

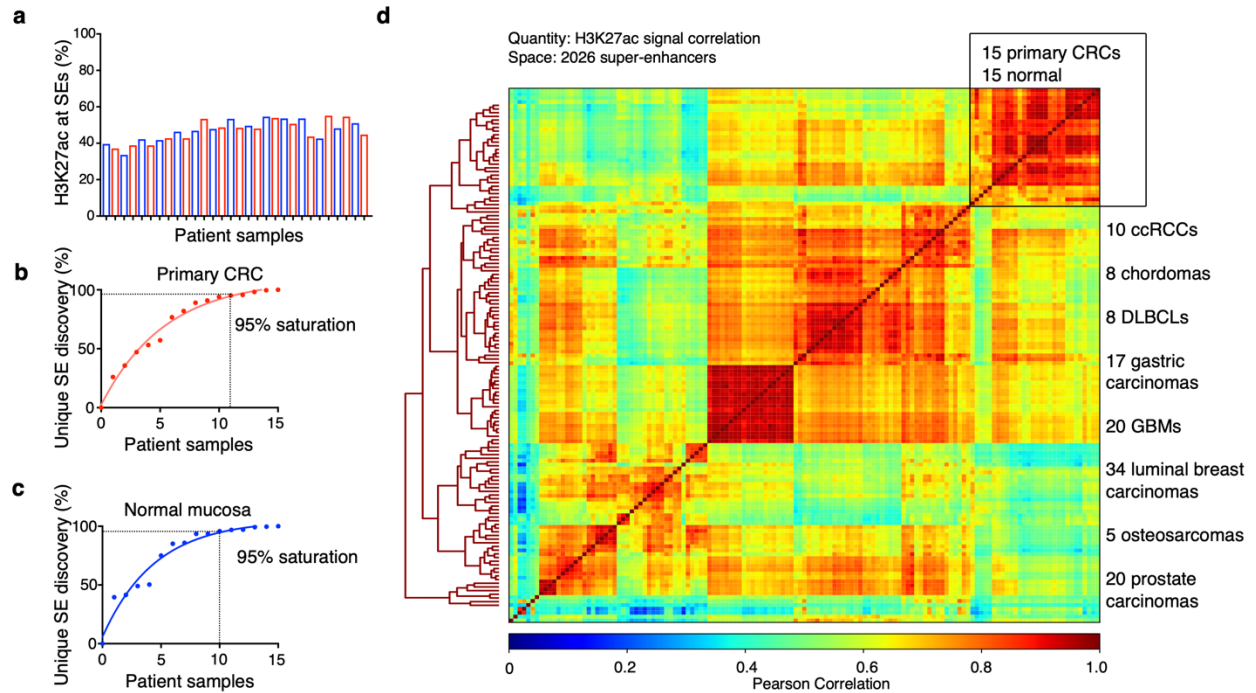


Fig. S1: The super-enhancer landscape in primary CRC and patient-matched adjacent normal colon epithelium. **a** Percentage of H3K27ac signal deposited solely at SEs. Each red or blue bar is an independent primary CRC ($n = 15$ independent samples) or normal colon epithelium sample ($n = 15$ independent samples), respectively. **b**, **c** Power analyses indicating cumulative percentage saturation of unique super-enhancer discovery with the addition of each patient in cohort. CRC in red, normal mucosa in blue. **d** Unsupervised hierarchical clustering, H3K27ac signal Pearson correlations at 2026 SEs from 30 colorectal samples in our cohort ($n = 15$ independent CRC, $n = 15$ independent normal mucosae) against clear cell renal cell carcinomas (ccRCC, $n = 10$ independent tumors), chordomas ($n = 8$ independent tumors), diffuse large B-cell lymphomas (DLBCL, $n = 4$ independent tumors), gastric carcinomas ($n = 17$ independent tumors), glioblastomas ($n = 20$ independent tumors), luminal breast cancer ($n = 34$ independent tumors),

osteosarcoma ($n = 5$ independent tumors), and prostate carcinomas ($n = 20$ independent tumors).

Please see Methods for accessions. Source data are provided as a Source Data file.

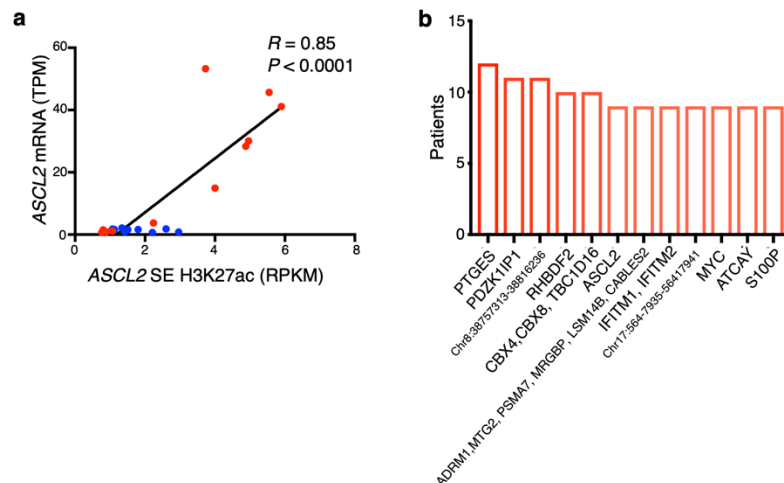


Fig. S2: The super-enhancer landscape in CRC identifies target genes. **a** Simple linear regression analysis of H3K27ac signal deposition at the *ASCL2* SE and *ASCL2* gene expression using sample matched CRC ($n = 11$ patients) and normal epithelium ($n = 10$ patients). Although 15 primary CRCs and 15 normal colons were used for ChIP-seq analyses, sample-matched RNA-seq data was only available for 11 CRCs and 10 normal colons, respectively. All available data was used in this analysis. Please see Methods for details. **b** Histogram of 12 candidate SEs ranked by gained recurrence (number of patients exhibiting SE gain, out of a total of 15). Please see Methods for accessions. Source data are provided as a Source Data file.

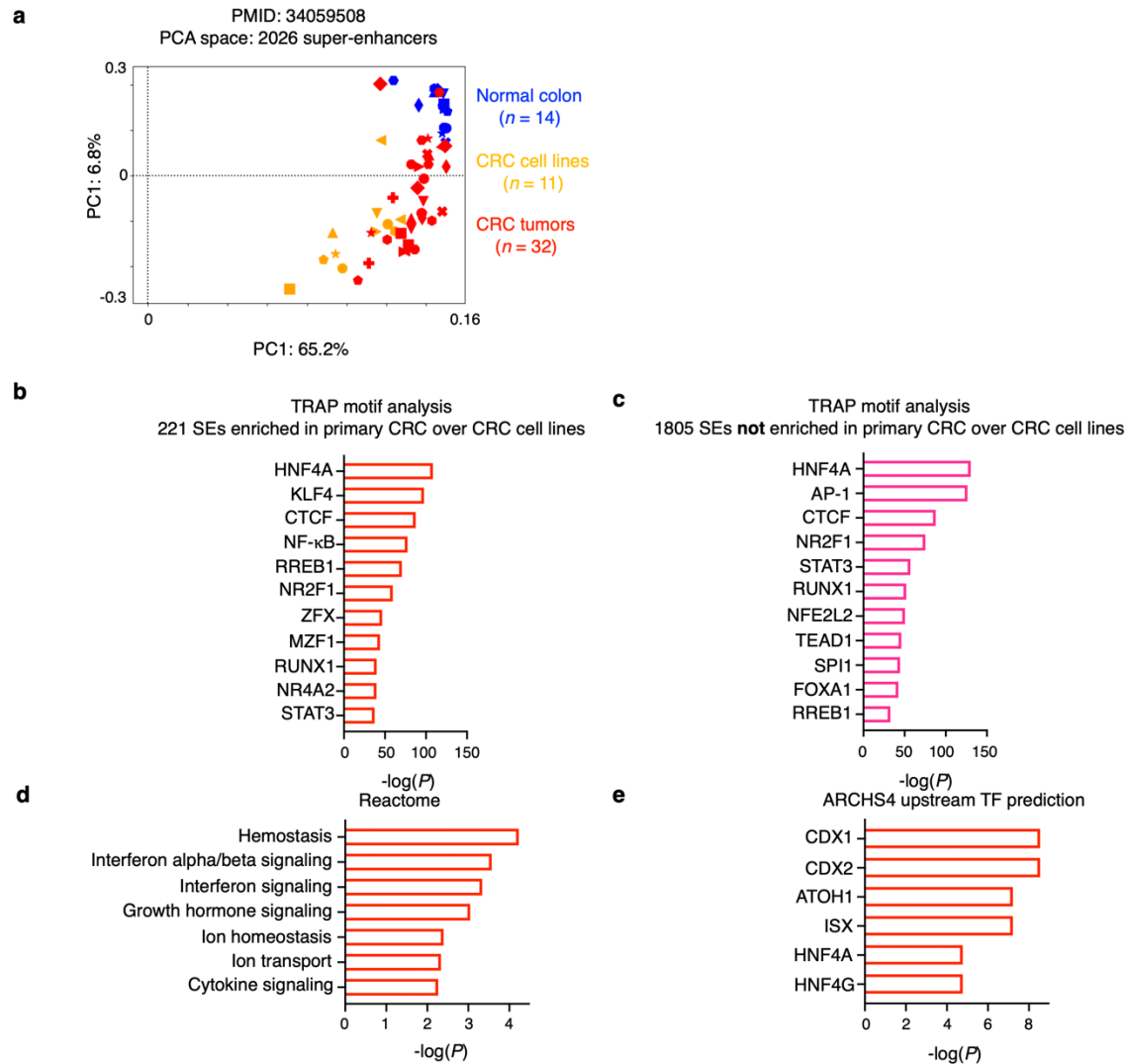
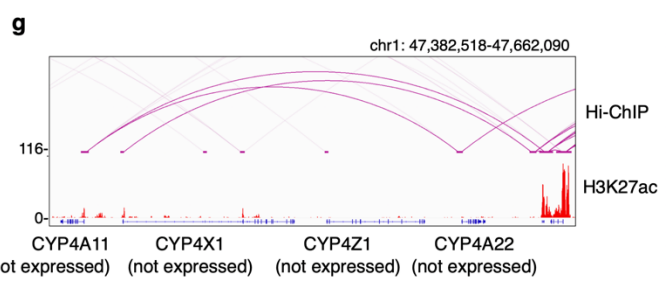
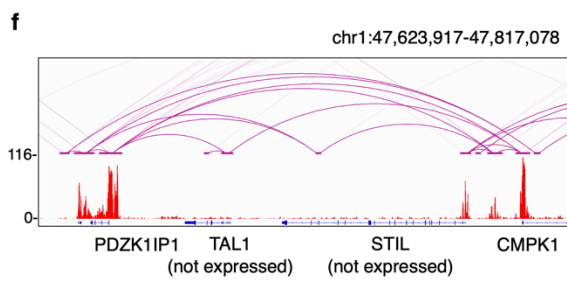
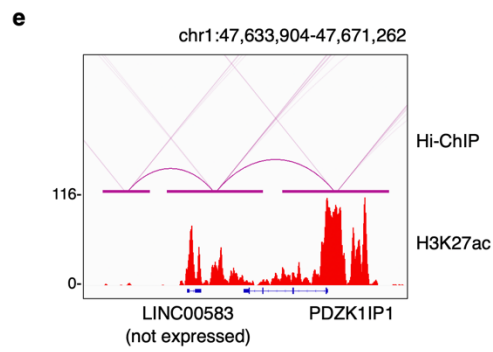
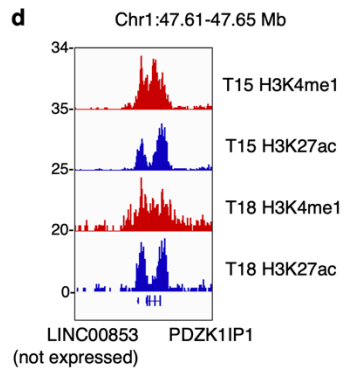
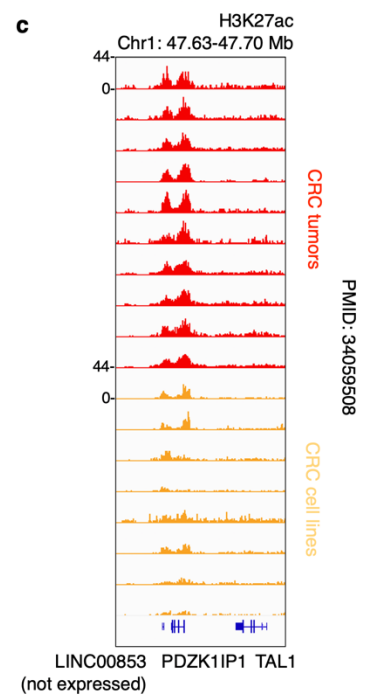
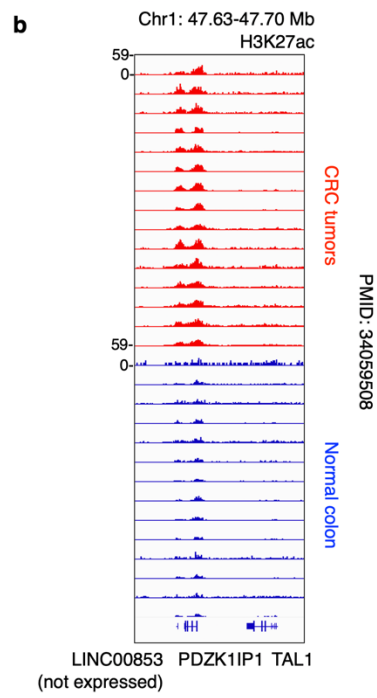
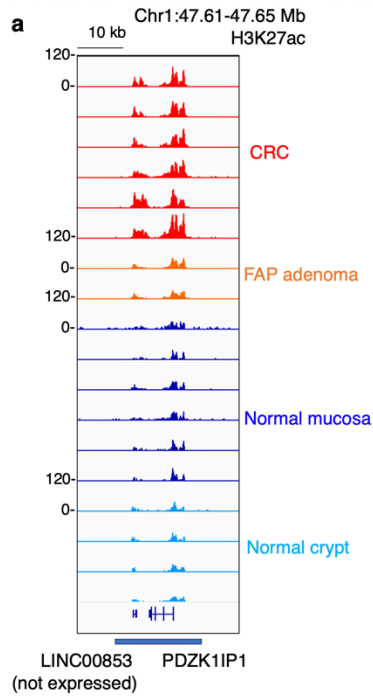


Fig. S3: Characterization of super-enhancers specific to primary CRC under-represented in CRC cell lines. **a** PCA of H3K27ac signal at 2026 SEs in CRC ($n = 32$ independent tissue samples), CRC cell lines ($n = 11$ independent cell lines), and normal colon mucosa ($n = 14$ independent tissue samples). Data from Orouji et al, please see Methods for accessions. **b** TRAP motif analysis of open chromatin regions within primary CRC-enriched SEs. Open chromatin regions defined by ATAC-seq data from 81 independent primary CRC tumors from TCGA. Please see Methods for accessions. Sequences are compared against all human promoters with a Benjamini-Hochberg correction to generate a P -value. **c** TRAP motif analysis of open chromatin regions within primary

CRC non-enriched SEs. Sequences are compared against all human promoters with a Benjamini-Hochberg correction to generate a *P*-value. **d** ENRICHR pathway analysis of a primary CRC-enriched SE gene signature, using the Reactome gene set database. The Fisher's exact test is used for *P*-value. **e** ENRICHR prediction of upstream transcription factors of the primary CRC-enriched SE gene signature using the ARCHS4 tool. The Fisher's exact test is used for *P*-value. Source data are provided as a Source Data file.



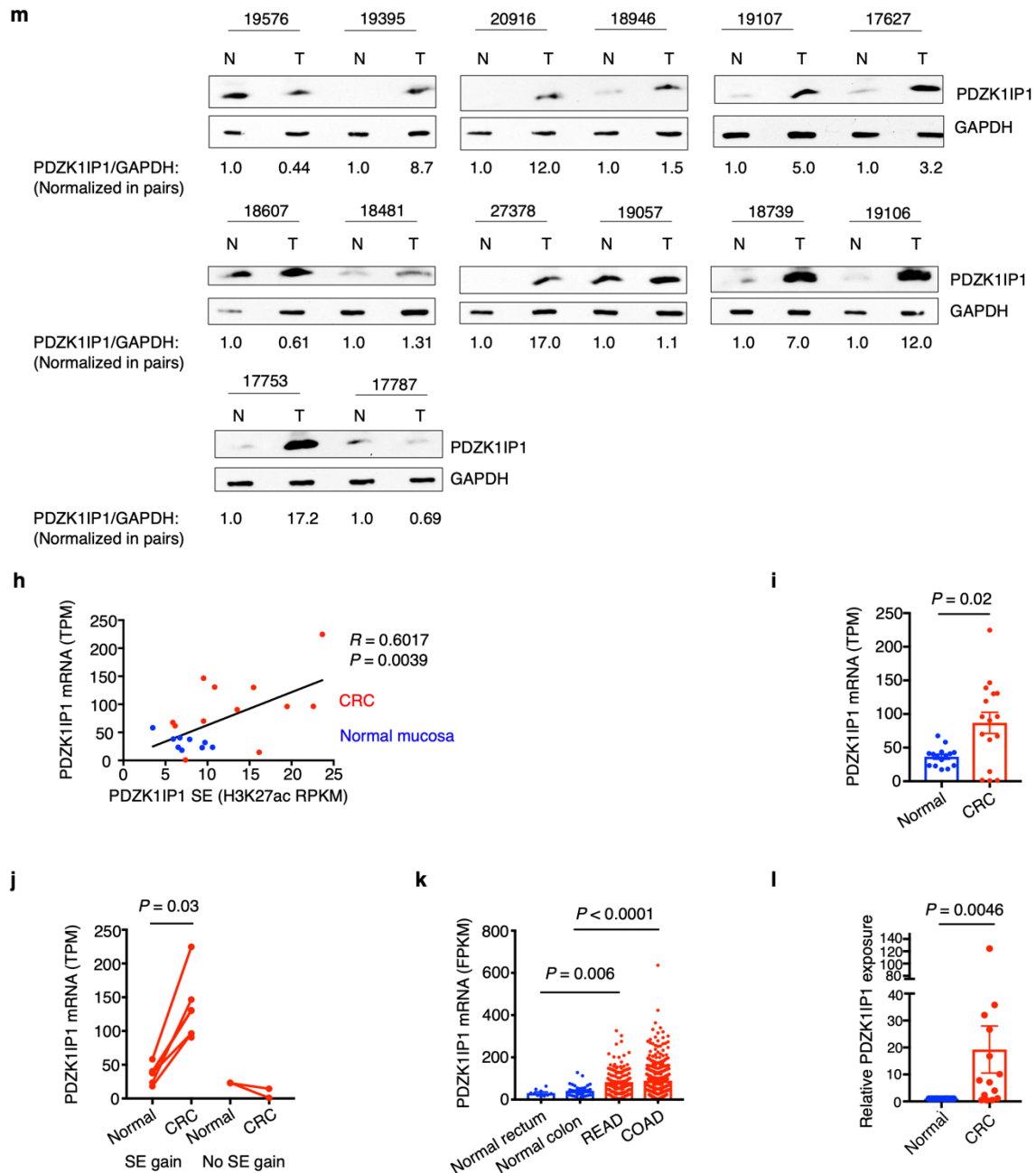


Fig. S4: *PDZK1IP1* and its super-enhancer are up-regulated in CRC. **a** H3K27ac ChIP-seq track at the *PDZK1IP1* SE (underlined) in 6 representative independent primary CRCs, 2 FAP adenomas, 6 representative independent normal colon epithelium samples, and 4 normal colon crypts. **b** H3K27ac ChIP-seq track at the *PDZK1IP1* SE in 15 representative independent primary CRCs and normal colon epithelium samples. Data from Orouji et al. **c** H3K27ac ChIP-seq track at

