Supplemental information

DNMT1 in *Six2* progenitor cells is essential for transposable element silencing and kidney development

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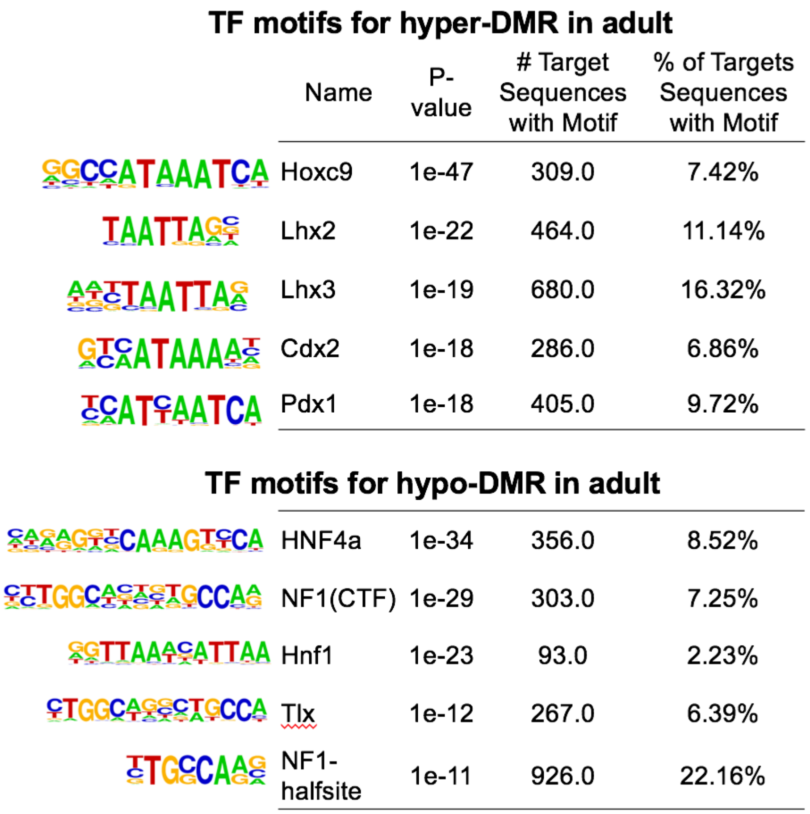


TF motifs for hyper-DMR in adult

Name	P-value	# Target Sequences with Motif	% of Targets Sequences with Motif
Hoxc9	1e-47	309.0	7.42%
Lhx2	1e-22	464.0	11.14%
Lhx3	1e-19	680.0	16.32%
Cdx2	1e-18	286.0	6.86%
Pdx1	1e-18	405.0	9.72%

TF motifs for hypo-DMR in adult

Name	P-value	# Target Sequences with Motif	% of Targets Sequences with Motif
HNF4a	1e-34	356.0	8.52%
NF1(CTF)	1e-29	303.0	7.25%
Hnf1	1e-23	93.0	2.23%
Tlx	1e-12	267.0	6.39%
NF1-halfsite	1e-11	926.0	22.16%

Figure S1. Transcription factor motif enrichment analysis of DMRs. TF motifs enriched in DMRs between P0 and adult mouse kidneys.

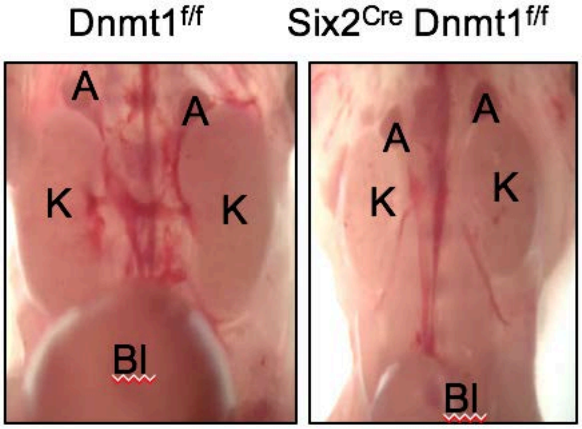


Figure S2. Gross morphology of *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice. Urinary bladder: UB, kidney: K and adrenal: A

