Supplementary materials for

Mouse embryonic stem cells exhibit cancer-like DNA methylation landscapes upon DNMT1 overexpression

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Figures S1 to S2

Tables S1 to S3

Other supplementary materials for this manuscript include the following:

Data S1 to S7

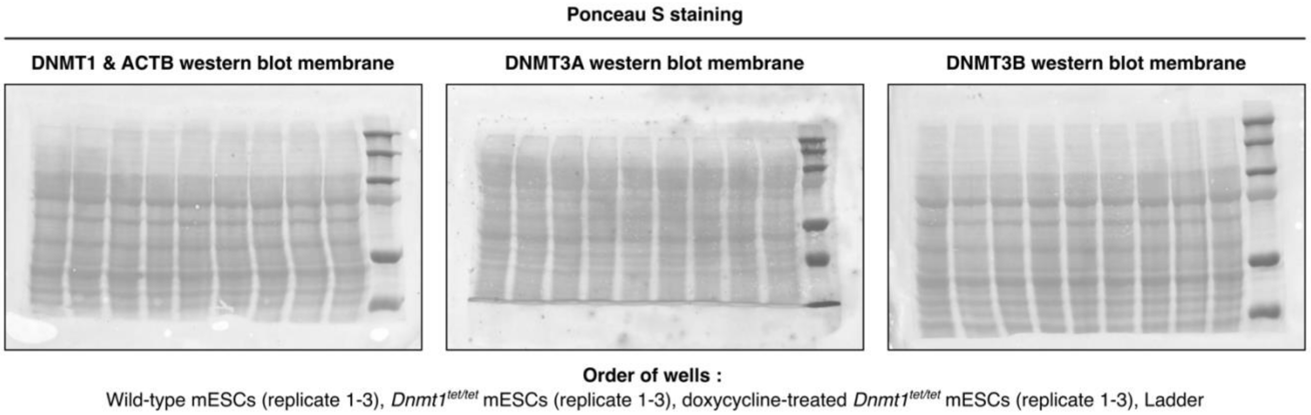


Figure S1. Perturbation of the DNA methylation machinery in *Dnmt1*$^{\text{tet/tet}}$ mESCs. Images of Ponceau S staining of western blot membranes used for normalizing the quantification of band intensities. *Related to Figure 1 and Data S2*.