the *PDZK1IP1* SE in 10 representative independent primary CRCs and 8 representative CRC cell lines. Data from Orouji et al. **d-g** H3K27ac ChIP-seq and Hi-ChIP integration showing genome interactions at the *PDZK1IP1* super-enhancer. Y-axes for all ChIP-seq tracks are scaled to the same range. Please see Methods for accessions. All data presented as mean $\pm$ s.e.m and significance determined using two-sided Student's *t*-test. **h** Simple linear regression analysis of *PDZK1IP1* SE H3K27ac signal and *PDZK1IP1* mRNA expression using sample-matched sequencing data. For CRC *n* = 11 independent patient samples, for normal mucosa *n* = 10. Although 15 primary CRCs and 15 normal colons were used for ChIP-seq analyses, sample-matched RNA-seq data was only available for 11 CRCs and 10 normal colons, respectively. All available data was used in this analysis. **i, j** *PDZK1IP1* mRNA expression by RNA-seq in our cohort of patients. For CRC *n* = 16 independent tumors; for normal mucosa *n* = 15 independent tissue samples. Two-sided Student's *t*-test. **k** *PDZK1IP1* mRNA expression by RNA-seq between normal colon (*n* = 42 independent cases), normal rectum (*n* = 10 independent cases) rectal adenocarcinoma (READ, *n* = 166 independent cases), and colon adenocarcinoma (COAD, *n* = 475 independent cases) from TCGA. Two-sided Student's *t*-test. **l, m** *PDZK1IP1* protein levels by immunoblot (fold change, CRC over normal for each pair). *n* = 14 de-identified patients, each with a matched tumor normal pair. T – tumor, N – matched normal. Five-digit de-identified patient number. Two-sided Student's *t*-test. **j** H3K4me1 and H3K27ac ChIP-seq tracks at the *PDZK1IP1* super-enhancer in two CRC samples, which met ROSE criteria for super-enhancer calling using either as input. Source data are provided as a Source Data file.

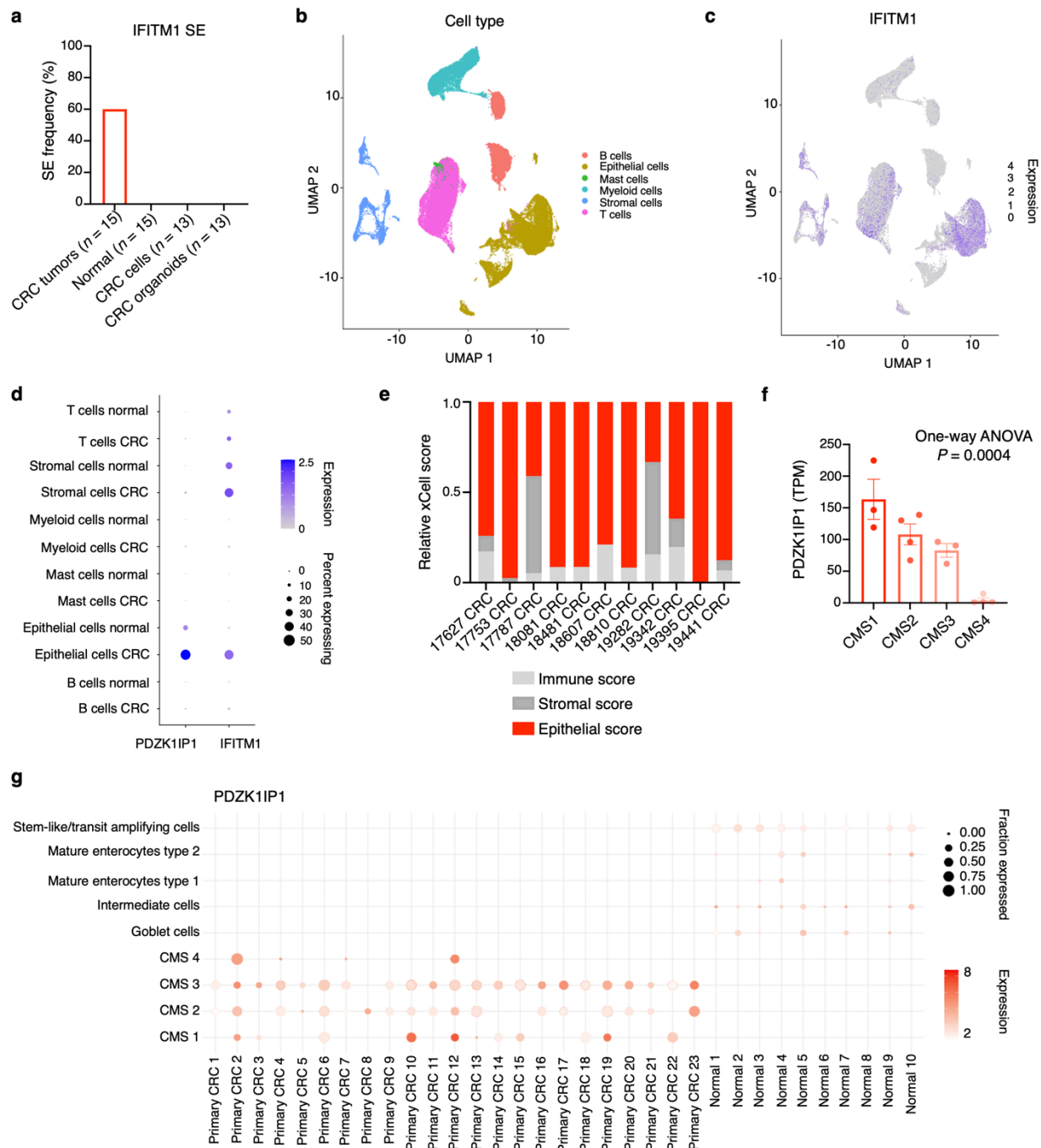


Fig. S5: Characterization of CRC-enriched SEs at *IFITM1* and *PDZK1IP1*. **a** Frequency of samples meeting ROSE criteria for SE calling at the *IFITM1* locus. $n = 15$ independent CRC tumors, $n = 15$ independent patient-matched normal colon mucosae, $n = 13$ independent CRC cell lines, $n = 9$ independent 3D CRC organoids. **b**, **c** UMAP of single cells from 23 independent

primary CRC tumors and 10 independent adjacent patient-matched normal colons merged into a single plot, annotated with cell type and *IFITM1* expression. Please see Methods for accessions. **d** Dot plot of *PDZK1IP1* or *IFITM1* expression in single cells from primary CRC or adjacent normal colon epithelium. **e** xCell de-convolution of bulk tumor RNA-seq into putative epithelial, immune, and stromal compositions. Out of the 15 primary CRCs for which H3K27ac ChIP-seq data is available, only 11 have sample-matched bulk tumor RNA-seq data. All available data was used in this analysis. **f** RNA-seq expression of *PDZK1IP1* by CMS. For CMS1 ($n = 3$ patients), for CMS2-4 ($n = 4$ patients per group). Data presented as mean $\pm$ s.e.m. **g** Dot plot of *PDZK1IP1* expression in single cells of epithelial origin, from either primary CRC ($n = 23$ independent cases) or patient-matched adjacent normal epithelium ($n = 10$ independent cases). CMS refers to the consensus molecular subtypes of CRC as previously assigned. Please see Methods for accessions. Source data are provided as a Source Data file.

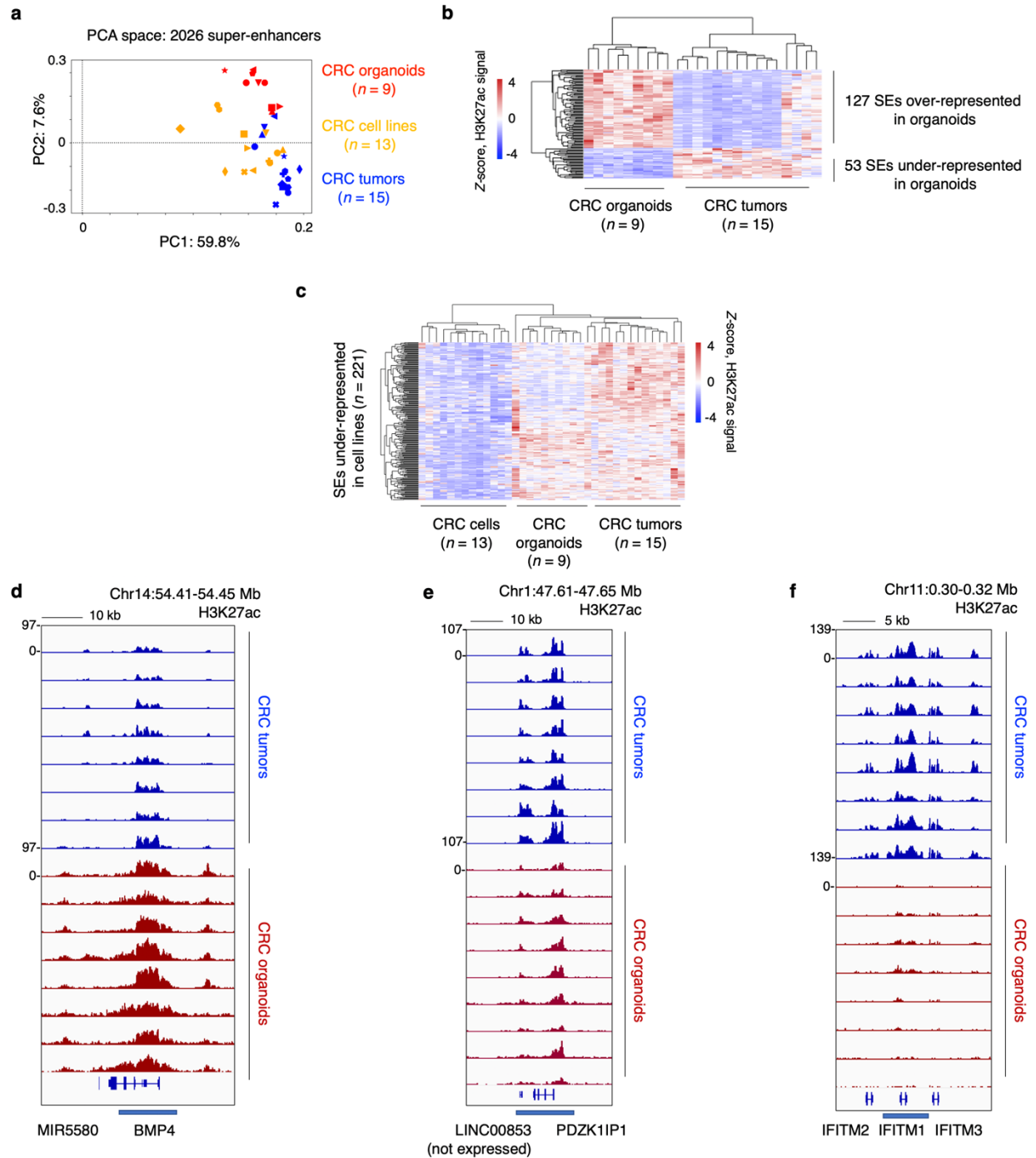


Fig. S6: Super-enhancers specific to primary CRC specimens and not recapitulated in 3D

CRC organoids. **a** PCA of H3K27ac signal at 2026 SEs in CRC ($n = 15$ independent tissue samples), CRC 3D organoids (derived from $n = 9$ independent patients), and CRC cell lines ($n = 13$ independent lines). Please see Methods for accessions. **b** Heatmap of H3K27ac signal (Z-score)

between CRC tumors and CRC 3D organoids with unsupervised hierarchical clustering at 180 differentially expressed SEs (absolute mean $\log_2$ fold change >1 , $P < 0.01$). **c** Incorporation of 3D CRC organoids into the heatmap of 221 SEs down-regulated in 2D CRC cell lines from Figure 2. **d** H3K27ac ChIP-seq track of the SE at *BMP4* (underlined) in $n = 8$ representative primary CRCs and $n = 8$ representative 3D CRC organoid cultures. Y-axes of all ChIP-seq tracks are scaled to the same range [0-97]. **e** H3K27ac ChIP-seq track of the SE at *PDZK1IP1* (underlined) in $n = 8$ representative primary CRCs and $n = 8$ representative 3D CRC organoid cultures. Y-axes of all ChIP-seq tracks are scaled to the same range [0-107]. **f** H3K27ac ChIP-seq track of the SE at *IFITM1* (underlined) in $n = 8$ representative primary CRCs and $n = 8$ representative 3D CRC organoid cultures. Y-axes of all ChIP-seq tracks are scaled to the same range [0-139].

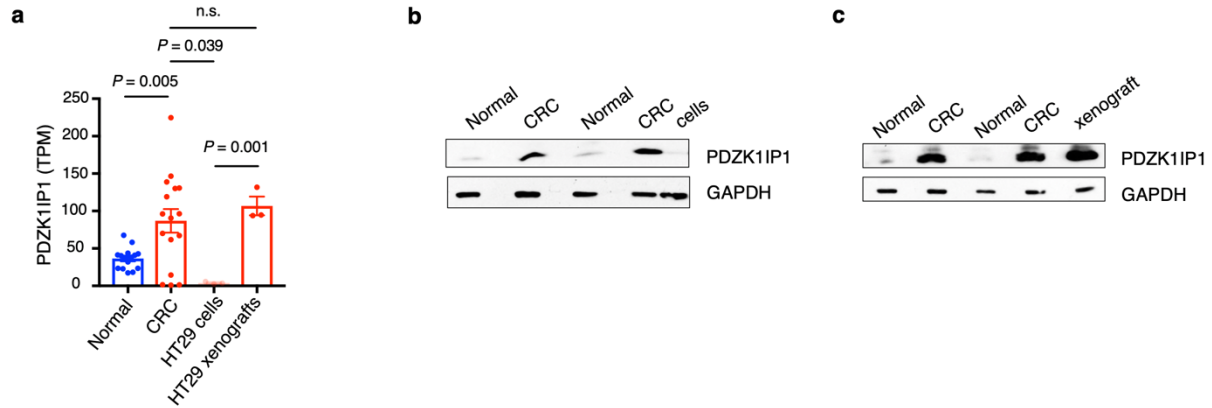
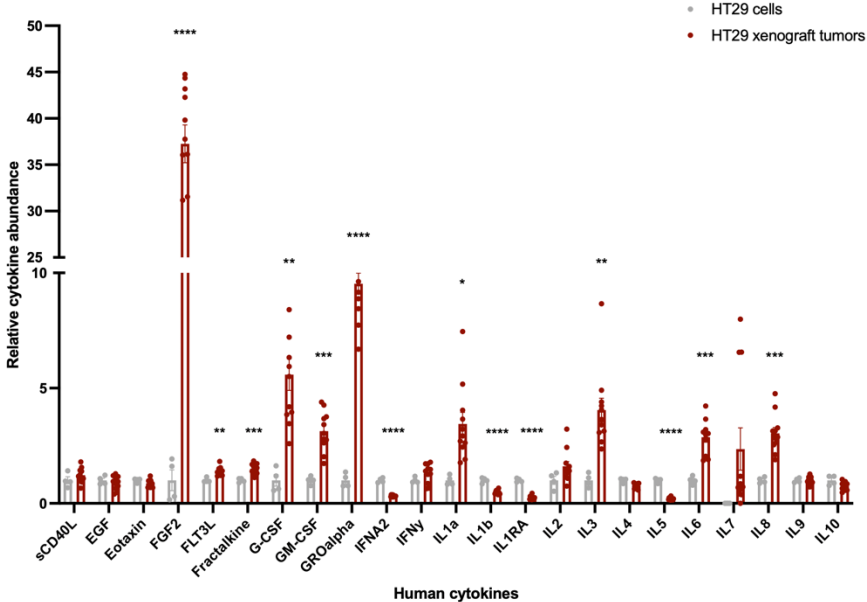


Fig. S7: *PDZK1IP1* expression levels in HT29 xenografts recapitulate those in primary CRC.

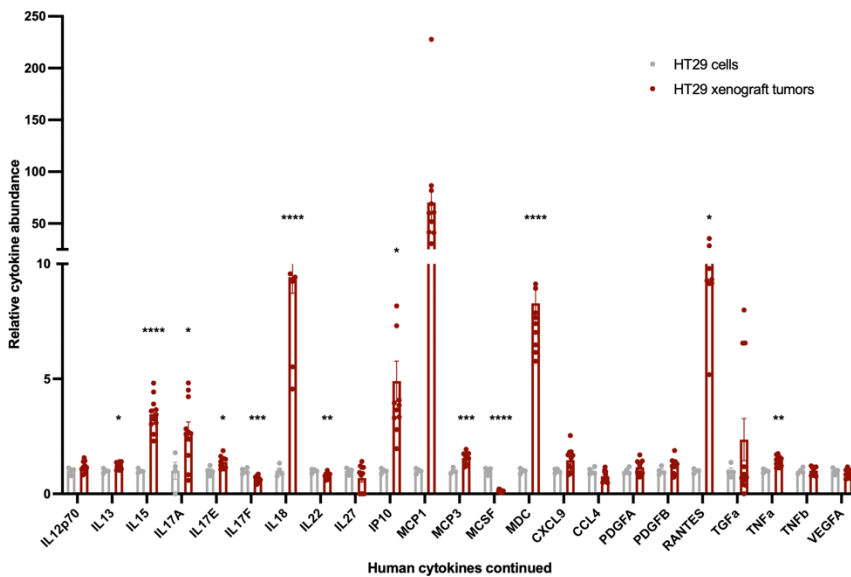
a *PDZK1IP1* expression by RNA-seq, HT29 cells ($n = 3$ biological replicates), HT29 xenografts ($n = 3$ independent tumors), normal mucosa ($n = 15$ independent tissue samples), and primary CRC ($n = 16$) independent tumors. Data presented as mean $\pm$ s.e.m. Significance was determined using two-sided Student's *t*-test. **b, c** *PDZK1IP1* expression by immunoblot across four independent patient-matched CRC-normal colon pairs, versus HT29 cells or HT29 xenograft tumors. Source data are provided as a Source Data file.