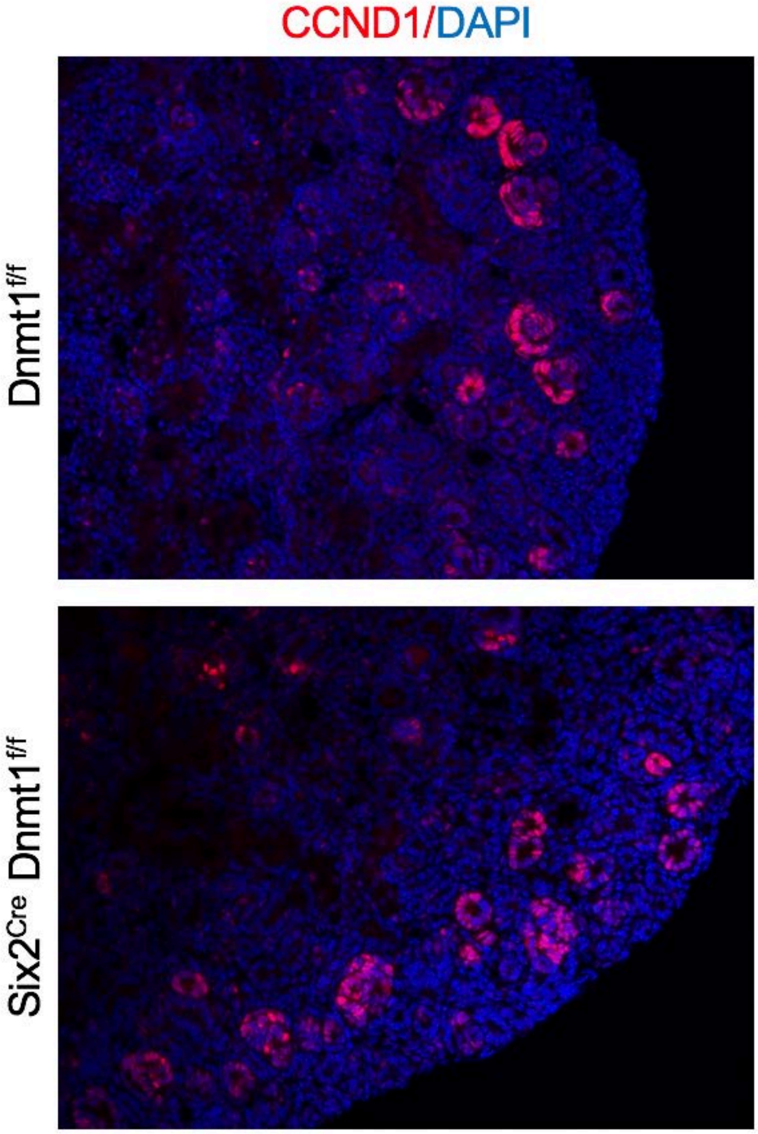


Figure S3. Immunofluorescence staining of CCND1 in *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ kidneys.

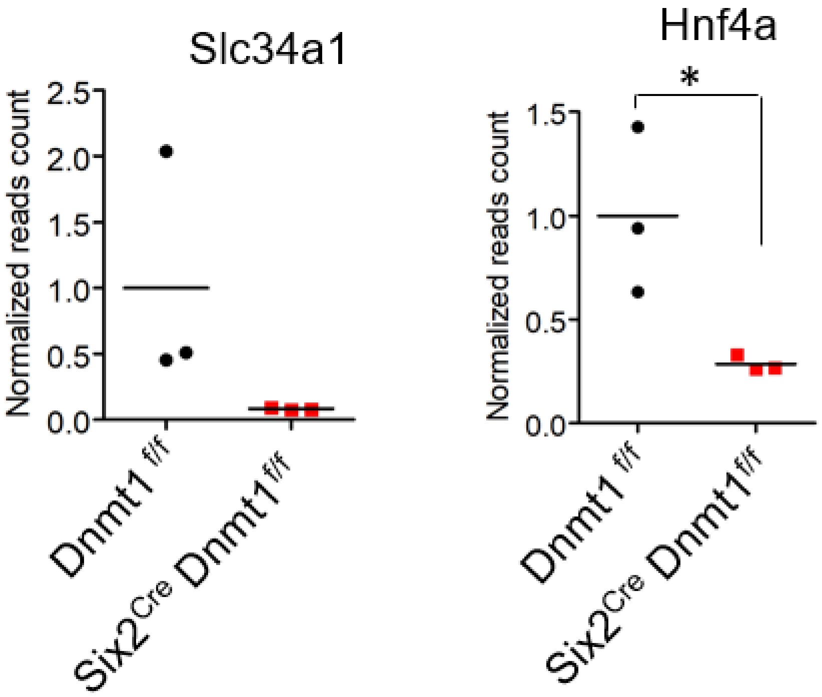


Figure S4. Expression of proximal tubule markers in *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ kidneys.

