GUIDANCE	-2.03312	0.0034044	
	HOXD3	KEGG_PRIMARY_IMMUNODEFICIENCY	-2.01399	0.0896912
		KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	-1.99349	0.0633269
		KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	-1.90681	0.1036424
KEGG_HOMOLOGOUS_RECOMBINATION		-1.8854	0.0965935	
KEGG_OTHER_GLYCAN_DEGRADATION		-1.87538	0.0862587	
KEGG_P53_SIGNALING_PATHWAY		-1.81851	0.1228653	
KEGG_AMINO_SUGAR_AND_NUCLEOTIDE_SUGAR_METABOLISM		-1.8068	0.117782	
KEGG_LYSOSOME		-1.77548	0.1374537	
KEGG_HEMATOPOIETIC_CELL_LINEAGE		-1.75654	0.142747	
KEGG_LEISHMANIA_INFECTION		-1.75604	0.1287359	
KEGG_ASTHMA		-1.75089	0.1216946	
KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY		-1.73736	0.1246306	
KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY		-1.71207	0.1401099	
KEGG_FC_GAMMA_R_MEDIATED_PHAGOCYTOSIS		-1.68064	0.1615436	
KEGG_GALACTOSE_METABOLISM		-1.65443	0.1444494	
KEGG_ALPHA_LINOLENIC_ACID_METABOLISM		-1.64698	0.1441016	
KEGG_GLYCOSPHINGOLIPID_BIOSYNTHESIS_LACTOAND_NEOLACTO_SERIES		-1.64465	0.1329486	
KEGG_RIBOFLAVIN_METABOLISM		-1.54373	0.1756841	
KEGG_NICOTINATE_AND_NICOTINAMIDE_METABOLISM		-1.52943	0.1793574	
KEGG_AMYOTROPHIC_LATERAL_SCLEROSIS_ALS		-1.49896	0.178269	
NFE2L3		KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	2.31502	9.90E-04
		KEGG_ASTHMA	2.22277	0.0013342
		KEGG_AUTOIMMUNE_THYROID_DISEASE	2.17964	0.0011303
	KEGG_VIRAL_MYOCARDITIS	2.12972	0.0018815	
	KEGG_LEISHMANIA_INFECTION	2.12131	0.0016267	
	KEGG_TYPE_I_DIABETES_MELLITUS	2.10432	0.0018113	
	KEGG_CELL_ADHESION_MOLECULES_CAMS	2.10239	0.0018426	
	KEGG_ALLOGRAFT_REJECTION	2.08947	0.0020694	
	KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	2.07726	0.0024161	
	KEGG_GRAFT_VERSUS_HOST_DISEASE	2.06089	0.0029941	

KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	2.05622	0.0028325
KEGG_CYTOSOLIC_DNA_SENSING_PATHWAY	2.01525	0.005017
KEGG_NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	1.98715	0.0075434
KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	1.98057	0.0080549
KEGG_PRIMARY_IMMUNODEFICIENCY	1.98037	0.0075179
KEGG_HOMOLOGOUS_RECOMBINATION	1.9418	0.0106902
KEGG_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	1.93468	0.0109227
KEGG_MISMATCH_REPAIR	1.87159	0.0213783
KEGG_T_CELL_RECEPTOR_SIGNALING_PATHWAY	1.85554	0.0233218
KEGG_P53_SIGNALING_PATHWAY	1.84839	0.0242923

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Abbreviations: Gene, gene symbol; NES, normalized enrichment score; FDR, false discovery rate.