Metagene of up-regulated H3K27ac enhancer peaks (mean $\log_2$ fold change > 1) in HT29 xenograft tumors ($n = 3$ independent tumors) over HT29 parental cells maintained in culture. The Fisher's exact test is used for P -value. **d** TRAP TF motif analysis output for H3K27ac enhancers shown in **c**. Sequences are compared against all human promoters with a Benjamini-Hochberg correction to generate a P -value. **e-h** Immunoblot of PDZK1IP1 levels in sgRELA or sgNeg HT29 cells treated with cytokines. **i** Immunoblot of PDZK1IP1 levels in sgSTAT3 or sgNeg HT29 cells treated with cytokines. Source data are provided as a Source Data file.

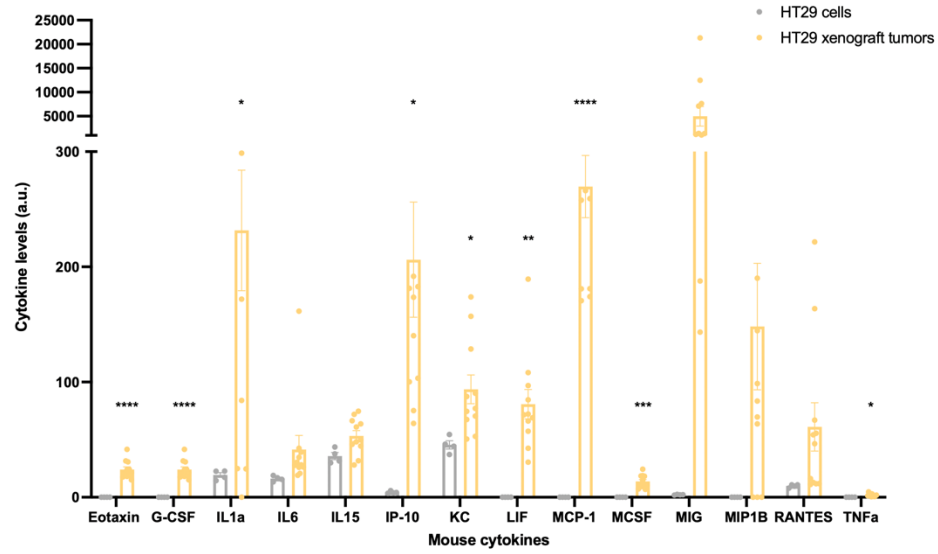
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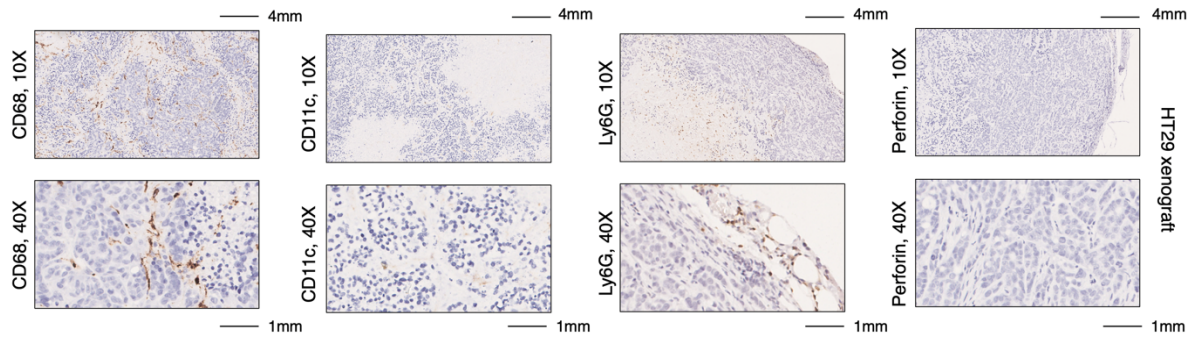
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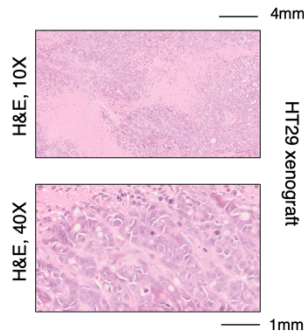
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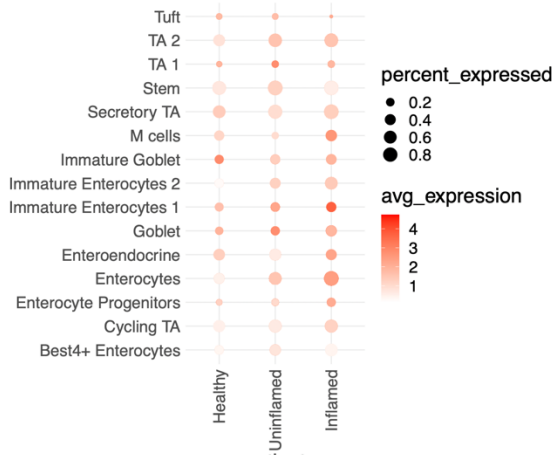


Fig. S9: Xenograft tumors exhibit increased pro-inflammatory cytokines, chemokines, and growth factors upstream of *PDZK1IP1*. a-b Luminex-based human and c mouse cytokine

profiling of HT29 xenograft tumor lysates ($n = 11$ biological replicates) and HT29 parental cells ($n = 4$ biological replicates) in culture (performed by EveTechnologies). Data presented as mean $\pm$ s.e.m. Significance was determined using two-sided Student's t -test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. Human IL-7 and mouse eotaxin, G-CSF, LIF, MCP-1, MCSF, MIP1B, and TNFa were undetectable in HT29 cells. **d, e** IHC and H&E staining of immune cell markers in HT29 xenograft tumors. **f** Dot plot of *PDZK1IP1* expression in single cells of epithelial origin from healthy patients without colitis, uninflamed colon of patients with colitis, and inflamed colon of patients with colitis. Source data are provided as a Source Data file.

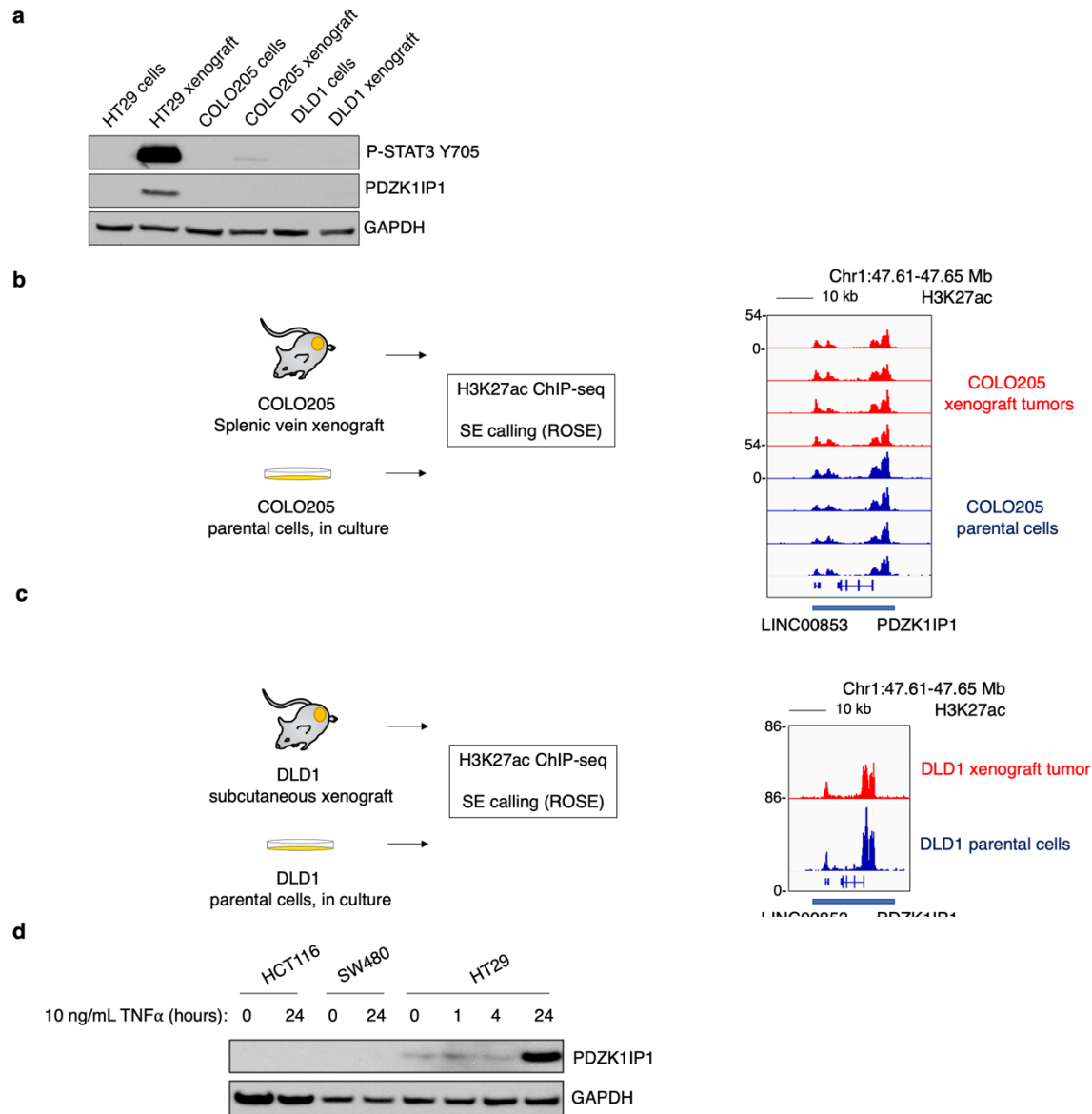


Fig. S10: Cell-specific super-enhancer reprogramming in response to microenvironment. a

PDZK1IP1 protein levels correlated with phosphorylation of STAT3 at the Y705 residue in

parental cells maintained in culture or subcutaneous xenografts in nude mice. **b** Experiment

overview. A xenograft model of COLO205 liver metastases in nude mice via splenic vein injection.

H3K27ac ChIP-seq of COLO205 xenograft tumors in nude mice ($n = 4$ independent tumors) and

COLO205 parental cells maintained in culture ($n = 4$ biological replicates). Y-axes of all ChIP-

seq tracks are scaled to the same range [0-54]. **c** Experiment overview. A subcutaneous xenograft

tumor model of DLD1 cells in nude mice. H3K27ac ChIP-seq of DLD1 xenograft tumors or DLD1 parental cells maintained in culture. Y-axes of all ChIP-seq tracks are scaled to the same range [0-86]. **d** *PDZK1IP1* protein levels by immunoblot with or without TNF α stimulation in HCT116, SW480, or HT29 cells. Panels **b**, **c** contain medical illustrations from SMART Servier Medical Art, reproduced with permission, licensed under a Creative Commons Attribution 3.0 unported license.

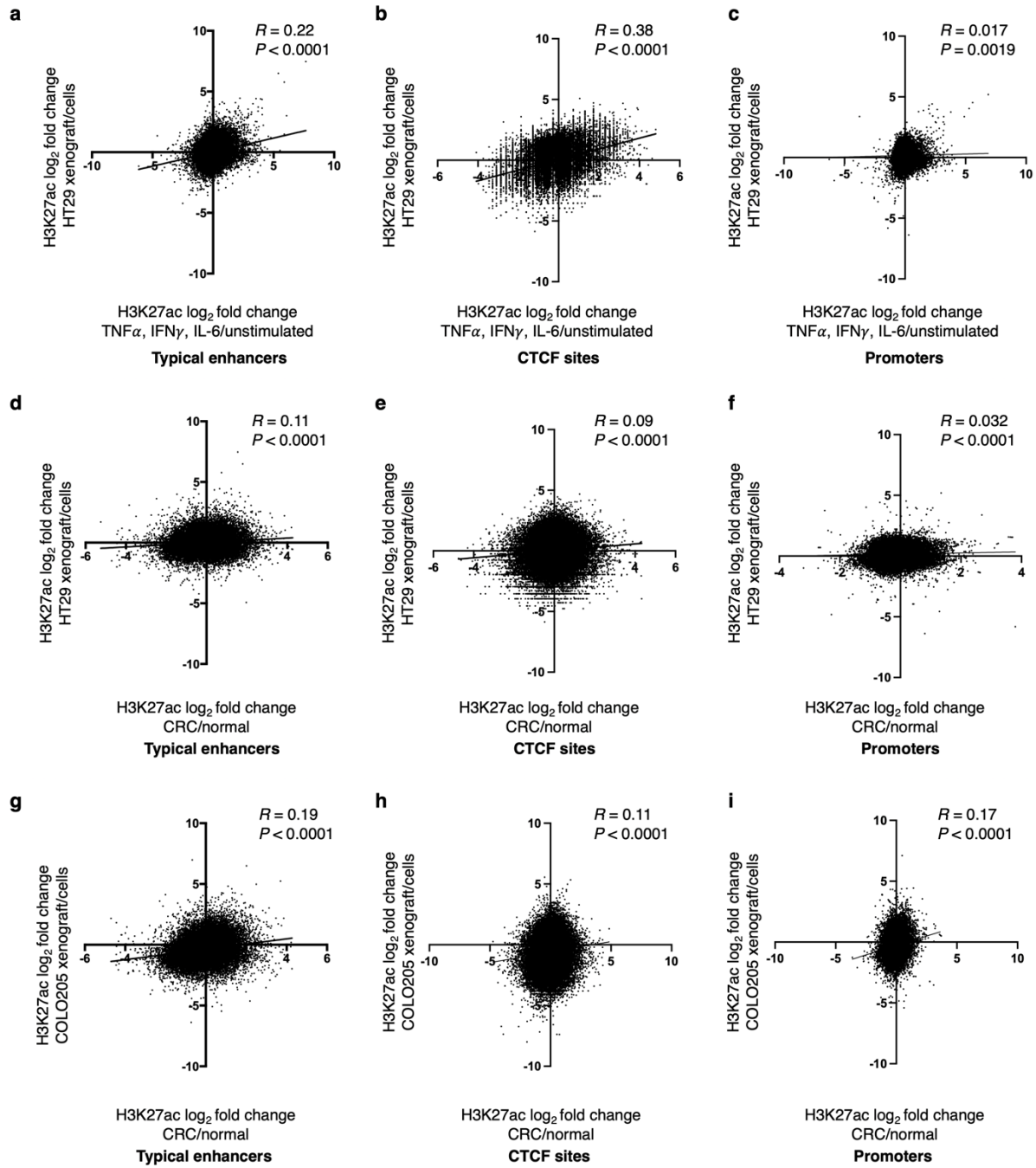


Figure S11. The tumor microenvironment recapitulates enhancer reprogramming in cancer.

a-c Simple linear regression analysis between $\log_2$ fold change H3K27ac signal in HT29 nude mice subcutaneous xenografts ($n = 3$ independent tumors) over parental cells *in vitro*, and $\text{TNF}\alpha$, $\text{IFN}\gamma$, IL-6 stimulated cells (10 ng/mL, 16 hours) over unstimulated cells. Each dot represents a unique typical enhancer, CTCF site, or promoter. **d-f** Simple linear regression analysis between $\log_2$ fold change H3K27ac signal in HT29 xenografts/parental cells and CRC/normal mucosa. Each dot represents a unique typical enhancer, CTCF site, or promoter. **g-i** Simple linear regression analysis between $\log_2$ fold change H3K27ac signal in COLO205 xenografts/parental cells and CRC/normal mucosa. Each dot represents a unique typical enhancer. Source data are provided as a Source Data file.

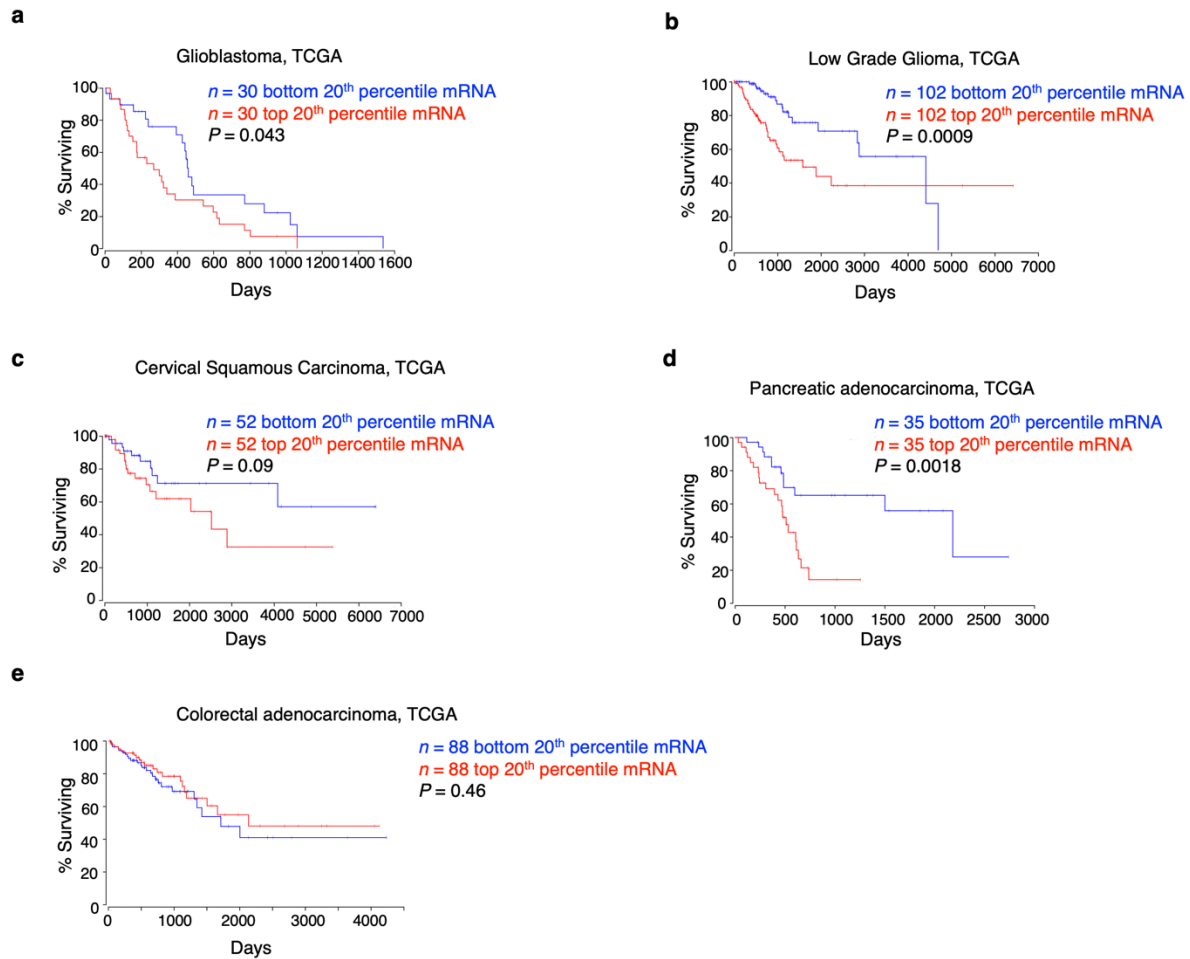


Fig. S12: High *PDZK1IP1* expression negatively prognosticates patient survival in multiple cancers but not CRC. a-e Kaplan-Meier analysis and survival curves of *PDZK1IP1* high (top 20% mRNA, in red) and low (bottom 20% mRNA, in blue) cancer cases. Patient survival and gene mRNA expression data from TCGA, visualized using OncoLnc.

