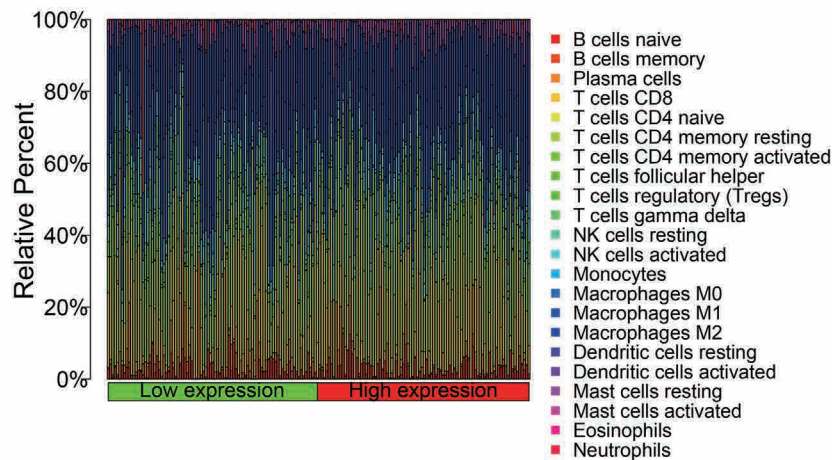
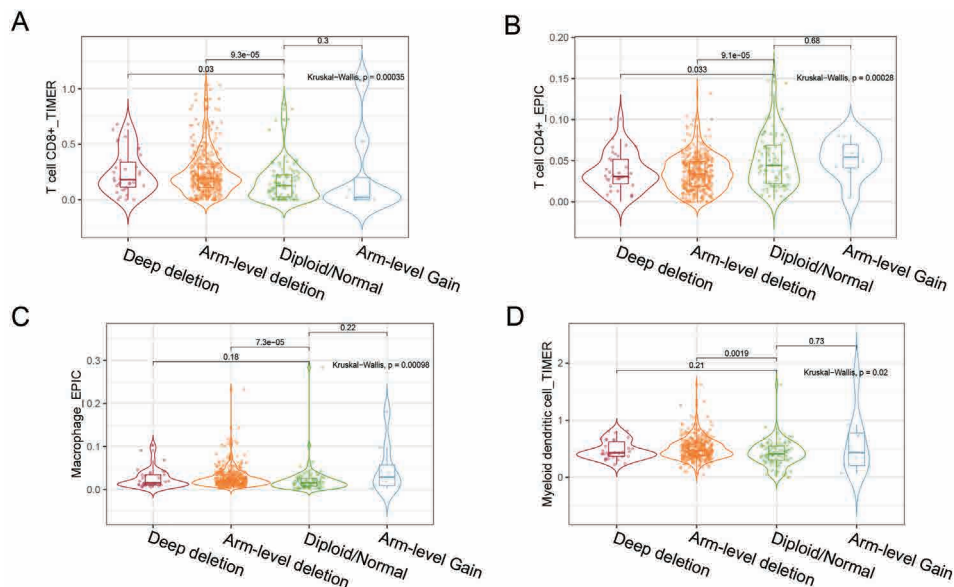


**Figure S1** The transduction efficacy of DNASE1L3 in ccRCC cells was determined using western blotting. ccRCC, clear cell renal cell carcinoma.



**Figure S2** Heatmap of relative immune cell infiltration levels between the high- and low-DNASE1L3 groups.



**Figure S3** Violin plots of the top 9 drugs with a significant difference in sensitivity between the high- and low-DNASE1L3 groups of ccRCC samples. ccRCC, clear cell renal cell carcinoma.

**Table S1** Univariate and multivariate analyses of clinicopathological characteristics and DNASE1L3 with overall survival in TCGA KIRC cohort

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.561 (0.403–0.779)	<0.001	0.61 (0.434–0.857)	0.0043
Gender	1.129 (0.813–1.568)	0.469	1.107 (0.786–1.558)	0.5616
Histologic grade	2.668 (1.829–3.893)	<0.001	1.679 (1.121–2.515)	0.012
Pathologic stage	3.99 (2.815–5.655)	<0.001	1.797 (0.812–3.981)	0.1484
Pathologic T	3.24 (2.329–4.507)	<0.001	1.25 (0.632–2.474)	0.5217
Pathologic N	0.822 (0.598–1.13)	0.228	0.867 (0.619–1.215)	0.4082
Pathologic M	3.474 (2.506–4.815)	<0.001	2.443 (1.653–3.61)	< 0.001
Tumor dimension	0.424 (0.3–0.599)	<0.001	0.943 (0.628–1.416)	0.7783
Tumor weight	0.562 (0.407–0.776)	<0.001	0.557 (0.394–0.788)	9e-04
DNASE1L3	0.505 (0.363–0.703)	<0.001	0.828 (0.585–1.17)	0.0285

TCGA, The Cancer Genome Atlas; HR, hazard ratio; CI, confidence interval.