**Table S3.** The GO functional annotation of candidate DNA methylation-driven gene with the use of GSEA

Gene	Gene sets	NES	FDR q-val	
LAT	GO_PROTEIN_TARGETING	-3.339404	0	
	GO_TRANSLATIONAL_INITIATION	-3.31827	0	
	GO_ESTABLISHMENT_OF_PROTEIN_LOCALIZATION_TO_ORGANELLES	-3.302083	0	
	GO_GOLGI_VESICLE_TRANSPORT	-3.287631	0	
	GO_AMIDE_BIOSYNTHETIC_PROCESS	-3.259312	0	
	GO_PROTEASOMAL_PROTEIN_CATABOLIC_PROCESS	-3.255723	0	
	GO_RRNA_METABOLIC_PROCESS	-3.252444	0	
	GO_PROTEIN_TARGETING_TO_MEMBRANE	-3.215333	0	
	GO_PROTEIN_FOLDING	-3.199061	0	
	GO_RIBOSOME_BIOGENESIS	-3.198145	0	
	GO_VACUOLAR_TRANSPORT	-3.178438	0	
	GO_VIRAL_LIFE_CYCLE	-3.172631	0	
	GO_ESTABLISHMENT_OF_PROTEIN_LOCALIZATION_TO_MEMBRANE	-3.168418	0	
	GO_PROTEIN_LOCALIZATION_TO_ENDOPLASMIC_RETICULUM	-3.167993	0	
	GO_RIBONUCLEOPROTEIN_COMPLEX_BIOGENESIS	-3.153517	0	
	GO_ESTABLISHMENT_OF_PROTEIN_LOCALIZATION_TO_ENDOPLASMIC_RETICULUM	-3.152013	0	
	GO_ER_TO_GOLGI_VESICLE_MEDIATED_TRANSPORT	-3.142889	0	
	GO_POSITIVE_REGULATION_OF_CATABOLIC_PROCESS	-3.135872	0	
	GO_REGULATION_OF_CELLULAR_PROTEIN_CATABOLIC_PROCESS	-3.124358	0	
	GO_ENDOMEMBRANE_SYSTEM_ORGANIZATION	-3.113897	0	
	GO_COFACTOR_METABOLIC_PROCESS	-3.092233	0	
	GO_PROTEIN_LOCALIZATION_TO_MEMBRANE	-3.089388	0	
	GO_NCRNA_METABOLIC_PROCESS	-3.08425	0	
	GO_POSTTRANSCRIPTIONAL_REGULATION_OF_GENE_EXPRESSION	-3.084227	0	
	GO_PROTEIN_POLYUBIQUITINATION	-3.082902	0	
	HOXD3	GO_ADAPTIVE_IMMUNE_RESPONSE	-2.971033	0
		GO_ACTIVATION_OF_IMMUNE_RESPONSE	-2.879108	0
		GO_B_CELL_MEDIATED_IMMUNITY	-2.758972	0
		GO_POSITIVE_REGULATION_OF_INTERFERON_GAMMA_PRODUCTION	-2.754612	0
		GO_B_CELL_RECEPTOR_SIGNALING_PATHWAY	-2.725312	0
		GO_ANTIGEN_RECEPTOR_MEDIATED_SIGNALING_PATHWAY	-2.722894	0
		GO_REGULATION_OF_INTERFERON_GAMMA_PRODUCTION	-2.72241	0
		GO_SISTER_CHROMATID_COHESION	-2.707151	0
GO_SISTER_CHROMATID_SEGREGATION		-2.654058	0	
GO_ADAPTIVE_IMMUNE_RESPONSE_BASED_ON_SOMATIC_RECOMBINATION_OF_IMMUNE_RECEPTORS_BUILT_FROM_IMMUNOGLOBULIN_SUPERFAMILY_DOMAINS		-2.64444	0	
GO_IMMUNE_EFFECTOR_PROCESS		-2.6421	0	
GO_LYMPHOCYTE_MEDIATED_IMMUNITY		-2.631601	0	
GO_LEUKOCYTE_MEDIATED_IMMUNITY		-2.627825	0	
GO_LYMPHOCYTE_COSTIMULATION		-2.611089	0	
GO_IMMUNE_RESPONSE_REGULATING_CELL_SURFACE_RECEPTOR_SIGNALING_PATHWAY		-2.588453	0	
GO_CHROMOSOME_SEGREGATION		-2.571246	0	
GO_NUCLEAR_CHROMOSOME_SEGREGATION		-2.560045	0	
GO_HUMORAL_IMMUNE_RESPONSE_MEDIATED_BY_CIRCULATING_IMMUNOGLOBULIN		-2.550792	0	
GO_REGULATION_OF_B_CELL_ACTIVATION		-2.542496	0	
GO_POSITIVE_REGULATION_OF_CELL_ACTIVATION		-2.53229	0	

	GO_LYMPHOCYTE_ACTIVATION	-2.525446	0
	GO_ACTIVATION_OF_INNATE_IMMUNE_RESPONSE	-2.525433	0
	GO_REGULATION_OF_T_CELL_PROLIFERATION	-2.50515	0
	GO_POSITIVE_REGULATION_OF_T_CELL_PROLIFERATION	-2.503446	0
	GO_PRODUCTION_OF_MOLECULAR_MEDIATOR_OF_IMMUNE_RESPONSE	-2.502215	0
NFE2L3	GO_REGULATION_OF_LYMPHOCYTE_MEDIATED_IMMUNITY	3.051679	0
	GO_ADAPTIVE_IMMUNE_RESPONSE	3.041467	0
	GO_LYMPHOCYTE_COSTIMULATION	3.014854	0
	GO_ACTIVATION_OF_IMMUNE_RESPONSE	2.995625	0
	GO_DEFENSE_RESPONSE_TO_VIRUS	2.982795	0
	GO_REGULATION_OF_INNATE_IMMUNE_RESPONSE	2.97711	0
	GO_POSITIVE_REGULATION_OF_CELL_CELL_ADHESION	2.975723	0
	GO_POSITIVE_REGULATION_OF_CELL_ACTIVATION	2.969666	0
	GO_POSITIVE_REGULATION_OF_LYMPHOCYTE_MEDIATED_IMMUNITY	2.959197	0
	GO_REGULATION_OF_INTERFERON_GAMMA_PRODUCTION	2.958476	0
	GO_REGULATION_OF_HOMOTYPIC_CELL_CELL_ADHESION	2.951035	0
	GO_POSITIVE_REGULATION_OF_INTERFERON_GAMMA_PRODUCTION	2.947577	0
	GO_POSITIVE_REGULATION_OF_T_CELL_PROLIFERATION	2.943495	0
	GO_POSITIVE_REGULATION_OF_INNATE_IMMUNE_RESPONSE	2.933921	0
	GO_REGULATION_OF_LEUKOCYTE_MEDIATED_IMMUNITY	2.927325	0
	GO_INTERFERON_GAMMA_MEDIATED_SIGNALING_PATHWAY	2.918686	0
	GO_LYMPHOCYTE_ACTIVATION	2.916385	0
	GO_LEUKOCYTE_ACTIVATION	2.90934	0
	GO_RESPONSE_TO_VIRUS	2.907774	0
	GO_REGULATION_OF_LEUKOCYTE_PROLIFERATION	2.889759	0
	GO_REGULATION_OF_T_CELL_PROLIFERATION	2.884331	0
	GO_REGULATION_OF_ADAPTIVE_IMMUNE_RESPONSE	2.879126	0
	GO_RESPONSE_TO_INTERFERON_GAMMA	2.878551	0
	GO_POSITIVE_REGULATION_OF_LEUKOCYTE_PROLIFERATION	2.87801	0
	GO_IMMUNE_EFFECTOR_PROCESS	2.876739	0

Abbreviations: Gene, gene symbol; NES, normalized enrichment score; FDR, false discovery rate.