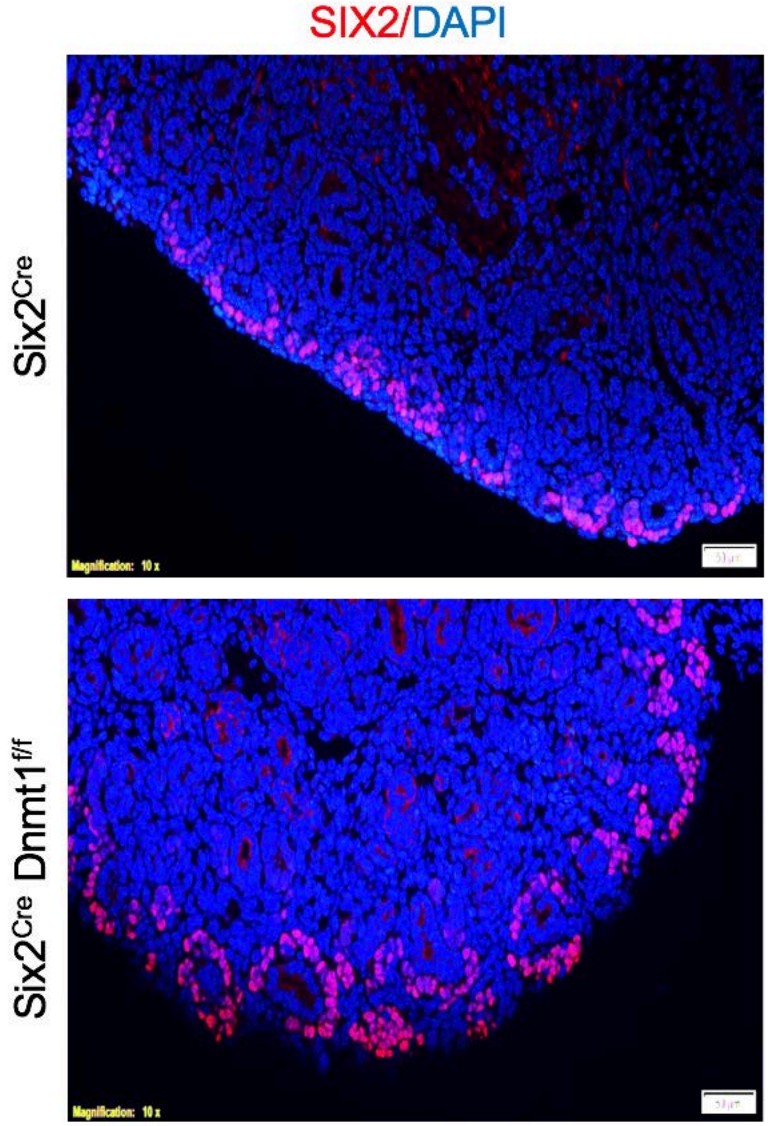


Figure S5. Immunofluorescence staining of SIX2 in *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ kidneys.