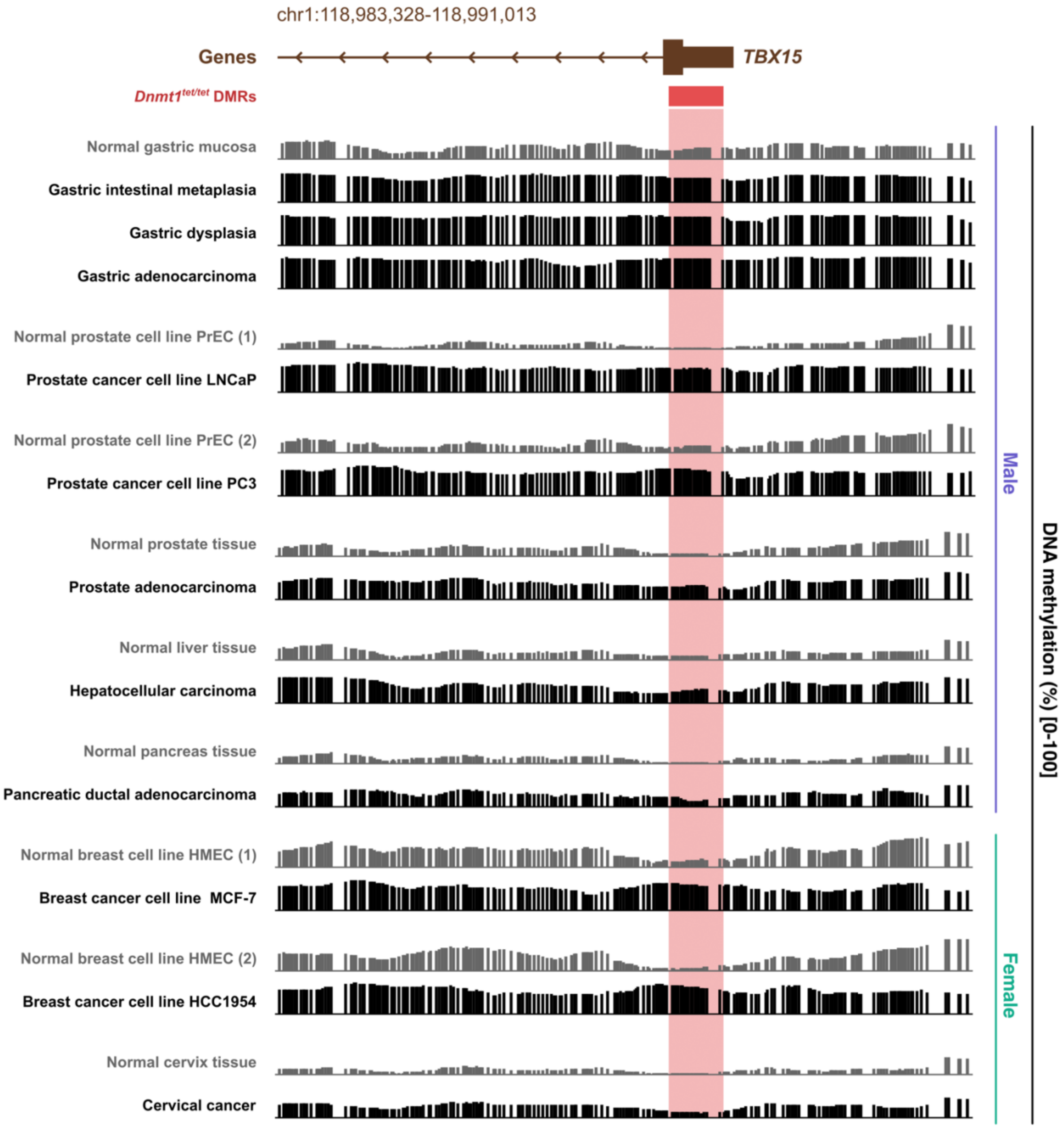
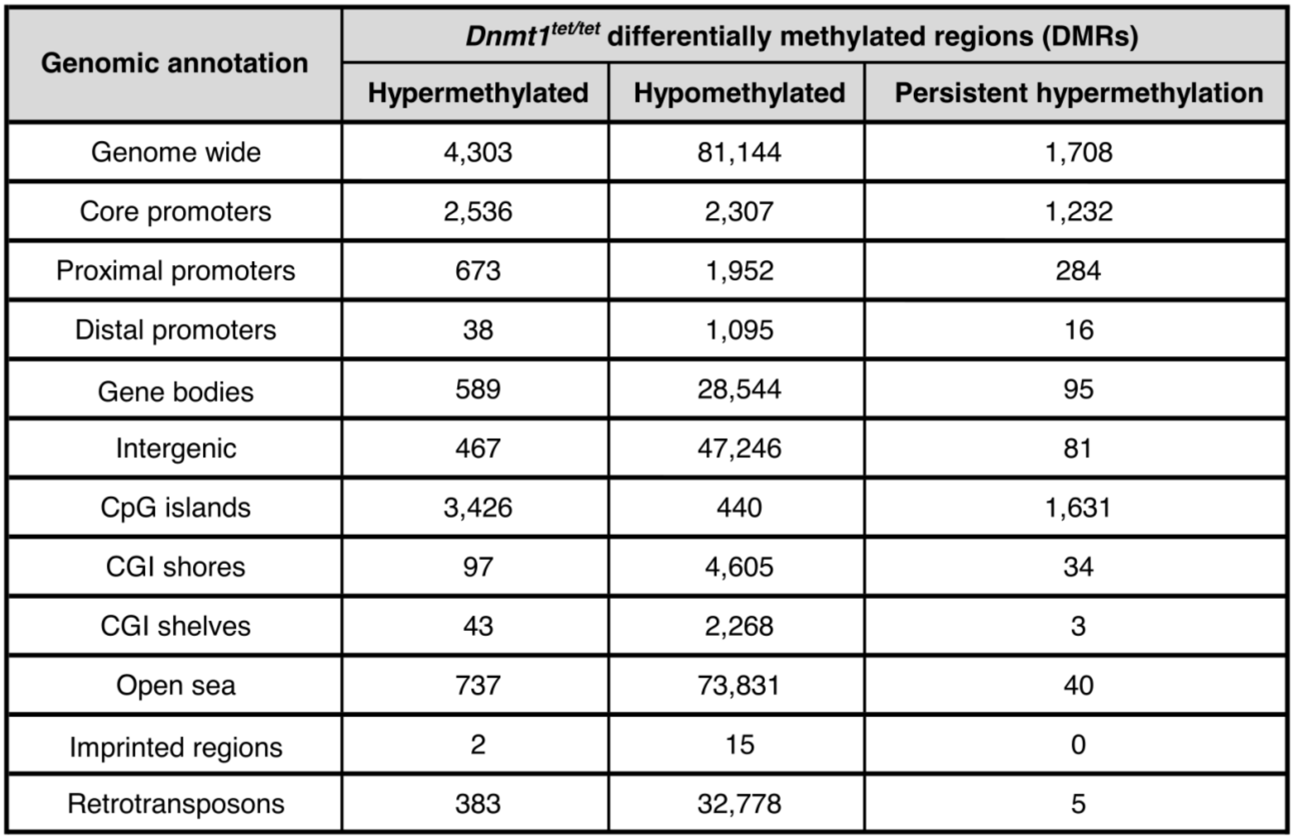