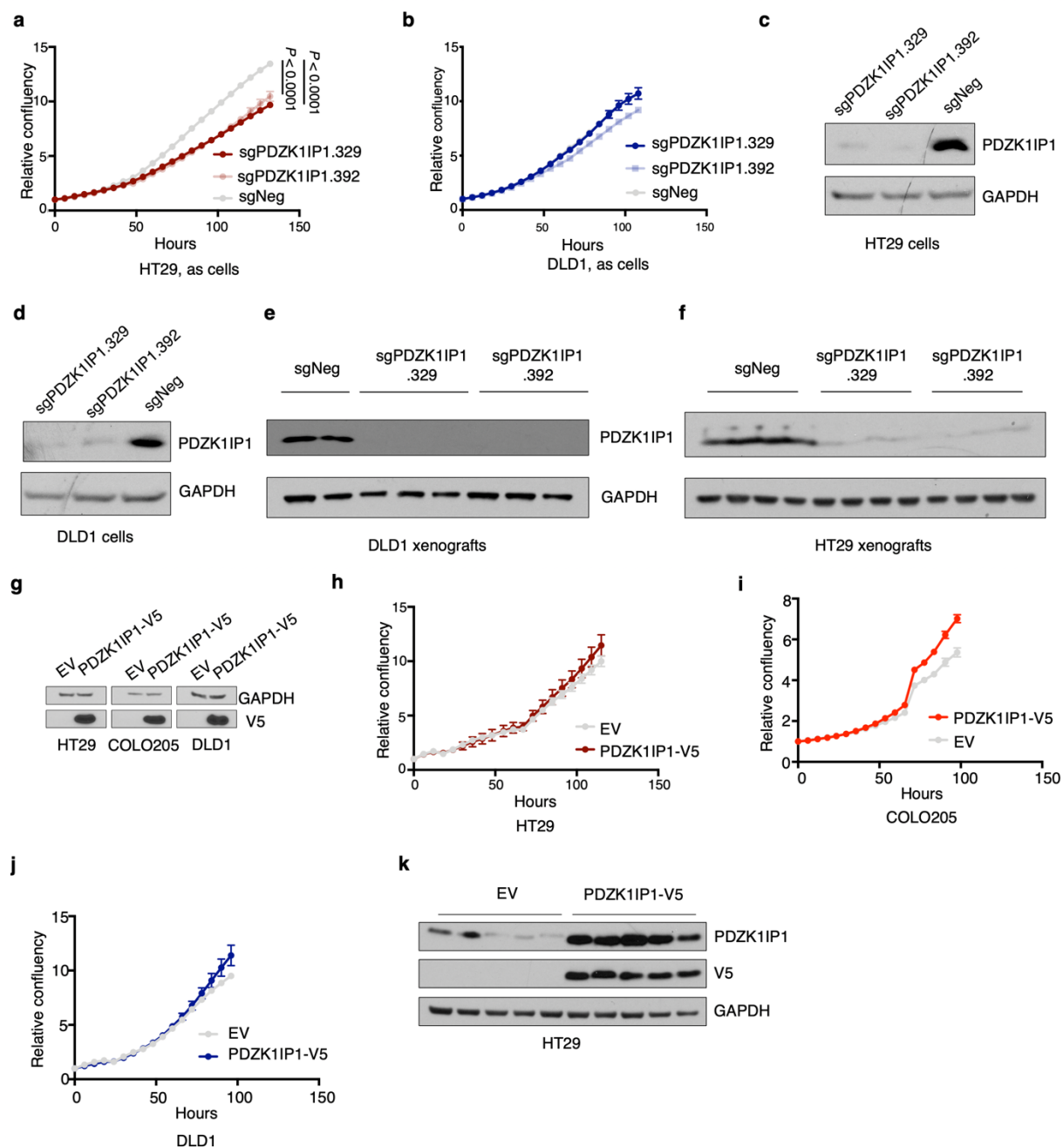


Fig. S13: *PDZK1IP1* does not affect CRC proliferation in culture. **a, b** Incucyte 2D growth curves of sgNeg or sgPDZK1IP1 cells ($n = 6$ biological replicates per group). Data presented as

mean $\pm$ s.e.m. Significance was determined using two-sided Student's *t*-test. **c, d** *PDZK1IP1* protein levels by immunoblot in HT29 and DLD1 cells between sgPDZK1IP1 and sgNeg. Data presented as mean $\pm$ s.e.m. **e, f** *PDZK1IP1* protein levels by immunoblot in HT29 and DLD1 subcutaneous xenograft tumors in nude mice between sgPDZK1IP1 and sgNeg. **g** Re-introducing exogenous *PDZK1IP1* expression *in vitro*. **h-j** Incucyte 2D growth curves of EV or PDZK1IP1-V5 expressing cells in HT29, COLO205, or DLD1 (*n* = 6 biological replicates per group). Data presented as mean $\pm$ s.e.m. **k** *PDZK1IP1* protein levels by immunoblot in HT29 subcutaneous xenograft tumors in nude mice between EV and PDZK1IP1-V5 expressing cells. Source data are provided as a Source Data file.

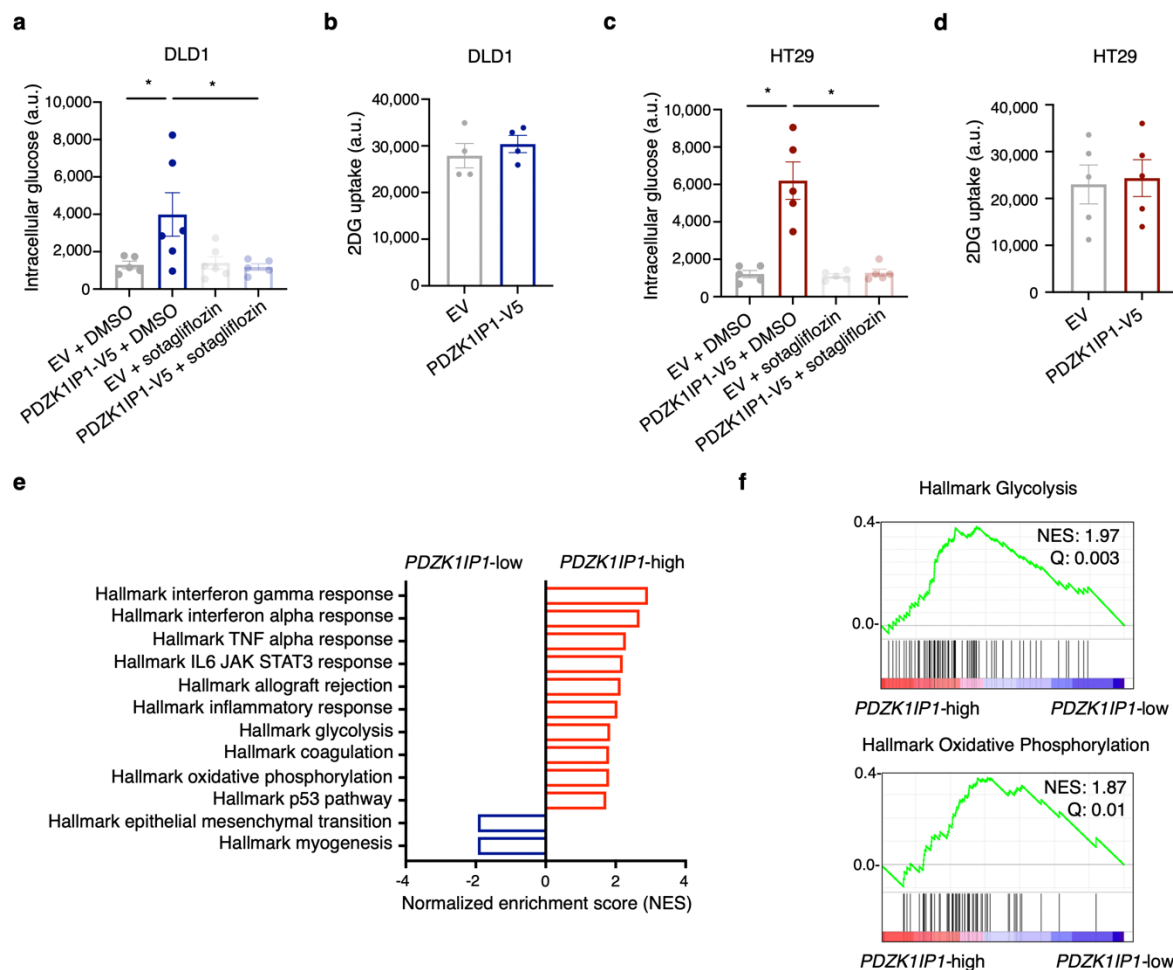


Fig. S14: *PDZK1IP1* increases glucose uptake and is linked to cancer metabolism. **a, c** Cellular glucose levels by fluorometric assay in cell lysates in the presence or absence of 25 μ M sotagliflozin. For HT29 ($n = 5$ biological replicates for per group) and DLD1 ($n = 5$ biological replicates for EV + DMSO and PDZK1IP1-v5 + sotagliflozin; $n = 6$ for PDZK1IP1-V5 + DMSO and EV + sotagliflozin). Data presented as mean $\pm$ s.e.m. Significance was determined using two-sided Student's t -test. * $P < 0.05$ **b, d** 2DG uptake by luminescent assay in cell lysates. For HT29 ($n = 5$ biological replicates per group) and DLD1 ($n = 4$ biological replicates per group). Data

presented as mean $\pm$ s.e.m. **e, f** Hallmarks of Cancer GSEA of RNA-seq expression data from *PDZK1IP1*-high (top 50% mRNA expression) versus *PDZK1IP1*-low (bottom 50% mRNA expression) primary CRCs from TCGA ($n = 342$ independent tumors). Source data are provided as a Source Data file.

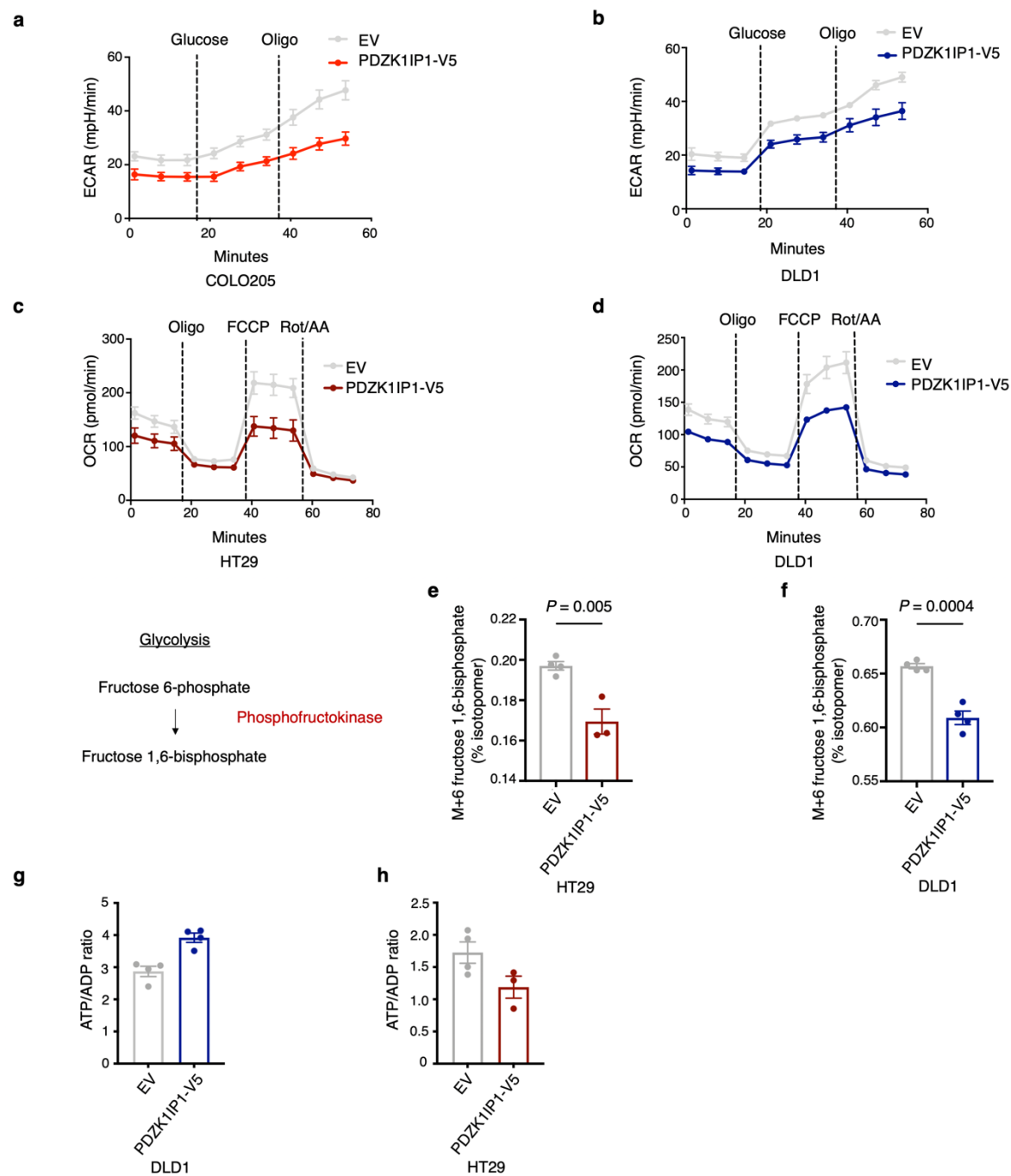


Fig. S15: *PDZK1IP1* decreases glycolytic and mitochondrial respiration rate. **a, b** Seahorse glycolytic stress test. ECAR – extracellular acidification rate, a readout of glycolysis rate ($n = 6$

biological replicates per group). Data presented as mean $\pm$ s.e.m. **c, d** Seahorse mitochondrial stress test. OCR – oxygen consumption rate, a readout of oxidative respiration rate ($n = 6$ biological replicates per group). Oligo – oligomycin, an ATP synthase inhibitor which decreases OCR and increase ECAR. FCCP – trifluoromethoxy carbonylcyanide phenylhydrazone, an inner mitochondrial membrane gradient decoupler that increases OCR. Rot/AA – Rotenone and antimycin A, complex I and complex III inhibitors, respectively, which decrease OCR. Data presented as mean $\pm$ s.e.m. **e, f** Relative peak area of uniformly labeled fructose 1,6-bisphosphate, reported as % of M+6 isotopomer of total labeled and unlabeled metabolite, from U- C^{13} glucose tracing ($n = 4$ biological replicates per group) as a readout of phosphofructokinase enzyme live-cell activity. Data presented as mean $\pm$ s.e.m. Significance was determined using two-sided Student's *t*-test. **g, h** ATP/ADP ratio from total polar metabolite peak area in HT29 and DLD1 cells ($n = 4$ biological replicates per group). Data presented as mean $\pm$ s.e.m. Significance was determined using two-sided Student's *t*-test. Source data are provided as a Source Data file.

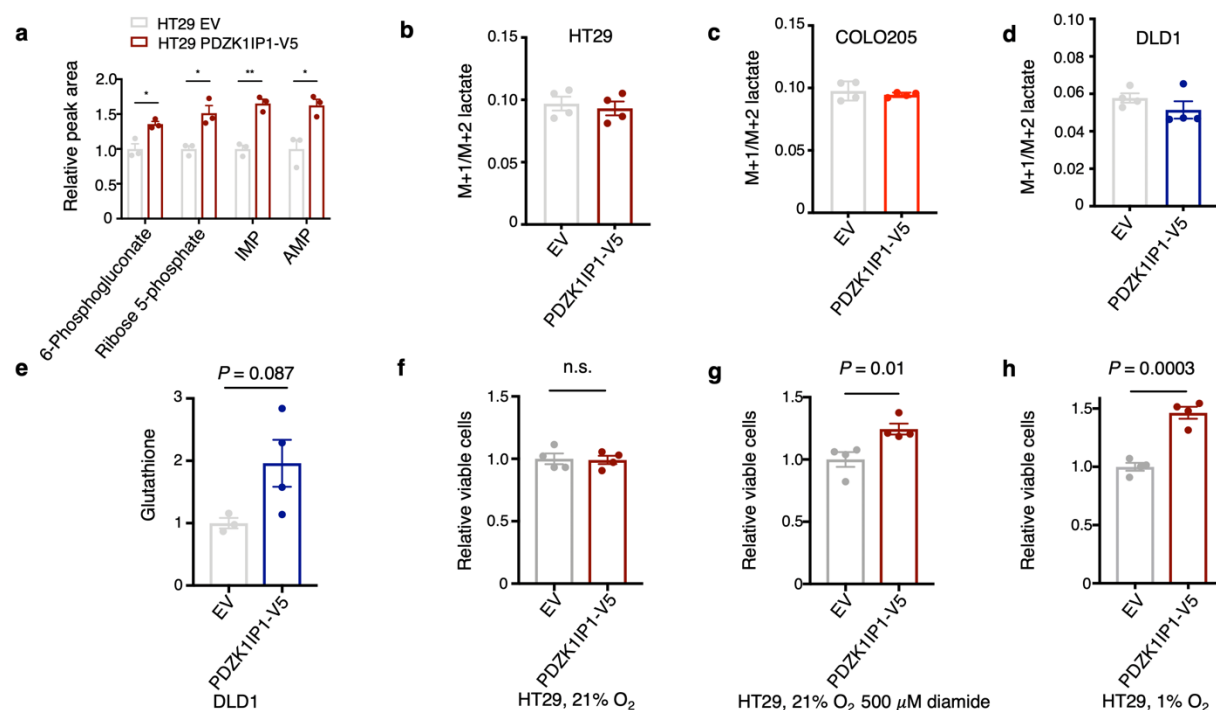


Fig. S16: *PDZK1IP1* maintains redox homeostasis. **a** Steady state levels (total peak area) of PPP intermediates and downstream metabolites ($n = 3$ per group). Data presented as mean $\pm$ s.e.m. Significance was determined using Student's t -test. * $P < 0.05$, ** $P < 0.01$. **b-d** Ratio of M+1/M+2 lactate levels by total peak area, from 5 mM 1,2C¹³-glucose labeling for 4 hours ($n = 4$ for all groups). Data presented as mean $\pm$ s.e.m. **e** Steady state levels of total glutathione peak area ($n = 4$ per group). Data presented as mean $\pm$ s.e.m. Significance was determined using Student's t -test. **f-h** Cell viability by colorimetric MTT assay under normoxia, hypoxia for 48 hours, or with 30 minutes of diamide treatment ($n = 4$ per group). Data presented as mean $\pm$ s.e.m. Significance was determined using Student's t -test. Source data are provided as a Source Data file.