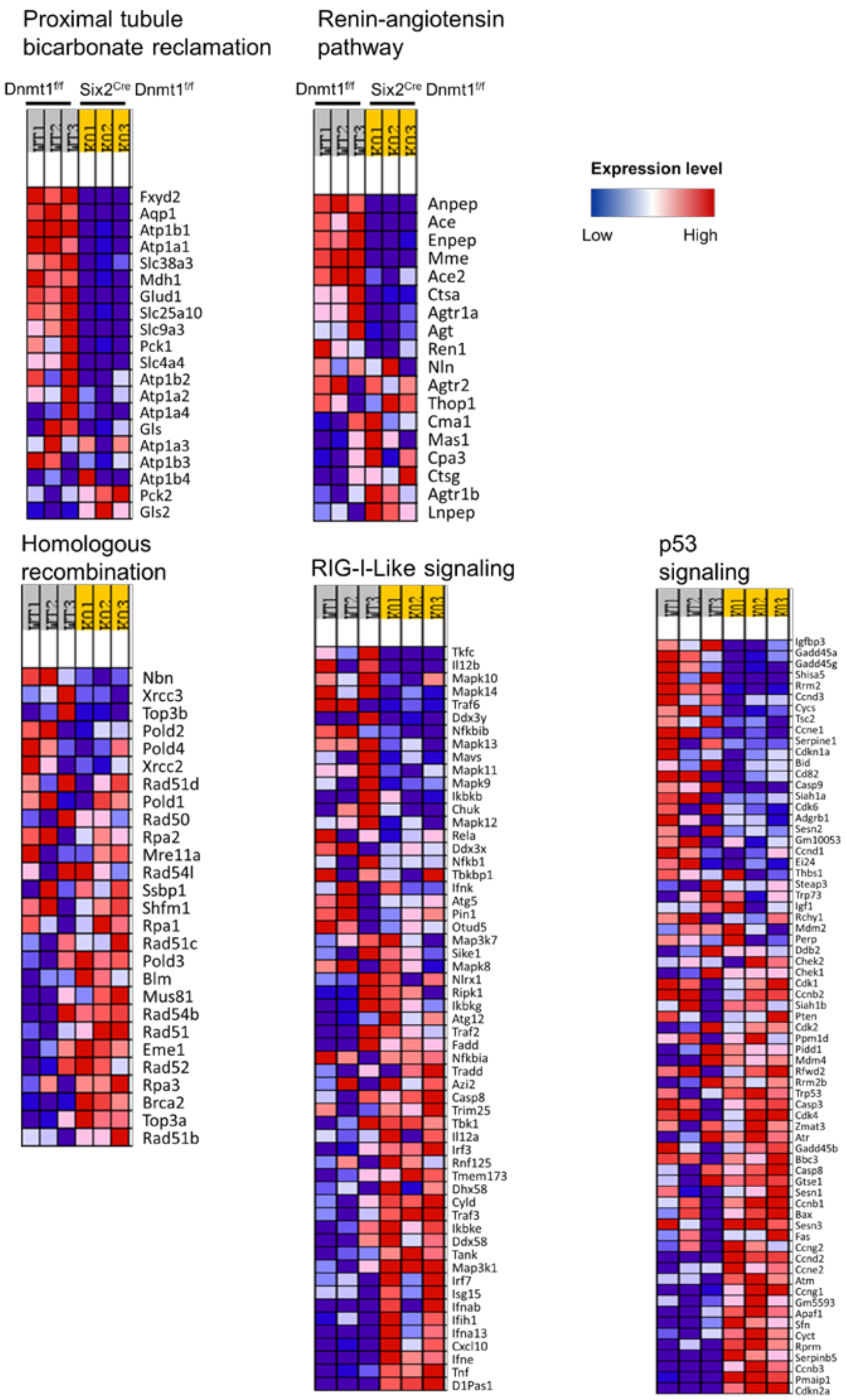
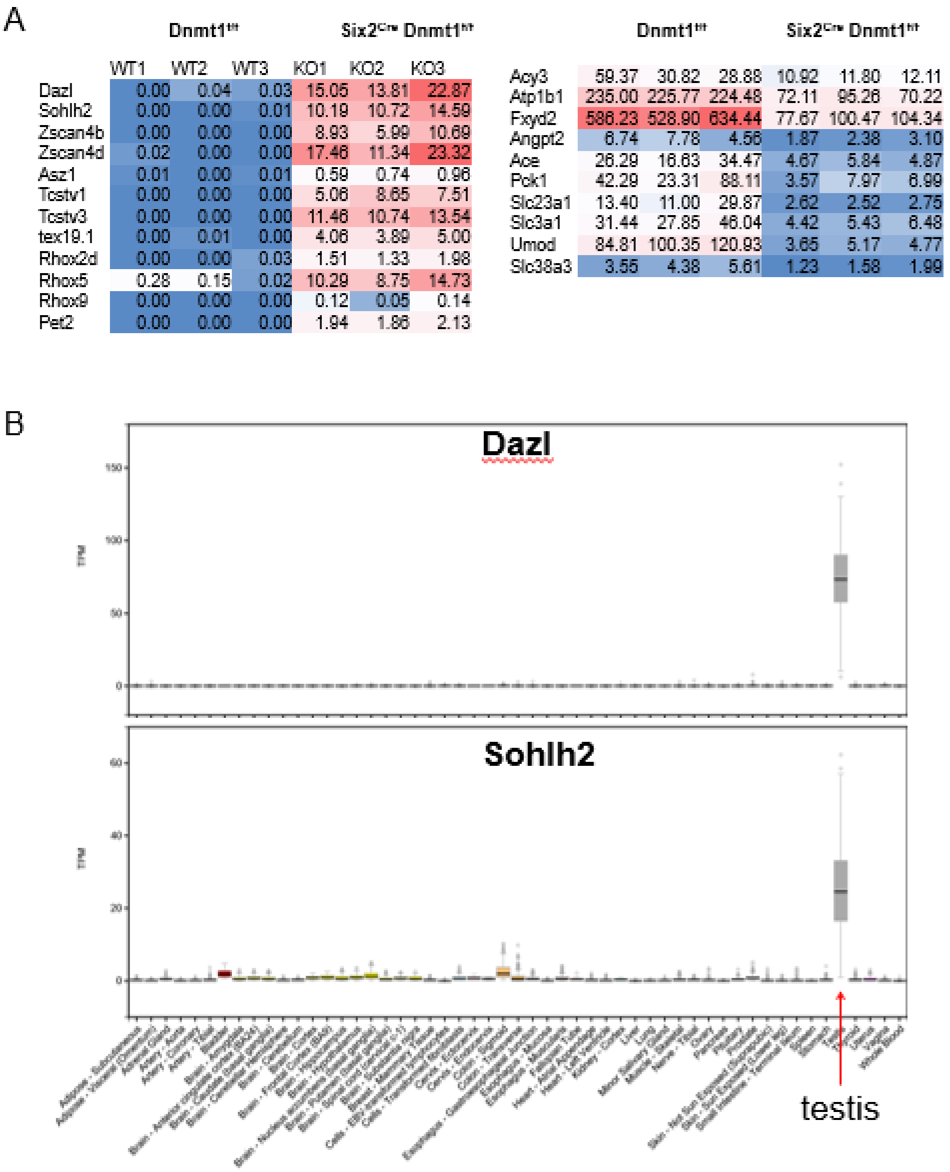