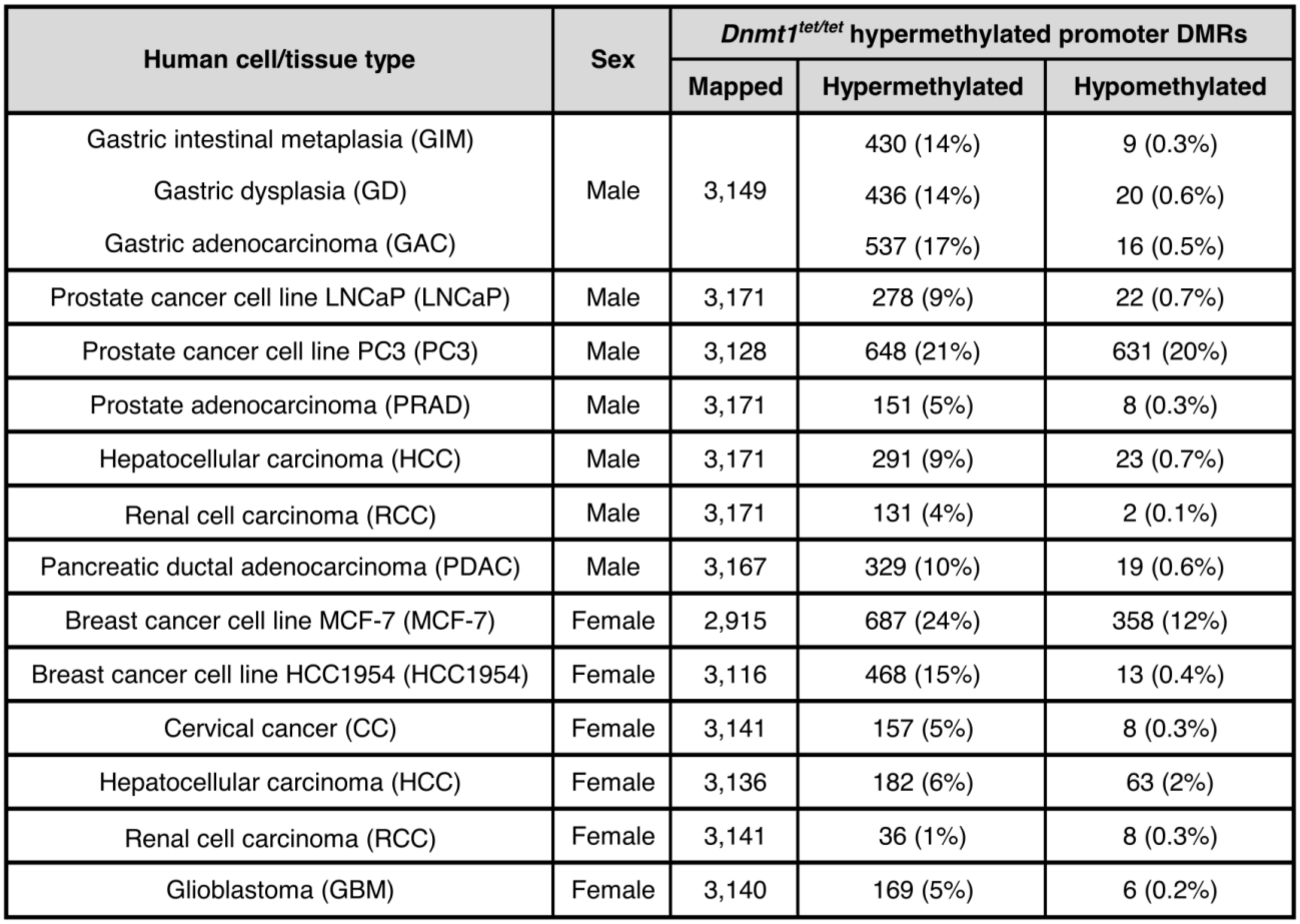