Supplementary Table 1: 2026 super-enhancers and putative gene associations by H3K27ac ChIP-seq signal and RNA-seq mRNA expression correlation.

#'chr'	'start'	'end'	Genes associated with super-enhancer by H3K27ac and mRNA correlation
chr1	839207	879441	CPSF3L
chr1	931032	942910	HES4
chr1	958033	1016775	
chr1	1056306	1073787	RNF223
chr1	1076920	1083409	RNF223
chr1	1092834	1107947	RNF223
chr1	1278680	1285456	CPSF3L

chr1	1364974	1379781	ACAP3, C1orf222, SCNN1D, MXRA8, VWA1, TNFRSF4, SLC35E2B, MIB2, TMEM240, SLC35E2, MMP23A, ANKRD65
chr1	1530021	1565186	
chr1	1680282	1729724	PRKCZ
chr1	1820906	1828473	PRKCZ
chr1	1954672	1985568	PLCH2
chr1	2063722	2092933	C1orf222, SLC35E2B, SLC35E2
chr1	2157893	2167812	PLCH2
chr1	2346593	2438208	PLCH2
chr1	2473058	2481551	PLCH2
chr1	2485426	2494310	PLCH2
chr1	3228780	3277512	MEGF6
chr1	3356135	3431583	LRRC47
chr1	6326718	6362599	ESPN
chr1	6379836	6456346	
chr1	6506270	6571895	ESPN
chr1	6639352	6664607	RPL22
chr1	8120867	8182464	
chr1	8207520	8285533	PARK7
chr1	8456022	8488406	
chr1	8931738	8960596	CA6
chr1	9221417	9243600	TMEM201
chr1	9326975	9508779	SPSB1
chr1	9858949	9909954	NMNAT1
chr1	10726087	10897857	MASP2
chr1	11766429	11867807	MAD2L2
chr1	12183318	12269678	MIIP
chr1	12651250	12690803	PRAMEF1, TNFRSF8

chr1	15455486	15557536	CASP9
chr1	15634011	15698833	CASP9
chr1	15735516	15760330	CASP9
chr1	16059949	16070046	CELA2A, TMEM82
chr1	16155997	16164227	CELA2A
chr1	16465112	16554574	SPATA21
chr1	17019382	17051807	ESPNP
chr1	17215262	17307660	NBPF1
chr1	17423509	17460118	PADI2, SDHB
chr1	17551677	17582041	SDHB
chr1	17828633	17961597	PADI2
chr1	19233804	19289265	ALDH4A1
chr1	19333613	19427107	ALDH4A1
chr1	19661379	19808674	
chr1	19909319	19947764	NBL1
chr1	19965334	19984929	AKR7L
chr1	20113568	20144846	RNF186
chr1	20796697	20823686	CAMK2N1
chr1	21574800	21669795	
chr1	21932541	22000272	CDC42
chr1	22213631	22265779	CDC42
chr1	22554966	22591190	CELA3B
chr1	23000040	23122584	
chr1	23744351	23780387	ASAP3, FUCA1, TCEA3
chr1	23840199	23920440	ID3
chr1	24117166	24138236	ZNF436
chr1	24426788	24449990	
chr1	25217166	25289408	C1orf63
chr1	25856096	25901176	C1orf63
chr1	26592392	26629600	
chr1	26662449	26705144	PIGV
chr1	26855685	26870766	PDIK1L
chr1	27017777	27034137	
chr1	27155163	27208661	PIGV
chr1	27316744	27360530	SYTL1
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chr9	131924858	131947259	CCBL1
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chr9	132143494	132269806	PTGES
chr9	132310662	132376115	PTGES
chr9	133223375	133329315	FNBP1
chr9	134103506	134158677	
chr9	134224427	134309073	
chr9	134496283	134555283	
chr9	134571356	134615946	
chr9	135924105	135940404	GBGT1, GTF3C5, ADAMTS1 3, CELP, CEL, ADAMTSL 2
chr9	135966206	136027438	
chr9	136099223	136160808	
chr9	136689130	136859572	DBH
chr9	136914345	136934837	
chr9	137144521	137367806	
chr9	138857212	138909902	SEC16A
chr9	138967415	139090962	CAMSAP1
chr9	139404968	139525089	
chr9	139578763	139591286	CCDC183
chr9	139683661	139691005	MAMDC4
chr9	139739767	139758297	CCDC183
chr9	139774959	139808829	TMEM210
chr9	139836298	139847672	C9orf172
chr9	140087151	140096306	C9orf172
chr9	140122472	140135480	CCDC183
chr9	140169673	140176591	NRARP
chr9	140186990	140203083	GRIN1

chr9	140203344	140212896	MAMDC4, LCN12, C9orf173
chr9	140500027	140510499	NRARP
chrX	12988547	13048990	
chrX	23811271	23841815	
chrX	39812121	39874657	
chrX	39941636	39969370	BCOR
chrX	40000296	40036731	BCOR
chrX	41189758	41195978	
chrX	68047881	68069392	
chrX	70835396	70848211	
chrX	118611219	118647263	
chrX	129193853	129255773	XPNPEP2
chrX	152950541	152975505	TMEM187
chrX	152988183	152993943	BCAP31
chrX	153186855	153196221	ARHGAP4
chrX	153236006	153240516	LAGE3
chrX	153264816	153326419	SRPK3
chrX	153576924	153613104	MECP2

**Supplementary Table 2:
2026 super-enhancers and putative gene associations by H3K27ac ChIP-seq signal and RNA-seq mRNA expression correlation, that are supported by Hi-ChIP looping contacts derived from primary CRC tumors.**

	'start'	'end'	Genes associated with super-enhancer by Hi-ChIP as well as H3K27ac by mRNA correlation
chr1	839207	879441	
chr1	931032	942910	
chr1	958033	1016775	
chr1	1056306	1073787	RNF223
chr1	1076920	1083409	RNF223
chr1	1092834	1107947	
chr1	1278680	1285456	
chr1	1364974	1379781	TNFRSF4, MIB2, ANKRD65
chr1	1530021	1565186	
chr1	1680282	1729724	PRKCZ
chr1	1820906	1828473	PRKCZ
chr1	1954672	1985568	
chr1	2063722	2092933	
chr1	2157893	2167812	
chr1	2346593	2438208	
chr1	2473058	2481551	

chr1	2485426	2494310	PLCH2
chr1	3228780	3277512	
chr1	3356135	3431583	LRRC47
chr1	6326718	6362599	ESPN
chr1	6379836	6456346	
chr1	6506270	6571895	ESPN
chr1	6639352	6664607	
chr1	8120867	8182464	
chr1	8207520	8285533	PARK7
chr1	8456022	8488406	
chr1	8931738	8960596	CA6
chr1	9221417	9243600	
chr1	9326975	9508779	SPSB1
chr1	9858949	9909954	NMNAT1
chr1	10726087	10897857	MASP2
chr1	11766429	11867807	MAD2L2
chr1	12183318	12269678	MIIP
chr1	12651250	12690803	
chr1	15455486	15557536	CASP9
chr1	15634011	15698833	CASP9
chr1	15735516	15760330	CASP9
chr1	16059949	16070046	CELA2A
chr1	16155997	16164227	
chr1	16465112	16554574	SPATA21
chr1	17019382	17051807	
chr1	17215262	17307660	NBPF1
chr1	17423509	17460118	PADI2, SDHB
chr1	17551677	17582041	SDHB
chr1	17828633	17961597	PADI2
chr1	19233804	19289265	ALDH4A1
chr1	19333613	19427107	ALDH4A1
chr1	19661379	19808674	
chr1	19909319	19947764	NBL1
chr1	19965334	19984929	AKR7L
chr1	20113568	20144846	RNF186
chr1	20796697	20823686	CAMK2N1

chr1	21574800	21669795	
chr1	21932541	22000272	CDC42
chr1	22213631	22265779	CDC42
chr1	22554966	22591190	CELA3B
chr1	23000040	23122584	
chr1	23744351	23780387	FUCA1, TCEA3
chr1	23840199	23920440	ID3
chr1	24117166	24138236	ZNF436
chr1	24426788	24449990	
chr1	25217166	25289408	
chr1	25856096	25901176	C1orf63 (RSRP1)
chr1	26592392	26629600	
chr1	26662449	26705144	PIGV
chr1	26855685	26870766	
chr1	27017777	27034137	
chr1	27155163	27208661	PIGV
chr1	27316744	27360530	
chr1	27424877	27489140	PIGV
chr1	27813161	27927216	XKR8
chr1	28184862	28219220	STX12
chr1	31202847	31297732	SNRNP40
chr1	31885596	31919499	SERINC2
chr1	31974209	32057981	TINAGL1
chr1	32127999	32154793	COL16A1
chr1	32387789	32429778	
chr1	32754249	32819404	BSDC1
chr1	33177547	33241527	KIAA1522
chr1	33342282	33373754	
chr1	33390274	33490740	TMEM54
chr1	33772194	33816350	
chr1	36614482	36653881	
chr1	37936562	37964770	
chr1	39570164	39599196	
chr1	40388079	40456214	
chr1	40494460	40525992	
chr1	41823076	41899496	

chr1	41916513	41984388	
chr1	42611417	42639350	GUCA2B, GUCA2A
chr1	43389469	43447054	C1orf210
chr1	43810360	43839648	C1orf210
chr1	43971999	44054819	SLC6A9
chr1	44448905	44509737	SLC6A9
chr1	44701316	44760395	ERI3
chr1	45097037	45154968	
chr1	45270933	45276806	
chr1	46631993	46660693	
chr1	46766371	46773007	
chr1	47644434	47659486	PDZK1IP1
chr1	47787864	47802416	
chr1	47896527	47918279	FOXD2
chr1	48150864	48195520	
chr1	51761624	51802404	
chr1	53758670	53794340	
chr1	54713922	54891305	TCEANC2
chr1	55024214	55073822	C1orf177 (LEXM)
chr1	55241442	55282938	TTC22, ACOT11, C1orf177 (LEXM)
chr1	59220979	59252104	
chr1	59268562	59291681	JUN
chr1	59314538	59409852	
chr1	61508480	61523688	
chr1	65530848	65534992	
chr1	68154381	68236593	
chr1	68268228	68299628	
chr1	85740062	85774046	
chr1	94031857	94090070	BCAR3
chr1	95239197	95290129	
chr1	10967477 3	10972962 3	GNAT2
chr1	11029971 5	11036698 8	GNAI3
chr1	11041965 6	11049088 6	
chr1	11173432 1	11174817 6	

chr1	11323053 0	11325044 4	
chr1	11373383 4	11379956 9	
chr1	11691477 7	11695267 3	ATP1A1
chr1	11699670 6	11706016 4	MAB21L3
chr1	12030670 1	12036106 7	
chr1	14541537 3	14545736 7	
chr1	15053037 3	15055318 3	C1orf51 (CIART)
chr1	15056835 6	15059538 8	C1orf51 (CIART)
chr1	15094296 8	15095210 7	PSMD4
chr1	15146690 5	15149168 1	
chr1	15150298 8	15152298 9	CELF3
chr1	15190735 9	15197428 3	
chr1	15200656 6	15202421 7	
chr1	15347893 3	15351173 0	S100A6
chr1	15353404 3	15355058 8	S100A4
chr1	15357102 9	15359053 1	S100A6
chr1	15373577 7	15377896 9	
chr1	15391534 4	15393749 1	
chr1	15437417 8	15446171 8	IL6R
chr1	15494246 5	15494925 9	
chr1	15496104 7	15499597 0	ZBTB7B
chr1	15500924 6	15502655 5	ZBTB7B
chr1	15505046 3	15505941 5	EFNA3
chr1	15509544 2	15511322 5	GBA
chr1	15516164 3	15516527 0	GBA
chr1	15589942 8	15591742 0	SLC25A44

chr1	15593134 9	15597941 1	C1orf85 (GLMP)
chr1	15604632 9	15611726 7	C1orf85 (GLMP)
chr1	15642572 0	15649822 1	C1orf85 (GLMP)
chr1	15662589 8	15666477 5	RHBG, NES, BCAN, CRABP2, PEAR1
chr1	15671198 1	15673029 7	C1orf85 (GLMP)
chr1	15981558 3	15986042 5	
chr1	15989130 4	15989608 6	
chr1	16098178 6	16099284 8	APOA2
chr1	16104289 8	16106014 4	USP21
chr1	16135898 9	16138032 4	
chr1	16454558 2	16465336 9	
chr1	16703247 3	16710596 9	GPA33
chr1	16718012 9	16719959 0	
chr1	16768124 4	16772739 8	
chr1	16901316 6	16909155 3	
chr1	18012320 4	18014347 4	QSOX1
chr1	18105718 7	18113031 7	
chr1	18235211 8	18236703 4	TEDDM1
chr1	19774012 3	19775745 7	
chr1	19999028 9	20002320 0	NR5A2
chr1	20085668 0	20089963 4	
chr1	20096101 4	20099834 2	
chr1	20126030 1	20128279 0	PKP1
chr1	20132239 2	20138389 9	PKP1
chr1	20141717 5	20148689 7	
chr1	20197380 8	20210495 8	ELF3

chr1	20275201 7	20278469 1	
chr1	20323660 1	20331691 5	FMOD
chr1	20404214 9	20410788 6	REN
chr1	20422824 5	20436858 6	
chr1	20441249 0	20448278 5	
chr1	20521689 8	20529130 8	
chr1	20539971 3	20551969 6	LEMD1
chr1	20553265 3	20556850 0	SLC45A3
chr1	20562843 8	20565004 4	ELK4, MFSD4
chr1	20683165 4	20691094 3	IL19
chr1	20709803 7	20715465 0	
chr1	20717474 8	20720897 4	IL19
chr1	20722345 4	20724424 5	
chr1	20791115 5	20792990 4	
chr1	20797927 2	20804335 2	
chr1	20827406 1	20835948 3	
chr1	20837393 9	20842465 0	PLXNA2
chr1	20976923 6	20983303 0	
chr1	21150217 6	21152768 8	
chr1	21168747 2	21172308 0	
chr1	21177650 6	21182854 5	TRAF5
chr1	21276861 4	21278347 0	
chr1	22389251 5	22393887 2	
chr1	22559601 0	22566882 2	DNAH14
chr1	22602982 6	22611027 3	
chr1	22628805 7	22632542 6	TMEM63A

chr1	22681525 5	22692709 9	
chr1	22807290 7	22814137 5	ZNF678
chr1	22824641 9	22827868 1	
chr1	22832698 1	22833108 8	
chr1	22834913 2	22835487 1	RNF187
chr1	22894028 9	22900462 7	RHOA
chr1	22922813 8	22930997 7	
chr1	22935633 1	22939007 9	
chr1	23020948 0	23029733 2	
chr1	23086443 6	23090494 3	
chr1	23153135 0	23155906 4	
chr1	23271446 3	23277139 1	
chr1	23374375 2	23376198 0	
chr1	23465752 3	23469597 5	
chr1	23472483 3	23476065 0	
chr1	23483434 8	23488830 4	
chr1	23495128 6	23506915 1	
chr1	23508874 8	23515829 7	
chr1	24420958 7	24424005 4	
chr1	24499599 3	24500236 5	C1orf101 (CATSPERE)
chr1	24511538 0	24513615 3	
chr1	24913706 4	24916853 5	
chr10	634473	710051	
chr10	972598	1001352	
chr10	3777459	3830408	
chr10	3846361	3854638	
chr10	3867604	3950023	
chr10	5506961	5706245	ASB13

chr10	11704540	11759069	
chr10	14564566	14667661	
chr10	15331568	15397491	FAM171A1
chr10	21455548	21464438	
chr10	24737364	24784244	
chr10	25004669	25021540	
chr10	27519398	27532774	
chr10	30706423	30726113	
chr10	32329666	32349392	
chr10	32383993	32479292	
chr10	32621022	32674058	
chr10	33227489	33272835	
chr10	43832131	43917416	
chr10	46990958	47058393	NPY4R
chr10	70976222	70993459	CCAR1
chr10	71081085	71149948	VPS26A
chr10	71164584	71267921	
chr10	71595936	71678030	
chr10	71885733	71903754	EIF4EBP2
chr10	72969762	73056436	UNC5B
chr10	73356961	73422741	UNC5B
chr10	73444381	73542810	
chr10	74002542	74100641	ANAPC16
chr10	74420932	74463640	
chr10	75603323	75677591	
chr10	76946014	76973090	VDAC2
chr10	76985609	77056330	ZNF503
chr10	77154927	77169743	ZNF503
chr10	79623645	79682923	
chr10	80710759	80737653	ZMIZ1
chr10	80804683	80922165	
chr10	80981446	81119139	EIF5AL1
chr10	81135308	81202484	SFTPA1
chr10	81895869	81968780	DYDC1
chr10	82187931	82269537	
chr10	85918778	85965078	GHITM, C10orf99

chr10	88424408	88476592	
chr10	88727013	88732486	
chr10	88851230	88865926	
chr10	89621087	89629308	CFL1P1
chr10	90639024	90664381	
chr10	95172495	95236263	
chr10	95301521	95351810	FFAR4
chr10	96990557	97074536	
chr10	98337456	98394081	
chr10	99086316	99097482	
chr10	99457428	99486837	
chr10	10212243 9	10213745 4	
chr10	10275559 4	10277910 3	PAX2
chr10	10279651 7	10283218 0	
chr10	10387218 2	10388136 3	FGF8
chr10	10415835 9	10418319 1	ARL3
chr10	10435334 3	10443898 3	
chr10	10530275 7	10538011 6	CNNM2
chr10	10539506 6	10561278 8	NEURL1
chr10	10564653 3	10568337 4	NEURL1
chr10	10605924 0	10611098 2	GSTO1
chr10	11175397 0	11177318 2	
chr10	11196297 9	11198186 9	MXI1
chr10	11211361 6	11219101 2	
chr10	11256225 8	11263945 2	PDCD4
chr10	11409005 7	11417311 8	
chr10	11470527 5	11472272 4	
chr10	11476032 3	11485704 5	
chr10	11570437 2	11572202 3	

chr10	11625404 3	11628405 2	
chr10	11910200 4	11913573 2	
chr10	12101154 5	12108049 5	BAG3, NANOS1, GRK5
chr10	12368635 1	12369639 1	NSMCE4A
chr10	12377304 1	12382454 3	
chr10	12386076 4	12391004 1	ATE1
chr10	12627507 2	12643705 3	
chr10	12668734 8	12685149 2	
chr10	12967001 1	12972150 3	
chr10	13419737 5	13424502 9	
chr10	13425777 3	13430178 4	
chr10	13438425 3	13442632 1	LRRC27
chr10	13507084 1	13509352 7	ZNF511
chr10	13515652 2	13517986 6	CALY, MTG1, PRAP1
chr11	199803	210282	
chr11	312970	318010	ANO9, IFITM1
chr11	390974	418670	ANO9
chr11	438101	448828	DEAF1, TMEM80, CEND1, ANO9
chr11	487117	519196	
chr11	557515	564610	ANO9
chr11	606195	622242	
chr11	701921	711865	ANO9
chr11	818110	822789	ANO9
chr11	823355	835562	CEND1
chr11	1027798	1158380	
chr11	1214325	1285146	
chr11	1525034	1597870	TOLLIP
chr11	1772068	1825281	ASCL2
chr11	1850339	1864639	ASCL2
chr11	2007426	2018993	KCNQ1, CD81, ASCL2
chr11	2222838	2227981	ASCL2