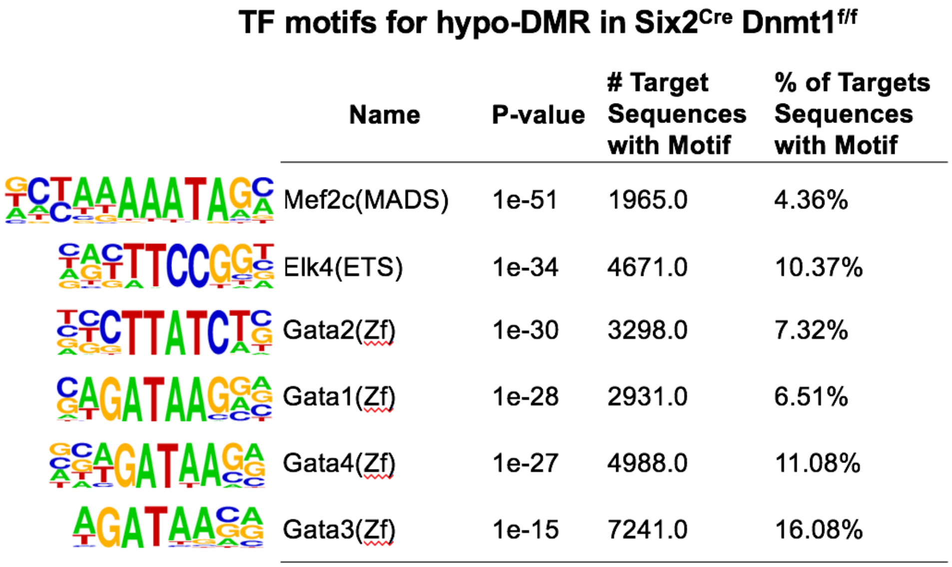
Figure S6. Heatmap of representative target genes showing gene expression differences. Gene set enrichment analysis of *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice showing expression of selected pathway genes.



	Dnmt1$^{f/f}$			Six2^{Cre} Dnmt1$^{f/f}$		
	WT1	WT2	WT3	KO1	KO2	KO3
Dazl	0.00	0.04	0.03	15.05	13.81	22.87
Sohlh2	0.00	0.00	0.01	10.19	10.72	14.59
Zscan4b	0.00	0.00	0.00	8.93	5.99	10.69
Zscan4d	0.02	0.00	0.00	17.46	11.34	23.32
Asz1	0.01	0.00	0.01	0.59	0.74	0.96
Tcstv1	0.00	0.00	0.00	5.06	8.65	7.51
Tcstv3	0.00	0.00	0.00	11.46	10.74	13.54
tex19.1	0.00	0.01	0.00	4.06	3.89	5.00
Rhox2d	0.00	0.00	0.03	1.51	1.33	1.98
Rhox5	0.28	0.15	0.02	10.29	8.75	14.73
Rhox9	0.00	0.00	0.00	0.12	0.05	0.14
Pet2	0.00	0.00	0.00	1.94	1.86	2.13