Figure S2. Conserved promoter hypermethylation between *Dnmt1*$^{tet/tet}$ mESCs and human cancer. Genomic tracks showing conserved *Dnmt1*$^{tet/tet}$ hypermethylation of the *TBX15* promoter across many human cancers.



Genomic annotation	***Dnmt1*$^{\textit{tet/tet}}$ differentially methylated regions (DMRs)**		
	Hypermethylated	**Hypomethylated**	**Persistent hypermethylation**
Genome wide	4,303	81,144	1,708
Core promoters	2,536	2,307	1,232
Proximal promoters	673	1,952	284
Distal promoters	38	1,095	16
Gene bodies	589	28,544	95
Intergenic	467	47,246	81
CpG islands	3,426	440	1,631
CGI shores	97	4,605	34
CGI shelves	43	2,268	3
Open sea	737	73,831	40
Imprinted regions	2	15	0
Retrotransposons	383	32,778	5

Table S1. Number of *Dnmt1*$^{\text{tet/tet}}$ DMRs by genomic annotation that were either hypermethylated or hypomethylated and that showed persistent hypermethylation. Persistent hypermethylation: hypermethylated DMRs showing a sustained increase in DNA methylation ≥ 10% in doxycycline-treated *Dnmt1*$^{\text{tet/tet}}$ mESCs. *Related to Figures 2 and 5*.



Human cell/tissue type	Sex	*Dnmt1*$^{tet/tet}$ hypermethylated promoter DMRs		
		Mapped	Hypermethylated	Hypomethylated
Gastric intestinal metaplasia (GIM)	Male	3,149	430 (14%)	9 (0.3%)
Gastric dysplasia (GD)			436 (14%)	20 (0.6%)
Gastric adenocarcinoma (GAC)			537 (17%)	16 (0.5%)
Prostate cancer cell line LNCaP (LNCaP)	Male	3,171	278 (9%)	22 (0.7%)
Prostate cancer cell line PC3 (PC3)	Male	3,128	648 (21%)	631 (20%)
Prostate adenocarcinoma (PRAD)	Male	3,171	151 (5%)	8 (0.3%)
Hepatocellular carcinoma (HCC)	Male	3,171	291 (9%)	23 (0.7%)
Renal cell carcinoma (RCC)	Male	3,171	131 (4%)	2 (0.1%)
Pancreatic ductal adenocarcinoma (PDAC)	Male	3,167	329 (10%)	19 (0.6%)
Breast cancer cell line MCF-7 (MCF-7)	Female	2,915	687 (24%)	358 (12%)
Breast cancer cell line HCC1954 (HCC1954)	Female	3,116	468 (15%)	13 (0.4%)
Cervical cancer (CC)	Female	3,141	157 (5%)	8 (0.3%)
Hepatocellular carcinoma (HCC)	Female	3,136	182 (6%)	63 (2%)
Renal cell carcinoma (RCC)	Female	3,141	36 (1%)	8 (0.3%)
Glioblastoma (GBM)	Female	3,140	169 (5%)	6 (0.2%)

Table S2. Number of human genomic regions corresponding to the *Dnmt1*$^{tet/tet}$ hypermethylated promoter DMRs that were mapped and that were either hypermethylated or hypomethylated in various male and female human cancer samples. *See also Data S7. Related to Figures 6 and 7.*

Sample	GIM	GD	GAC	LNCaP	PC3	PRAD	HCC (M)	RCC (M)	PDAC	MCF-7	HCC1954	CC	HCC (F)	RCC (F)	GBM
GIM	406	381	398	137	368	96	168	95	232	244	270	122	73	15	97
GD	381	431	413	136	385	93	168	94	237	248	281	126	78	17	94
GAC	398	413	513	163	447	107	189	97	257	290	318	133	90	19	102
LNCaP	137	136	163	277	174	115	124	69	118	177	203	58	63	20	76
PC3	368	385	447	174	633	112	200	103	252	303	328	131	101	23	113
PRAD	96	93	107	115	112	148	83	48	84	107	131	41	39	15	48
HCC (M)	168	168	189	124	200	83	288	80	132	154	181	66	91	19	80
RCC (M)	95	94	97	69	103	48	80	129	86	90	103	49	47	23	58
PDAC	232	237	257	118	252	84	132	86	325	182	209	98	64	18	83
MCF-7	244	248	290	177	303	107	154	90	182	687	284	108	76	19	90
HCC1954	270	281	318	203	328	131	181	103	209	284	468	123	87	22	99
CC	122	126	133	58	131	41	66	49	98	108	123	157	36	11	44
HCC (F)	73	78	90	63	101	39	91	47	64	76	87	36	182	14	43
RCC (F)	15	17	19	20	23	15	19	23	18	19	22	11	14	36	22
GBM	97	94	102	76	113	48	80	58	83	90	99	44	43	22	169

Table S3. Number of regions of conserved *Dnmt1*$^{tet/tet}$ promoter hypermethylation that were shared between different human cancer samples. Regions on chromosomes X and Y were not included in this analysis. M: male, F: female. *See also Table S2*. *Related to Figure 7*.