chr11	2228439	2233334	ASCL2
chr11	2233511	2240175	ASCL2
chr11	2277708	2293051	ASCL2
chr11	2531969	2557416	ASCL2
chr11	2745510	2769952	ASCL2
chr11	2782893	2865875	CD81
chr11	2922397	2926733	TRPM5
chr11	2930168	2936397	OSBPL5
chr11	2947884	2955533	SLC22A18
chr11	3143708	3192459	ZNF195
chr11	7593139	7644873	
chr11	8708696	8755650	
chr11	8768419	8836787	
chr11	10306635	10374218	
chr11	12065965	12303424	
chr11	16921358	16947833	
chr11	16967632	17032859	KCNJ11
chr11	27485463	27494502	
chr11	34066224	34077172	
chr11	34171953	34296972	
chr11	34605603	34627752	
chr11	34641466	34676856	
chr11	35159997	35201316	
chr11	36366405	36403697	
chr11	44589671	44656439	CD82
chr11	44952460	45004436	TP53I11
chr11	45167037	45204540	PRDM11, TSPAN18
chr11	46258923	46340902	ATG13
chr11	47395923	47437968	ATG13
chr11	48004523	48088987	
chr11	57037148	57094593	ZDHHC5
chr11	57528674	57569477	
chr11	58939074	58975027	DTX4, GLYATL1
chr11	59521144	59568809	
chr11	60885373	60933207	ZP1
chr11	61298131	61396818	

chr11	61460952	61469382	CPSF7
chr11	61519574	61526232	MYRF
chr11	61721960	61749932	FADS3
chr11	62303222	62328979	HNRNPUL2
chr11	63529313	63537924	C11orf84 (SPINDOC)
chr11	63602327	63659507	
chr11	63682671	63690515	RTN3
chr11	64004653	64012011	MARK2
chr11	64084259	64091917	MARK2
chr11	64654508	64663543	SNX15
chr11	65043034	65085130	DPF2, CDC42EP2, TM7SF2, LTBP3, MAP4K2, EHBP1L1, SIPA1
chr11	65146042	65153316	MAP3K11
chr11	65182698	65196358	MAP3K11
chr11	65235731	65278300	KCNK7
chr11	65336369	65346081	SYVN1
chr11	65541984	65595884	DPF2
chr11	65609879	65638159	OVOL1
chr11	66621798	66651079	
chr11	66799161	66863232	PITPNM1
chr11	66880913	66897995	RBM14
chr11	67000685	67058673	CABP4
chr11	67118214	67125134	
chr11	67138085	67142641	CABP4
chr11	67231049	67237376	CABP4
chr11	67253402	67276815	PITPNM1
chr11	67396050	67415560	CABP4
chr11	67775272	67783134	
chr11	67803411	67811072	
chr11	67857262	67933103	CHKA
chr11	67963386	67984625	
chr11	68063591	68237978	
chr11	68577616	68638315	CPT1A, TPCN2
chr11	68861560	68905716	IGHMBP2, TPCN2, MRGPRF
chr11	69036308	69080715	IGHMBP2, MRGPRF, TPCN2
chr11	69142617	69324571	CCND1, MRGPRF, TPCN2, FGF19
chr11	69451044	69483535	CCND1

chr11	69777158	69847417	CTTN, PPFIA1, FGF19, FADD
chr11	70961547	71022977	
chr11	71932563	71952314	
chr11	72414607	72501733	ATG16L2
chr11	72518642	72544162	
chr11	72884579	72953894	
chr11	73076627	73104220	
chr11	73668076	73731342	
chr11	74854195	74915339	SLCO2B1
chr11	75012037	75064571	MOGAT2
chr11	75176812	75248626	GDPD5
chr11	75264295	75306314	SERPINH1
chr11	76447841	76517502	TSKU
chr11	76773786	76787721	
chr11	76796563	76803020	TSKU
chr11	77170698	77186470	
chr11	94258920	94283685	
chr11	11705224 0	11710062 0	APOA5
chr11	11767966 2	11771481 8	CEP164, FXVD6, SCN2B
chr11	11794426 0	11796399 9	
chr11	11848008 9	11851359 0	MPZL3
chr11	11865913 2	11866349 8	
chr11	11874046 6	11881118 4	DDX6
chr11	11922714 6	11924735 5	USP2, PDZD3, C2CD2L
chr11	11953362 2	11962017 8	
chr11	11998043 2	12001819 6	TRIM29
chr11	12003901 4	12010506 6	OAF
chr11	12131595 3	12135371 2	
chr11	12461537 0	12463961 6	
chr11	12618061 6	12635074 2	ST3GAL4
chr11	12831735 1	12838964 2	

chr11	12985635 5	12987464 6	
chr11	13001176 1	13009073 0	APLP2
chr12	607333	620505	SLC6A12
chr12	633556	685948	SLC6A12
chr12	718228	756396	
chr12	1682523	1718555	
chr12	1764325	1791236	LRTM2
chr12	1904657	1956059	
chr12	2210461	2280312	DCP1B, CACNA1C, LRTM2
chr12	3813953	3867210	
chr12	4378093	4417824	
chr12	6267425	6351305	PLEKHG6
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chr8	13425663 3	13431593 4	NDRG1
chr8	13433547 0	13439100 7	
chr8	13584306 1	13584590 0	
chr8	14151642 8	14152324 2	
chr8	14155271 4	14164251 5	CHRA1
chr8	14208259 9	14217494 4	
chr8	14220398 5	14225604 6	SLC45A4
chr8	14227392 1	14229995 7	SLC45A4, PTP4A3, DENND3, PTK2
chr8	14231560 3	14235742 8	PTP4A3
chr8	14242227 2	14242962 2	PTP4A3
chr8	14408948 1	14410988 2	ZC3H3, RHPN1, LY6E, LY6D, ZFP41
chr8	14434253 3	14436894 3	ZC3H3, RHPN1, CYP11B2, TIGD5, MAPK15, MAFA, TOP1MT
chr8	14446416 6	14452932 5	ZC3H3, RHPN1, TIGD5, MAPK15, MAFA

chr8	14465344 4	14466389 1	RHPN1
chr8	14481341 9	14482397 4	ZC3H3, TOP1MT, ZFP41, SCRIB, GRINA, RHPN1
chr8	14488667 0	14490852 0	ZC3H3
chr8	14493895 2	14498921 6	ZC3H3
chr8	14500570 3	14502956 7	ZC3H3
chr8	14504367 4	14505259 0	ZC3H3
chr8	14553693 6	14556279 1	ARHGAP39
chr8	14557760 2	14558479 8	
chr8	14563753 2	14565983 5	ZNF34
chr8	14572487 5	14573655 1	
chr9	2014195	2023271	
chr9	14309511	14323573	
chr9	19229675	19233894	
chr9	27360698	27473689	
chr9	33128522	33168546	AQP3
chr9	33202488	33255307	SPINK4, AQP3
chr9	33287280	33298803	
chr9	33813398	33820021	
chr9	35904158	35925009	HRCT1
chr9	36120900	36166748	
chr9	36290824	36329566	HRCT1
chr9	37911456	38075786	
chr9	71324166	71364433	
chr9	73006949	73036884	KLF9
chr9	74373059	74384783	
chr9	74977205	74981427	
chr9	77686385	77727120	
chr9	80618409	80650066	
chr9	91968129	92116567	CKS2
chr9	92134062	92172043	
chr9	92263575	92302155	GADD45G
chr9	93909435	93975909	

chr9	95492230	95537743	NOL8
chr9	95929205	96033139	
chr9	96211941	96274344	
chr9	96312205	96383980	
chr9	97362246	97412003	
chr9	97765305	97771070	C9orf3 (AOPEP)
chr9	98248725	98275129	
chr9	99175902	99183433	CDC14B
chr9	10082157 4	10090950 5	
chr9	10092514 1	10095825 1	
chr9	10097105 7	10101651 2	
chr9	10800953 2	10809564 5	
chr9	11024378 8	11026817 3	KLF4
chr9	11034857 0	11040236 7	
chr9	11200847 1	11210875 0	EPB41L4B
chr9	11294344 0	11298431 6	
chr9	11301423 9	11302261 2	
chr9	11465320 4	11467138 7	PTGR1
chr9	11490885 1	11494330 6	
chr9	11506773 0	11510162 3	
chr9	11613196 4	11616140 8	
chr9	11626529 5	11639686 9	
chr9	11712474 5	11716572 0	
chr9	12361829 9	12369889 5	PHF19
chr9	12402338 0	12410202 5	GSN
chr9	12436020 4	12452877 1	
chr9	12608127 4	12614403 2	ZBTB26
chr9	12701873 7	12708502 6	

chr9	12909204 6	12914227 0	
chr9	13014929 5	13016525 6	SH2D3C, LRSAM1, ENG, SLC2A8, GARNL3, LRSAM1
chr9	13025629 4	13035154 1	
chr9	13058714 1	13064707 0	STXBP1
chr9	13066451 3	13068455 4	ST6GALNAC6
chr9	13070434 9	13075549 1	NAIF1
chr9	13086449 0	13088071 4	FAM102A
chr9	13090597 6	13091442 4	
chr9	13162252 7	13168014 7	
chr9	13181145 5	13185037 2	
chr9	13189542 0	13190983 5	PHYHD1
chr9	13192485 8	13194725 9	
chr9	13209441 1	13212486 8	PTGES
chr9	13214349 4	13226980 6	PTGES
chr9	13231066 2	13237611 5	PTGES
chr9	13322337 5	13332931 5	FNBP1
chr9	13410350 6	13415867 7	
chr9	13422442 7	13430907 3	
chr9	13449628 3	13455528 3	
chr9	13457135 6	13461594 6	
chr9	13592410 5	13594040 4	ADAMTSL2, GBGT1, GTF3C5, ADAMTS13, CELP, CEL
chr9	13596620 6	13602743 8	
chr9	13609922 3	13616080 8	
chr9	13668913 0	13685957 2	DBH
chr9	13691434 5	13693483 7	
chr9	13714452 1	13736780 6	

chr9	13885721 2	13890990 2	
chr9	13896741 5	13909096 2	CAMSAP1
chr9	13940496 8	13952508 9	
chr9	13957876 3	13959128 6	CCDC183
chr9	13968366 1	13969100 5	MAMDC4
chr9	13973976 7	13975829 7	CCDC183
chr9	13977495 9	13980882 9	TMEM210
chr9	13983629 8	13984767 2	C9orf172 (AJM1)
chr9	14008715 1	14009630 6	C9orf172 (AJM1)
chr9	14012247 2	14013548 0	CCDC183
chr9	14016967 3	14017659 1	NRARP
chr9	14018699 0	14020308 3	GRIN1
chr9	14020334 4	14021289 6	MAMDC4, C9orf173 (STPG3), LCN12
chr9	14050002 7	14051049 9	NRARP
chrX	12988547	13048990	
chrX	23811271	23841815	
chrX	39812121	39874657	
chrX	39941636	39969370	BCOR
chrX	40000296	40036731	BCOR
chrX	41189758	41195978	
chrX	68047881	68069392	
chrX	70835396	70848211	
chrX	11861121 9	11864726 3	
chrX	12919385 3	12925577 3	XPNPEP2
chrX	15295054 1	15297550 5	TMEM187
chrX	15298818 3	15299394 3	
chrX	15318685 5	15319622 1	ARHGAP4
chrX	15323600 6	15324051 6	LAGE3

chrX	15326481 6	15332641 9	SRPK3
chrX	15357692 4	15361310 4	MECP2

Supplementary Table 3:
List of commercially
available CRC cell lines
commonly used in
laboratory studies.

HCT15
HCT116
COLO320
CACO2
HT29
DLD1
LS180
RKO
SW480
SW620
COLO741
SW480
COLO205

Supplementary Table 4: Hg19 coordinates of super-enhancers identified in primary CRC and normal colon tissue that are over- or under-represented in 13 commercial CRC cell lines.

'chr'	'start'	'end'	log2 cell lines/ ₁	P-value
chr2	219921304	219926326	-3.933334181	4.75E-06
chr19	1282741	1294598	-3.032709913	7.60E-05
chr16	49886677	49893398	-2.949821466	0.000519631
chr19	42210448	42221456	-2.898911644	0.004772279
chr11	312970	318010	-2.894756705	1.76E-05
chr8	142422272	142429622	-2.644337941	0.001276849
chr19	950367	958117	-2.495988143	0.007449326
chr5	149539500	149568866	-2.335044971	1.38E-06
chr7	27226673	27235671	-2.171925116	0.002112967
chr7	100607523	100631215	-2.158768857	7.53E-06
chr11	76773786	76787721	-2.116481306	9.32E-10
chr3	38025920	38036323	-2.084897042	1.80E-06
chr1	47644434	47659486	-2.078868512	1.74E-06
chr7	113722871	113728455	-2.054225966	0.003951842
chr16	31137030	31147852	-2.037706389	1.65E-08
chr19	1129240	1134649	-2.035016076	5.13E-09
chr17	3856496	3892930	-2.015277075	9.50E-07
chr11	76796563	76803020	-2.005698624	1.14E-06
chr10	85918778	85965078	-1.956797767	6.89E-07
chr16	67460809	67504574	-1.945311673	1.21E-07
chr9	130905976	130914424	-1.91203976	0.000189521
chr14	94848020	94862793	-1.890862615	0.009692258
chr20	22548732	22567099	-1.887185684	0.001244224
chrX	70835396	70848211	-1.868040926	0.000105237

chr17	74485442	74490614	-1.851351981	2.51E-05
chr7	70158103	70166365	-1.815465956	2.41E-05
chr7	73180110	73189479	-1.810669041	1.10E-05
chr2	14762896	14776676	-1.803198778	0.000146674
chr8	142315603	142357428	-1.803098563	0.00033056
chr1	205532653	205568500	-1.800685286	0.000129067
chr8	48646118	48651966	-1.760217332	6.43E-08
chr7	156393561	156419142	-1.759424939	0.000451767
chr7	150477778	150505955	-1.753099976	1.77E-05
chr16	85449100	85526770	-1.752547912	0.000214569
chr16	582919	587823	-1.75068509	5.44E-06
chr4	15002818	15007221	-1.704048064	8.80E-08
chr19	18611824	18621473	-1.694070408	8.11E-07
chr19	40419549	40457265	-1.692289026	0.000447315
chr9	140186990	140203083	-1.674837677	8.94E-05
chr1	33342282	33373754	-1.670767379	3.25E-06
chr4	149348610	149367220	-1.66504665	4.70E-07
chr17	73634586	73644264	-1.663655009	0.000271978
chr8	76314903	76322046	-1.663653639	0.000200429
chr4	160023546	160026111	-1.660029638	2.21E-06
chr19	50668992	50738128	-1.654229726	1.39E-05
chr20	60979569	60991115	-1.651679206	0.001274464
chr16	31487207	31500133	-1.646142188	2.01E-05
chr1	1056306	1073787	-1.625633377	4.37E-05
chr7	27140197	27149295	-1.590910353	0.002221693
chr15	68479899	68503417	-1.588524898	3.11E-08
chr22	31666929	31694556	-1.583014828	6.13E-07
chr19	33723635	33815979	-1.576082011	4.14E-06
chr16	53163214	53168804	-1.562522215	0.001147531
chr16	68384973	68432029	-1.562204677	1.68E-07
chr17	37779956	37790775	-1.552808833	3.36E-05
chr21	43718828	43759283	-1.549372024	0.000136642
chr22	38493842	38517899	-1.539972117	5.68E-07
chr20	17902067	17921342	-1.522326512	2.30E-06
chr16	30123335	30135353	-1.518808525	9.54E-06
chr2	241540948	241546332	-1.517004878	0.000736344
chr8	144938952	144989216	-1.503213086	6.17E-06
chr19	35599346	35623141	-1.500696097	0.000173606
chr22	50319146	50364826	-1.495054142	2.29E-06
chr9	92263575	92302155	-1.49031086	1.83E-06
chr18	28676993	28682939	-1.489553055	0.001023615
chr11	2930168	2936397	-1.486304394	1.34E-05
chr9	130864490	130880714	-1.485125129	8.31E-05
chr4	1748180	1818534	-1.482977267	0.000172748
chr1	16059949	16070046	-1.480374457	0.000183684

chr9	95929205	96033139	-1.480201283	3.42E-06
chr2	219148537	219162345	-1.476482263	0.001992198
chr19	41914345	41942398	-1.473144331	1.38E-07
chr18	19741865	19781074	-1.464659281	0.000491763
chr17	38327873	38351879	-1.464426274	6.49E-05
chr2	239169490	239219160	-1.463708595	1.68E-07
chr7	29601890	29607677	-1.452014835	0.001734837
chr17	81005827	81069196	-1.442303168	1.51E-05
chr2	242704267	242763347	-1.441783842	7.54E-06
chr13	27522316	27597035	-1.42852943	0.008113301
chr15	31616912	31698718	-1.42833867	2.07E-07
chr19	55756765	55767392	-1.42726789	0.006850812
chr10	134197375	134245029	-1.427197048	5.09E-09
chr1	61508480	61523688	-1.412822061	2.25E-05
chr9	140087151	140096306	-1.410234098	0.006737055
chr16	67423853	67447927	-1.407506127	1.04E-05
chr17	79763639	79788092	-1.388498587	8.97E-08
chr10	134257773	134301784	-1.380589018	7.23E-06
chr1	199990289	200023200	-1.374864468	0.002411763
chr3	53166834	53230973	-1.374491386	8.47E-08
chr8	142203985	142256046	-1.372888112	6.06E-05
chr3	71612437	71634637	-1.372196278	0.000179723
chr19	54979246	54985496	-1.363581356	0.000548464
chr14	38052216	38072548	-1.363489967	0.002279186
chr9	134496283	134555283	-1.35721224	0.005416658
chr22	37406071	37423323	-1.357177296	4.84E-05
chr7	30322996	30327105	-1.355003336	6.64E-06
chr12	6468473	6473930	-1.354950301	0.000145933
chr4	140096935	140110107	-1.354221017	1.10E-07
chr4	7957954	7988605	-1.340452856	1.33E-05
chr17	26120397	26151772	-1.335406068	0.000614658
chr11	1525034	1597870	-1.334335	6.89E-06
chr5	40676729	40700663	-1.333969521	0.005834136
chr7	27236867	27251265	-1.333213185	0.008969102
chr5	149586118	149597726	-1.327771064	0.000134751
chr1	155050463	155059415	-1.32584885	0.000636383
chr19	4034556	4150644	-1.318671308	4.72E-08
chr17	73568797	73577073	-1.314979465	3.52E-05
chr14	55031455	55035147	-1.314499318	0.00014642
chr9	117124745	117165720	-1.313797327	0.000198119
chr17	37827160	37837462	-1.311567369	0.000914851
chr7	991118	994980	-1.306250732	0.006732574
chr8	1913890	1926709	-1.295545411	0.000272981
chr12	121650947	121685811	-1.29244219	0.001279391
chr19	1247317	1256284	-1.290320659	7.94E-05