**Table S2** Enriched pathways identified by gene set variation analysis

Enrichment pathway	logFC	AveExpr	t	PValue	B
HALLMARK_INFLAMMATORY_RESPONSE	-0.666411929	-0.042680113	-11.09173643	1.30E-25	47.26352526
HALLMARK_PI3K_AKT_SIGNALING	-0.355398535	-0.00803295	-8.005119501	9.04E-15	22.62776178
HALLMARK_IL2_STAT5_SIGNALING	0.375038246	0.019892002	7.078565282	5.19E-12	16.39408757
HALLMARK_APOPTOSIS	-0.223903386	0.00121603	5.149911711	3.81E-07	5.491271249
HALLMARK_COMPLEMENT	-0.192004368	-0.028986423	5.136586074	4.07E-07	5.426427293
HALLMARK_UV_RESPONSE_DN	0.172732956	0.014415888	4.924004275	1.17E-06	4.412415036
HALLMARK_MYOGENESIS	0.18997163	-0.015052083	4.754523374	2.63E-06	3.631769163
HALLMARK_NOTCH_SIGNALING	0.191859924	0.020362396	4.649311134	4.31E-06	3.159669916
HALLMARK_APICAL_JUNCTION	0.215732098	0.017976647	4.529249881	7.47E-06	2.632747157
HALLMARK_BILE_ACID_METABOLISM	0.21017882	0.002412222	4.503938433	8.38E-06	2.523274498
HALLMARK_CHOLESTEROL_HOMEOSTASIS	0.127391723	0.023398391	3.980730458	7.93E-05	0.387799408
HALLMARK_HYPOXIA	-0.180752546	-0.045033923	-3.201705765	0.001456654	-2.331246004
HALLMARK_ALLOGRAFT_REJECTION	0.110602798	0.016886653	2.93869075	0.00345449	-3.121851806
HALLMARK_KRAS_SIGNALING_UP	-0.125074195	0.008714008	-2.740486394	0.006363122	-3.674439969
HALLMARK_HEME_METABOLISM	-0.131915054	-0.012703651	-2.677777628	0.007664804	-3.841489401
HALLMARK_ADIPOGENESIS	-0.092579588	-0.00809113	-2.387895763	0.017330251	-4.564797316
HALLMARK_FATTY_ACID_METABOLISM	-0.12498338	-0.022695805	-2.325213712	0.020475813	-4.710579718
HALLMARK_TGF_BETA_SIGNALING	-0.099997657	-0.003749942	-2.072604799	0.038741326	-5.259578265
HALLMARK_E2F_TARGETS	-0.09369153	-0.015703605	-1.98801535	0.04737661	-5.429577429
HALLMARK_XENOBIOTIC_METABOLISM	-0.108768526	-0.005630683	-1.927383658	0.054520591	-5.547141625
HALLMARK_PEROXISOME	-0.069199396	-0.027588037	-1.290287285	0.197571064	-6.56474049
HALLMARK_SPERMATOGENESIS	0.058876175	0.003957631	1.171246154	0.242079921	-6.710551194
HALLMARK_GLYCOLYSIS	-0.055958993	-0.026284211	-1.1147388	0.26551922	-6.774857826
HALLMARK_ESTROGEN_RESPONSE_LATE	0.038413851	0.008076799	0.854226229	0.393405029	-7.030383484
HALLMARK_ANDROGEN_RESPONSE	-0.039432266	-0.008307564	-0.839358563	0.401685238	-7.042933983
HALLMARK_KRAS_SIGNALING_DN	-0.036312776	-0.021754717	-0.838926409	0.401927475	-7.043295499
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	0.04175892	0.012279035	0.790635862	0.429546286	-7.082523126
HALLMARK_P53_PATHWAY	0.036245963	-0.011319057	0.666435346	0.505452501	-7.172759301
HALLMARK_G2M_CHECKPOINT	0.025410291	0.008484358	0.601358806	0.547884425	-7.213909222
HALLMARK_MTORC1_SIGNALING	0.030257615	-0.006865279	0.587601258	0.557075801	-7.222068446
HALLMARK_UV_RESPONSE_UP	0.01707857	-0.009392713	0.335351598	0.737506135	-7.338230311
HALLMARK_TNFA_SIGNALING_VIA_NFKB	-0.007791369	-0.017992909	-0.14451614	0.885153464	-7.383937138
HALLMARK_MITOTIC_SPINDLE	-0.005301183	-0.011054946	-0.140510359	0.888315609	-7.384507059
HALLMARK_IL6_JAK_STAT3_SIGNALING	0.001264934	-0.015509815	0.028854342	0.976992732	-7.393946725