chr7	25979727	26008574	-1.288425537	0.005901451
chr16	11290981	11360138	-1.28593865	2.36E-06
chr8	145536936	145562791	-1.282480618	2.95E-05
chr5	1073524	1188157	-1.28018389	0.000552488
chr2	43035897	43038998	-1.279825977	7.20E-09
chr9	139578763	139591286	-1.278519633	5.51E-05
chr1	51761624	51802404	-1.276336427	7.99E-06
chr19	35485150	35505427	-1.273803969	2.21E-06
chr21	42866102	42955540	-1.271553665	0.003990368
chr9	140203344	140212896	-1.268492344	0.003718446
chr7	948975	956672	-1.267631416	0.000589779
chr7	100482826	100510426	-1.262130127	4.80E-06
chr11	64654508	64663543	-1.26061998	0.001093014
chr9	110243788	110268173	-1.251133259	0.000442417
chr1	226288057	226325426	-1.248226489	8.32E-07
chr12	32543708	32556907	-1.244848297	1.23E-06
chr18	60381757	60385355	-1.235852828	3.79E-05
chr20	57463250	57471189	-1.214365622	0.000611273
chr5	32433949	32447867	-1.213848352	0.000267944
chr19	923608	929931	-1.211890102	0.004619643
chr21	45658980	45670752	-1.200354979	0.001115286
chr17	76988200	76995813	-1.19781147	0.002996369
chr3	169375755	169387326	-1.197762721	0.00030491
chr15	40634403	40643032	-1.192001967	0.003206032
chr9	100821574	100909505	-1.19111333	7.61E-05
chr11	818110	822789	-1.190429173	1.76E-05
chr1	19965334	19984929	-1.189885971	0.00011409
chr3	127449108	127543524	-1.181684473	0.000712362
chr17	73519791	73524830	-1.179960513	4.78E-05
chr5	172195280	172206972	-1.177488882	6.76E-05
chr11	117944260	117963999	-1.175196218	0.001450218
chr20	62164679	62175099	-1.174885529	0.002258229
chr19	12892449	12906321	-1.172881308	1.57E-06
chr6	35438934	35474161	-1.172216596	4.52E-06
chr1	1092834	1107947	-1.171099652	0.002064843
chr17	18864569	18923164	-1.170180749	0.005223225
chr1	17828633	17961597	-1.162184065	0.000116939
chr1	32127999	32154793	-1.1590256	0.001938253
chr1	233743752	233761980	-1.158896275	0.001413337
chrX	68047881	68069392	-1.15695134	0.001230527
chr16	81299560	81312418	-1.156884193	3.83E-05
chr2	206948329	206952121	-1.152646404	2.07E-07
chr6	157097603	157103712	-1.152413919	0.000154177
chr1	1076920	1083409	-1.149284102	0.002793414
chr15	31725421	31791946	-1.146208447	0.000106421

chr22	46497766	46507175	-1.144533411	0.005056484
chr15	31546526	31573312	-1.1437809	7.76E-06
chr7	1568954	1574711	-1.142482389	0.000235901
chr8	134335470	134391007	-1.136072787	0.002367042
chr6	35691386	35701797	-1.134733443	6.62E-05
chr1	207098037	207154650	-1.131390166	0.003585078
chr11	2922397	2926733	-1.127961438	0.000137631
chr9	14309511	14323573	-1.125174648	0.002250256
chr20	56104107	56204341	-1.122036256	0.00336621
chr20	56229753	56295325	-1.118689646	0.004286441
chr19	49178577	49202140	-1.111287415	8.88E-05
chr17	73529524	73542716	-1.109659761	0.008782904
chr21	44858977	44873702	-1.109649262	0.001078597
chr9	2014195	2023271	-1.108875373	7.58E-06
chr14	105944150	105959031	-1.106254332	0.002882295
chr19	11353793	11380147	-1.104940631	1.87E-06
chr8	81397760	81421513	-1.104026822	0.000173483
chr8	145724875	145736551	-1.102944841	0.000375006
chr10	135156522	135179866	-1.10253336	0.004821712
chr19	45220249	45288652	-1.101828316	0.000358198
chr1	155161643	155165270	-1.101255846	0.006195042
chr11	2531969	2557416	-1.099006162	0.000600571
chr10	112562258	112639452	-1.095353097	0.00213485
chr16	88443224	88621560	-1.094897966	0.002762185
chr17	10676053	10719009	-1.094674354	0.004648038
chr11	606195	622242	-1.094121442	5.99E-05
chr5	172327125	172346151	-1.093982888	2.61E-05
chr22	50962309	50971267	-1.093835024	0.003064404
chr6	168413323	168503148	-1.09366734	2.41E-05
chr8	145043674	145052590	-1.093621486	0.000623648
chr17	57442508	57459901	-1.092540175	0.003262118
chr1	228349132	228354871	-1.091068244	0.000204448
chr6	89788647	89793074	-1.089729814	8.93E-09
chr2	28542414	28677214	-1.088175117	9.13E-05
chr22	46406761	46411260	-1.088019864	0.000118634
chr1	65530848	65534992	-1.086156021	0.000454408
chr13	41237892	41242018	-1.08574238	0.000736638
chr1	37936562	37964770	-1.084054544	0.000176254
chr1	20796697	20823686	-1.080299094	0.004959933
chr8	61811816	61840052	-1.080121891	4.15E-05
chr12	106620916	106644657	-1.079291391	3.69E-05
chr14	103367432	103415466	-1.07815608	2.61E-05
chr3	169755228	169768436	-1.072797034	7.41E-06
chr14	100569955	100660583	-1.069741409	0.000293944
chr2	208027703	208032208	-1.068574986	0.00013338

chr5	149941195	150017647	-1.064230609	5.23E-06
chr4	124315353	124341272	-1.055196918	0.001277395
chr9	139739767	139758297	-1.045706755	4.37E-05
chr4	141157126	141174915	-1.044484983	0.00687941
chr1	226029826	226110273	-1.037503403	7.21E-06
chr9	139683661	139691005	-1.034391734	9.92E-05
chr5	32298136	32333194	-1.033402799	0.003793373
chr16	57118390	57188393	-1.032752273	2.17E-05
chr2	242280263	242316360	-1.030467192	0.002928121
chr1	48150864	48195520	-1.024145926	2.27E-05
chr19	39887706	39902964	-1.023371562	0.000581726
chr2	238380339	238457019	-1.019570375	0.00548691
chr12	57519739	57575138	-1.017545226	0.000325957
chr2	241895868	241951777	-1.014868666	0.004083038
chr20	62150329	62155053	-1.010226977	0.000818134
chr19	49114785	49123342	-1.009885182	0.000928071
chr19	17875523	17914613	-1.007297164	9.04E-05
chr10	98337456	98394081	1.007035335	0.002355826
chr14	91817703	91881574	1.054473572	0.001319197
chr2	242784751	242844988	1.055869807	0.000500672
chr6	30691362	30762214	1.06354511	0.001788619
chr8	27189458	27266603	1.105089489	0.006499779
chr1	839207	879441	1.23821519	0.008747137
chr4	1492816	1584306	1.253051461	0.003244989
chr18	3583274	3626174	1.292623519	4.47E-05
chr7	130567798	130646840	1.301600783	0.000842286
chr12	46761555	46797433	1.368447694	0.00332708
chr17	48176137	48195174	1.393480425	0.000480532
chr17	17795500	17864058	1.41147405	0.007475802

Supplementary Table 5: Gene signature downstream of tumor-enriched SEs. Genes are mRNA up-regulated in primary CRCs over CCLE cell lines.

PTP4A3
IFITM2
SERPINA1
TMEM176B
COL16A1
C10orf99
PDZK1IP1
NOS2
SLC7A10
TMEM82
FXWD3
SHC2
GADD45G
CEACAM6
TMEM220
SOCS1
NR3C2
CYP27A1
ATP2A3
PALM
HSD11B2
FKBP5
PADI2
LRRC36
IFITM1
KIF25
PDE4C
SMPD3
MATK
TST
SMIM5
MAPK3
AMN
LCN12
CCDC183
CAMK2N1
KLF4

**Supplemen
tary Table**

6: Super-
enhancers
up-regulated
in primary
CRC over
patient-
matched
normal
tissue, and
also up-
regulated in
primary
specimens
over CRC
cell lines.

	'start'	'end'
chr11	312970	318010
chr8	142422272	142429622
chr19	950367	958117
chr1	47644434	47659486
chr17	74485442	74490614
chr8	142203985	142256046
chr19	923608	929931
chr20	56229753	56295325
chr2	208027703	208032208

Supplementary Table 7:
Juxtaposition of primary CRC cases with mutational status and *PDZK1IP1* SE status.
All patients for which data are available are shown.

Patient	PDZK1IP1 SE	Gene	Mutation	Variant_Classif	Variant Allele Frequency
18481T	Yes	PRDM2	c.4027G>A	Missense_Mut	0.150344828
18481T	Yes	SZT2	c.2138del	Frame_Shift_D	0.383838384
18481T	Yes	CACNA1S	c.5012G>A	Missense_Mut	0.182072829
18481T	Yes	KISS1	c.225del	Frame_Shift_D	0.41025641
18481T	Yes	PIK3C2B	c.2698C>T	Missense_Mut	0.399463807
18481T	Yes	C2orf71	c.3839C>T	Missense_Mut	0.2
18481T	Yes	CASP8	c.1557del	Frame_Shift_D	0.350308642
18481T	Yes	CASP8	c.1586T>C	Missense_Mut	0.396258503
18481T	Yes	TGFBR2	c.644G>A	Missense_Mut	0.351687389
18481T	Yes	TGFBR2	c.1043T>C	Missense_Mut	0.364628821
18481T	Yes	PBRM1	c.1961A>G	Missense_Mut	0.189873418
18481T	Yes	PBRM1	c.518T>C	Missense_Mut	0.390728477
18481T	Yes	ATR	c.7375C>T	Missense_Mut	0.155555556
18481T	Yes	TET2	c.371A>G	Missense_Mut	0.179447853
18481T	Yes	TET2	c.4354C>T	Nonsense_Mut	0.377919321
18481T	Yes	TET2	c.4871A>G	Missense_Mut	0.208805031
18481T	Yes	FAT1	c.12608G>A	Missense_Mut	0.376744186
18481T	Yes	FAT1	c.7366G>A	Missense_Mut	0.352859135
18481T	Yes	ARID1B	c.1988A>G	Missense_Mut	0.19895288
18481T	Yes	EGFR	c.2029C>T	Missense_Mut	0.193548387
18481T	Yes	EGFR	c.2930G>A	Missense_Mut	0.393333333
18481T	Yes	MET	c.40C>T	Missense_Mut	0.418390805
18481T	Yes	KMT2C	c.7238C>T	Missense_Mut	0.18814433
18481T	Yes	WRN	c.2743T>C	Missense_Mut	0.181081081
18481T	Yes	ANK1	c.1231G>A	Missense_Mut	0.420454545

18481T	Yes	SMARCA2	c.980G>A	Missense_Muta	0.333333333
18481T	Yes	GATA3	c.1134del	Frame_Shift_D	0.408333333
18481T	Yes	RET	c.169C>T	Missense_Muta	0.343023256
18481T	Yes	ADK	c.731C>T	Missense_Muta	0.152777778
18481T	Yes	KAT6B	c.4121G>A	Missense_Muta	0.37628866
18481T	Yes	TCF7L2	c.1485del	Frame_Shift_D	0.452830189
18481T	Yes	FGFR2	c.181C>T	Missense_Muta	0.368512111
18481T	Yes	DRD4	c.763del	Frame_Shift_D	0.344827586
18481T	Yes	FAT3	c.971A>G	Missense_Muta	0.158798283
18481T	Yes	KMT2A	c.5338del	Frame_Shift_D	0.179824561
18481T	Yes	CHD4	c.2402T>C	Missense_Muta	0.338461538
18481T	Yes	KMT2D	c.9417del	Frame_Shift_D	0.401574803
18481T	Yes	KMT2D	c.7061del	Frame_Shift_D	0.25
18481T	Yes	KMT2D	c.1300del	Frame_Shift_D	0.227272727
18481T	Yes	ERBB3	c.2033G>A	Missense_Muta	0.332129964
18481T	Yes	POLE	c.1309G>A	Missense_Muta	0.370481928
18481T	Yes	POLE	c.1280C>T	Missense_Muta	0.341397849
18481T	Yes	BRCA2	c.2957del	Frame_Shift_D	0.33611691
18481T	Yes	RB1	c.971T>A	Missense_Muta	0.333333333
18481T	Yes	PCDH8	c.1975C>T	Missense_Muta	0.36
18481T	Yes	PCDH8	c.1432C>T	Missense_Muta	0.413043478
18481T	Yes	PCDH8	c.1397C>T	Missense_Muta	0.295454545
18481T	Yes	PCDH8	c.277G>A	Missense_Muta	0.371273713
18481T	Yes	PCDH17	c.1898A>G	Missense_Muta	0.394160584
18481T	Yes	PCDH17	c.2714A>T	Missense_Muta	0.364
18481T	Yes	DICER1	c.4458del	Frame_Shift_D	0.368088468
18481T	Yes	DICER1	c.1859A>G	Missense_Muta	0.123214286
18481T	Yes	AXIN1	c.1565C>T	Missense_Muta	0.28
18481T	Yes	PIGQ	c.1679G>A	Missense_Muta	0.142857143
18481T	Yes	TSC2	c.1723C>A	Missense_Muta	0.333333333
18481T	Yes	PLEKHG4	c.1574del	Frame_Shift_D	0.214285714
18481T	Yes	PLEKHG4	c.1575C>G	Missense_Muta	0.214285714
18481T	Yes	C16orf86	c.461A>G	Missense_Muta	0.191780822
18481T	Yes	CD68	c.84del	Frame_Shift_D	0.368181818
18481T	Yes	TP53	c.998G>A	Missense_Muta	0.355102041
18481T	Yes	NF1	c.8158A>G	Missense_Muta	0.310344828
18481T	Yes	ERBB2	c.2516T>C	Missense_Muta	0.169934641
18481T	Yes	KEAP1	c.1639G>A	Missense_Muta	0.35978836
18481T	Yes	DAND5	c.37C>T	Missense_Muta	0.222222222
18481T	Yes	FCHO1	c.2354T>C	Missense_Muta	0.436170213
18481T	Yes	JAK3	c.911A>T	Missense_Muta	0.48
18481T	Yes	PIK3R2	c.862C>T	Missense_Muta	0.150943396
18481T	Yes	KMT2B	c.1833G>A	Nonsense_Muta	0.443820225
18481T	Yes	ASXL1	c.2993C>T	Missense_Muta	0.34765625
18481T	Yes	SRC	c.659G>A	Missense_Muta	0.356321839

18481T	Yes	SRC	c.800G>A	Missense_Muta	0.473684211
18481T	Yes	SMC1A	c.2701G>A	Missense_Muta	0.373608903
18481T	Yes	SMC1A	c.1732-1G>T	Splice_Site	0.363914373
18481T	Yes	SMC1A	c.401T>C	Missense_Muta	0.320486815
18481T	Yes	AR	c.2086G>A	Missense_Muta	0.349887133
18481T	Yes	STAG2	c.3584G>A	Missense_Muta	0.323943662
17627T	Yes	APC	c.3733A>T	Nonsense_Muta	0.395480226
17627T	Yes	ATM	c.6679C>T	Missense_Muta	0.310559006
17627T	Yes	SETBP1	c.4511C>T	Missense_Muta	0.363636364
17627T	Yes	SMAD2	c.1272_1279dup	Frame_Shift_In	0.643410853
17627T	Yes	NXNL1	c.376C>G	Missense_Muta	0.142857143
18946T	No	NRAS	c.34G>T	Missense_Muta	0.726744186
18946T	No	APC	c.1495C>T	Nonsense_Muta	0.441201717
18946T	No	APC	c.4339del	Frame_Shift_D	0.459482038
18946T	No	SMC3	c.212C>T	Missense_Muta	0.41686747
18946T	No	ATM	c.2084T>C	Missense_Muta	0.45041816
18946T	No	ATM	c.9022C>T	Missense_Muta	0.443911793
18946T	No	CHD4	c.4216C>T	Missense_Muta	0.419981499
18946T	No	FLT3	c.106G>T	Missense_Muta	0.620921802
18946T	No	ERBB2	c.2033G>A	Missense_Muta	0.550724638
19395T	Yes	PIK3CA	c.323G>A	Missense_Muta	0.376528117
19395T	Yes	PIK3CA	c.1634A>C	Missense_Muta	0.251655629
19395T	Yes	APC	c.2336dup	Frame_Shift_In	0.39544808
19395T	Yes	APC	c.4459_4460ins	Frame_Shift_In	0.393899204
19395T	Yes	APC	c.4460C>A	Missense_Muta	0.394946809
19395T	Yes	BRAF	c.1799T>A	Missense_Muta	0.269349845
19395T	Yes	FAT3	c.2762C>A	Missense_Muta	0.3671875
19395T	Yes	FAT3	c.4718C>T	Missense_Muta	0.352380952
19395T	Yes	KMT2D	c.2021C>T	Missense_Muta	0.307692308
19395T	Yes	AGRP	c.262G>A	Missense_Muta	0.486631016
19395T	Yes	TP53	c.743G>A	Missense_Muta	0.6125
19395T	Yes	SOX9	c.736C>T	Nonsense_Muta	0.363888889
19395T	Yes	SMAD2	c.1389C>A	Nonsense_Muta	0.379496403
19395T	Yes	SMAD2	c.904T>C	Missense_Muta	0.380514706
19395T	Yes	KMT2B	c.2732C>T	Missense_Muta	0.41509434
19442T	Yes	PRDM2	c.2933C>T	Missense_Muta	0.121718377
19442T	Yes	PRDM2	c.4184G>A	Missense_Muta	0.170694864
19442T	Yes	ARID1A	c.2402dup	Frame_Shift_In	0.102857143
19442T	Yes	IGFN1	c.10258G>A	Missense_Muta	0.175
19442T	Yes	FH	c.535G>A	Missense_Muta	0.176870748
19442T	Yes	ALK	c.474dup	Frame_Shift_In	0.190082645
19442T	Yes	ALS2	c.4136_4138del	In_Frame_Del	0.178907721
19442T	Yes	ERBB4	c.3817C>T	Missense_Muta	0.151821862
19442T	Yes	BAP1	c.1628G>A	Missense_Muta	0.154185022
19442T	Yes	PBRM1	c.1601G>A	Missense_Muta	0.209191759

19442T	Yes	PIK3CA	c.331A>G	Missense_Muta	0.180987203
19442T	Yes	FGFR3	c.1075C>T	Nonsense_Muta	0.144230769
19442T	Yes	TET2	c.4317dup	Frame_Shift_In	0.193014706
19442T	Yes	TET2	c.5597C>T	Missense_Muta	0.196048632
19442T	Yes	FAT1	c.9857C>G	Missense_Muta	0.173780488
19442T	Yes	FAT1	c.4184G>A	Missense_Muta	0.121510673
19442T	Yes	FAT1	c.2833G>A	Missense_Muta	0.201787995
19442T	Yes	APC	c.4666dup	Frame_Shift_In	0.210526316
19442T	Yes	KMT2C	c.13940dup	Frame_Shift_In	0.166276347
19442T	Yes	ACTR3B	c.829C>A	Missense_Muta	0.197740113
19442T	Yes	FGFR1	c.1588G>A	Missense_Muta	0.177446103
19442T	Yes	KAT6A	c.76C>T	Missense_Muta	0.180327869
19442T	Yes	SMARCA2	c.4354dup	Frame_Shift_In	0.243589744
19442T	Yes	FAM166B	c.470C>T	Missense_Muta	0.5625
19442T	Yes	PTCH1	c.3793G>A	Missense_Muta	0.155555556
19442T	Yes	PTCH1	c.3622G>A	Missense_Muta	0.185714286
19442T	Yes	TSC1	c.1257del	Frame_Shift_D	0.217687075
19442T	Yes	NOTCH1	c.4828G>A	Missense_Muta	0.203389831
19442T	Yes	KAT6B	c.4523del	Frame_Shift_D	0.195439739
19442T	Yes	OR2D3	c.234dup	Frame_Shift_In	0.19524618
19442T	Yes	NRXN2	c.2011C>T	Missense_Muta	0.223300971
19442T	Yes	EHD1	c.490C>T	Missense_Muta	0.18694362
19442T	Yes	FAT3	c.3998A>G	Missense_Muta	0.244705882
19442T	Yes	FAT3	c.6679C>T	Missense_Muta	0.12424608
19442T	Yes	KMT2D	c.7109G>A	Missense_Muta	0.216216216
19442T	Yes	KMT2D	c.7061del	Frame_Shift_D	0.351351351
19442T	Yes	KMT2D	c.4841G>A	Missense_Muta	0.174563591
19442T	Yes	KMT2D	c.2993del	Frame_Shift_D	0.170731707
19442T	Yes	NCOR2	c.6923C>T	Missense_Muta	0.141304348
19442T	Yes	RB1	c.1478T>A	Missense_Muta	0.149797571
19442T	Yes	PCDH17	c.2579C>T	Missense_Muta	0.202925046
19442T	Yes	AKT1	c.745C>T	Missense_Muta	0.285714286
19442T	Yes	BLM	c.2268del	Frame_Shift_D	0.213296399
19442T	Yes	AXIN1	c.1523del	Frame_Shift_D	0.407407407
19442T	Yes	CREBBP	c.2469G>T	Missense_Muta	0.111111111
19442T	Yes	FANCA	c.623C>T	Missense_Muta	0.18018018
19442T	Yes	MAP2K2	c.329C>T	Missense_Muta	0.209923664
19442T	Yes	SMARCA4	c.2714G>A	Missense_Muta	0.166240409
19442T	Yes	SMARCA4	c.4336C>G	Missense_Muta	0.156593407
19442T	Yes	OR7A17	c.113C>T	Missense_Muta	0.156097561
19442T	Yes	SLC27A1	c.1259G>A	Missense_Muta	0.183431953
19442T	Yes	PIK3R2	c.107C>T	Missense_Muta	0.2
19442T	Yes	SRC	c.1259C>T	Missense_Muta	0.174496644
19442T	Yes	RUNX1	c.1108G>T	Missense_Muta	0.193548387
19442T	Yes	EP300	c.5375A>C	Missense_Muta	0.177570093

19442T	Yes	SMC1A	c.2695G>A	Missense_Muta	0.203262233
19442T	Yes	AMER1	c.3009A>G	Missense_Muta	0.197101449
19442T	Yes	ATRX	c.3682C>T	Missense_Muta	0.169724771
19442T	Yes	PLXNB3	c.1970G>A	Missense_Muta	0.11627907
17787T	No	TP53	c.701A>G	Missense_Muta	0.618421053
17787T	No	KEAP1	c.1133G>A	Missense_Muta	0.663793103
18081T	Yes	APC	c.646C>T	Nonsense_Muta	0.635416667
18081T	Yes	PDE6A	c.2302G>A	Missense_Muta	0.333333333
18081T	Yes	POLE	c.5573G>A	Missense_Muta	0.381294964
19106T	Yes	PRDM16	c.1898C>T	Missense_Muta	0.951612903
19106T	Yes	PRDM16	c.3369_3371dup	In_Frame_Ins	0.92
19106T	Yes	IDH1	c.532G>A	Missense_Muta	0.302449414
19106T	Yes	MLH1	c.655A>G	Missense_Muta	0.372986369
19106T	Yes	TACC3	c.427G>A	Missense_Muta	0.358422939
19106T	Yes	UGT2B7	c.801_802del	Missense_Muta	0.319034853
19106T	Yes	FAT1	c.8535G>A	Missense_Muta	0.355665025
19106T	Yes	PNPLA1	c.1268C>A	Missense_Muta	0.914285714
19106T	Yes	TSC1	c.1079C>A	Missense_Muta	0.337777778
19106T	Yes	ATE1	c.499C>T	Missense_Muta	0.378723404
19106T	Yes	TACC2	c.2488C>T	Missense_Muta	0.363043478
19106T	Yes	FAT3	c.8983C>A	Missense_Muta	0.290087464
19106T	Yes	TECTA	c.1111A>G	Missense_Muta	0.33492823
19106T	Yes	TP53BP1	c.1074C>G	Missense_Muta	0.949874687
19106T	Yes	MPDU1	c.685G>A	Missense_Muta	0.969465649
19106T	Yes	TP53	c.326dup	Frame_Shift_In	0.910714286
19282T	No	SMO	c.2081del	Frame_Shift_D	0.117021277
18607T	Yes	ADCY3	c.2387G>A	Missense_Muta	0.167630058
18607T	Yes	MSH6	c.2079del	Frame_Shift_D	0.16286645
18607T	Yes	CASP8	c.1596del	Frame_Shift_D	0.121794872
18607T	Yes	PIK3CA	c.3140A>G	Missense_Muta	0.159292035
18607T	Yes	TET2	c.3157C>T	Nonsense_Muta	0.166666667
18607T	Yes	FAT1	c.13717G>A	Missense_Muta	0.153439153
18607T	Yes	EGFR	c.1282G>A	Missense_Muta	0.174208145
18607T	Yes	PVRIG	c.892del	Frame_Shift_D	0.115942029
18607T	Yes	BRAF	c.1799T>A	Missense_Muta	0.165254237
18607T	Yes	WT1	c.496G>A	Missense_Muta	0.142857143
18607T	Yes	CCDC73	c.1341del	Frame_Shift_D	0.363636364
18607T	Yes	KMT2D	c.1940del	Frame_Shift_D	0.24
18607T	Yes	BRCA2	c.10248del	Frame_Shift_D	0.136842105
18607T	Yes	C14orf79	c.83C>A	Missense_Muta	0.171929825
18607T	Yes	IDH2	c.435del	Frame_Shift_D	0.184466019
18607T	Yes	SPNS1	c.1133G>A	Missense_Muta	0.217391304
18607T	Yes	TRADD	c.286C>T	Missense_Muta	0.285714286
18607T	Yes	ERBB2	c.2446C>T	Missense_Muta	0.154589372
18607T	Yes	ERBB2	c.3235G>A	Missense_Muta	0.159663866

18607T	Yes	SMARCE1	c.903G>T	Missense_Muta	0.157258065
18607T	Yes	SOX9	c.984_1036del	Frame_Shift_D	0.121428571
18607T	Yes	RGL3	c.925G>A	Missense_Muta	0.141025641
18607T	Yes	CHEK2	c.1081C>T	Missense_Muta	0.158798283
18810T	Yes	PIK3CA	c.1633G>A	Missense_Muta	0.406779661
18810T	Yes	FAT1	c.7699C>T	Missense_Muta	0.437694704
18810T	Yes	APC	c.1958+2T>G	Splice_Site	0.42019544
18810T	Yes	APC	c.4464_4467del	Frame_Shift_D	0.382075472
18810T	Yes	KRAS	c.38G>A	Missense_Muta	0.426273458
18810T	Yes	FZD10	c.1127C>T	Missense_Muta	0.446327684
18810T	Yes	SMAD2	c.961C>T	Nonsense_Muta	0.112676056
18810T	Yes	SMAD4	c.1065C>A	Missense_Muta	0.535947712
18739T	Yes	PIK3CA	c.1624G>A	Missense_Muta	0.290187891
18739T	Yes	FBXW7	c.941del	Frame_Shift_D	0.367454068
18739T	Yes	APC	c.4166_4167ins	Frame_Shift_In	0.430107527
18739T	Yes	KRAS	c.35G>A	Missense_Muta	0.486166008
18739T	Yes	TP53	c.743G>A	Missense_Muta	0.696296296
19441T	Yes	APC	c.2711_2712del	Frame_Shift_D	0.392703863
19441T	Yes	NOTCH1	c.4864C>T	Missense_Muta	0.465116279
19441T	Yes	TP53	c.880G>T	Nonsense_Muta	0.361313869
19441T	Yes	FAM129C	c.1967G>A	Missense_Muta	0.380614657
19342T	Yes	SMARCA2	c.2363G>A	Nonsense_Muta	0.339756592
19342T	Yes	TP53	c.853G>T	Nonsense_Muta	0.611515553
19342T	Yes	TP53	c.659A>G	Missense_Muta	0.231943629
19342T	Yes	SUZ12	c.1105T>C	Missense_Muta	0.601747815
19342T	Yes	SMAD4	c.1594_1596del	In_Frame_Del	0.573435504

**Supplementary Table
8:
Juxtaposition of
primary
CRC cases
with
patient
demographics and
PDZK1IP1
SE status.**

Samples	Has <i>PDZK1IP1</i>	Sex	Age	Colon Anatomy
18481T	Yes	no data		
17753T	Yes	Male		63 Sigmoid colon and rectum
18607T	Yes	Male		71 Terminal ileum appendix and ascending colon
18810T	Yes	Male		67 Terminal ileum and cecum
19441T	Yes	Male		71 Descending colon
19282T	No	Female		82 Terminal ileum and ascending colon
19106T	Yes	Male		74 Sigmoid colon and rectum
19342T	Yes	Male		53 Transverse colon
18739T	Yes	Male		63 Sigmoid colon
18946T	No	Male		83 Descending colon
18081T	Yes	Male		62 Sigmoid colon and rectum

19442T	Yes	Female	61	Terminal ileum appendix and ascending colon
19395T	Yes	Male	61	Terminal ileum, cecum, appendix, and ascending colon
17627T	Yes	Male	64	Sigmoid colon
17787T	No	Male	67	Descending and sigmoid colon

**Supplementary Table 9:
Juxtaposition of primary CRC cases with pathological features and *PDZK1IP1* SE status.**

Samples	Has <i>PDZK1IP1</i> super-enhancer?	Tumor Staging	Primary Tumor Description
18481T	Yes		No data
17753T	Yes	pT4aN2a	Invasive, moderately differentiated adenocarcinoma with mucinous features. The tumor invades through the wall to the serosal surface with acute inflammatory reaction. Lymphovascular and perineural invasion identified. Extramural large vessel invasion identified.
18607T	Yes	pT3N1a	Invasive poorly differentiated adenocarcinoma with medullary feature. Invades into subserosal soft tissue. Perineural invasion also present. Extensive lymphatic invasion seen. IHC shows MLH1 and PMS2 loss, possible MSI.

18810T	Yes	pT1N0	Invasive moderately differentiated adenocarcinoma. The tumor invades the submucosa. Foci suspicious for lymphovascular invasion are identified. Perineural invasion is not identified.
19441T	Yes	pT4aN0	Invasive moderately differentiated adenocarcinoma extending through the serosal surface. Perineural and lymphovascular space invasion are present. Peritumoral abscess with foreign body giant cell reaction. Large extramural vein invasion.
19282T	No	no data	Poorly differentiated adenocarcinoma. No adenomatous component is found to confirm primary colonic origin. The tumor is almost entirely intralymphatic and there is focal intramural venous invasion. The tumor is CDX2 negative which is uncommon for primary CRC but not exclusionary. Additional immunostains are negative for primary breast, GYN, or pulmonary origin.

19106T	Yes	pT3N1a	Invasive moderately differentiated adenocarcinoma with invasion to the pericorectal adipose tissue. Lymphovascular and neural invasions present.
19342T	Yes	pT2N0	Moderately differentiated mucinous adenocarcinoma with invasion into the muscularis propria. India ink tattoo noted.
18739T	Yes	pT4aN0	Moderately differentiated adenocarcinoma with transmural invasion to the visceral peritoneum. Focal high-grade tumor budding and extramural large vein invasion are identified.
18946T	No	pT4N0	Invasive, moderately differentiated adenocarcinoma extending to the serosal surface. Submucosal ink tattoo. Lymphovascular or perineural space invasion is not identified. Exuberant fibrohistiocytic reaction of the subserosal soft tissue.
18081T	Yes	pT3N0	Invasive moderately differentiated adenocarcinoma. The tumor invades the muscularis propria and into subserosal soft tissue. Tumor budding.

19442T	Yes	pT4aN0	Invasive moderately differentiated mucinous adenocarcinoma. Extended through the serosal surface into the visceral peritoneum with associated fibroinflammatory response. Lymphovascular or perineural space invasion is not identified. No evidence of large extramural vein invasion.
19395T	Yes		Moderately differentiated mucinous adenocarcinoma. The tumor invades through muscularis propria into pericolic fat. Vascular invasion is not identified. Perineural invasion is not identified.
17627T	Yes	no data	No data
17787T	No	pT4bN2b	Moderate to poorly differentiated carcinoma with mixed morphology. Extensive lymphovascular and perineural invasion are noted. Extramural large vessel invasion is identified. Background colon with mildly active chronic colitis and melanosis coli. Long history with quiescent ulcerative colitis.

Supplementary Table 10: H3K27ac ChIP-seq metrics.

17627T: 74,355 called peaks stitched to 17,726 enhancers.
17627N: 75,466 called peaks stitched to 21,636 enhancers.
17753T: 59,688 called peaks stitched to 13,726 enhancers.
17753N: 175,589 called peaks stitched to 5,392 enhancers.
17787T: 76,011 called peaks stitched to 20,341 enhancers.
17787N: 66,728 called peaks stitched to 17,567 enhancers.
18081T: 54,343 called peaks stitched to 15,075 enhancers.
18081N: 52,082 called peaks stitched to 14,110 enhancers.
18481T: 29,640 called peaks stitched to 7,921 enhancers.
18481N: 75,102 called peaks stitched to 24,268 enhancers.
18607T: 47,801 called peaks stitched to 24,704 enhancers.
18607N: 80,274 called peaks stitched to 19,847 enhancers.
18739T: 56,757 called peaks stitched to 15,073 enhancers.
18739N: 34,545 called peaks stitched to 5,692 enhancers.
18946T: 51,652 called peaks stitched to 19,214 enhancers.
18946N: 27,010 called peaks stitched to 15,655 enhancers.
18810T: 72,790 called peaks stitched to 13,804 enhancers.
18810N: 57,932 called peaks stitched to 6,217 enhancers.
19106T: 58,973 called peaks stitched to 16,857 enhancers.
19106N: 61,476 called peaks stitched to 15,331 enhancers.
19282T: 63,909 called peaks stitched to 17,020 enhancers.
19282N: 59,106 called peaks stitched to 15,434 enhancers.
19342T: 53,155 called peaks stitched to 14,616 enhancers.
19342N: 52,206 called peaks stitched to 13,616 enhancers.
19395T: 63,693 called peaks stitched to 18,157 enhancers.
19395N: 47,387 called peaks to 13,483 enhancers.
19441T: 70,089 called peaks stitched to 18,884 enhancers.
19441N: 63,324 called peaks stitched to 16,074 enhancers.
19442T: 62,613 called peaks stitched to 16,760 enhancers.
19442N: 77,621 called peaks stitched to 19,239 enhancers.
HT29 cells: 43,055 called peaks stitched to 10,784 enhancers.
HT29 xenograft tumor rep. 1: 47,940 called peaks stitched to 13,097 enhancers.
HT29 xenograft tumor rep. 2: 61,713 called peaks stitched to 18,869 enhancers.
HT29 xenograft tumors rep. 3: 27,347 called peaks stitched to 7,049 enhancers.
HT29 TNF-alpha, IFN-gamma, and IL-6 treated cells: 60,741 called peaks stitched to 15,139 enhancers.

Supplementary Table 11:
Consensus molecular subtypes of primary CRCs and PDZK1IP1 expression by RNA-seq.

Primary CRC	prediction	P value	FDR	PDZK1IP1 mRNA expression (TPM)
X17243T	CMS2	0.001	0.00133333	138.915
X17547T	CMS4	0.001	0.00133333	1.31922
X17561T	CMS1	0.002997	0.00368862	118.964
X17627T	CMS3	0.001	0.00133333	96.4203
X17753T	CMS1	0.00499501	0.00570858	224.632
X17787T	CMS4	0.001	0.00133333	14.4398
X18081T	CMS2	0.001	0.00133333	130.041
X18481T	CMS3	0.001	0.00133333	61.7672
X18607T	CMS1	0.001	0.00133333	146.586
X18810T	CMS3	0.001	0.00133333	90.4694
X19057T	CMS4	0.001	0.00133333	1.48811
X19107T	CMS2	0.001	0.00133333	67.1396
X19282T	CMS4	0.001	0.00133333	0.865068
X19342T	NA	0.94205794	0.94205794	130.711
X19395T	NA	0.44155844	0.47099567	70.1376

**Supplementary Table
12:
H3K27ac
and
H3K4me1
calling of
the
PDZK1IP1
super-
enhancer
using
ROSE.**

Sample	H3K27ac?	H3K4me1?
N1 (normal)	No	No
N3 (normal)	No	No
N4 (normal)	No	No
N5 (normal)	No	No
N6 (normal)	No	No
N8 (normal)	No	No
N11 (normal)	No	No
N12 (normal)	No	No
N13 (normal)	No	No
N15 (normal)	No	No
N17 (normal)	No	No
N18 (normal)	No	No
N20 (normal)	No	No

T1 (tumor)	Yes	No
T3 (tumor)	No	No
T4 (tumor)	Yes	No
T5 (tumor)	No	No
T7 (tumor)	No	No
T8 (tumor)	No	No
T11 (tumor)	No	No
T12 (tumor)	No	No
T13 (tumor)	No	No
T14 (tumor)	Yes	No
T15 (tumor)	Yes	Yes
T16 (tumor)	No	No
T17 (tumor)	Yes	No
T18 (tumor)	Yes	Yes