	Dnmt1$^{f/f}$			Six2^{Cre} Dnmt1$^{f/f}$		
Acy3	59.37	30.82	28.88	10.92	11.80	12.11
Atp1b1	235.00	225.77	224.48	72.11	95.26	70.22
Fxyd2	586.23	528.90	634.44	77.67	100.47	104.34
Angpt2	6.74	7.78	4.56	1.87	2.38	3.10
Ace	26.29	16.63	34.47	4.67	5.84	4.87
Pck1	42.29	23.31	88.11	3.57	7.97	6.99
Slc23a1	13.40	11.00	29.87	2.62	2.52	2.75
Slc3a1	31.44	27.85	46.04	4.42	5.43	6.48
Umod	84.81	100.35	120.93	3.65	5.17	4.77
Slc38a3	3.55	4.38	5.61	1.23	1.58	1.99

Figure S7. Gene expression patterns in *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice. (A) RNA sequencing FPKM of gene expression in *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice. FPKM stands for Fragments Per Kilobase of transcript per Million mapped reads. (B) Transcript level of *Dazl* and *Sohlh2* in different human tissue samples. Data is from GTEx Analysis Release V7.



TF motifs for hypo-DMR in Six2^{Cre} Dnmt1$^{f/f}$

Name	P-value	# Target Sequences with Motif	% of Targets Sequences with Motif
Mef2c(MADS)	1e-51	1965.0	4.36%
Elk4(ETS)	1e-34	4671.0	10.37%
Gata2(Zf)	1e-30	3298.0	7.32%
Gata1(Zf)	1e-28	2931.0	6.51%
Gata4(Zf)	1e-27	4988.0	11.08%
Gata3(Zf)	1e-15	7241.0	16.08%

Figure S8. Transcription factor motif enrichment analysis of DMRs. TF motifs enriched in hypo-DMRs between *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mouse kidneys.

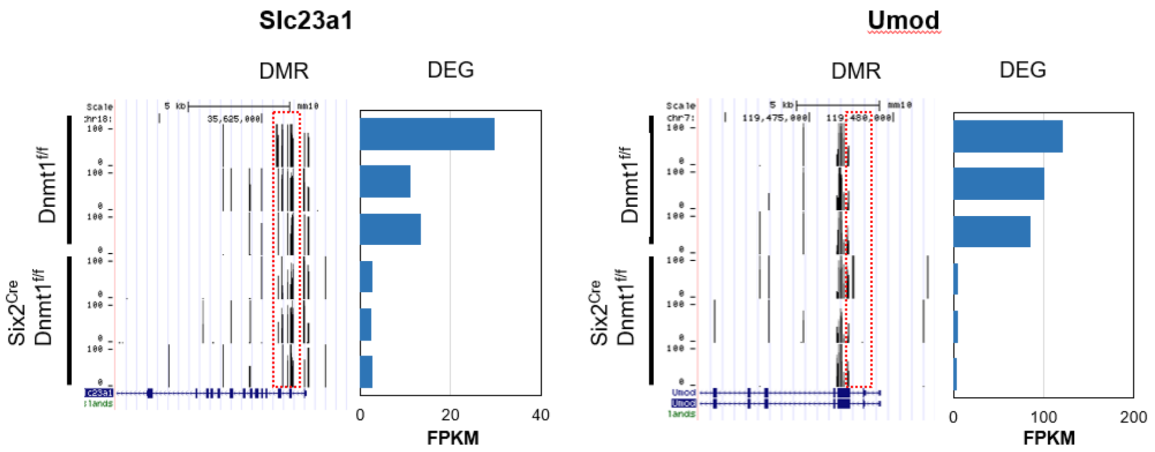


Figure S9. Representative DMRs and their target gene expression changes. DMRs are marked by red boxes. Left panel shows a UCSC genome browser screenshot with DNA methylation patterns and Y-axis represents methylation level from 0% to 100%. Right panel shows gene expression level and X-axis represents FPKM. FPKM stands for Fragments Per Kilobase of transcript per Million mapped reads.

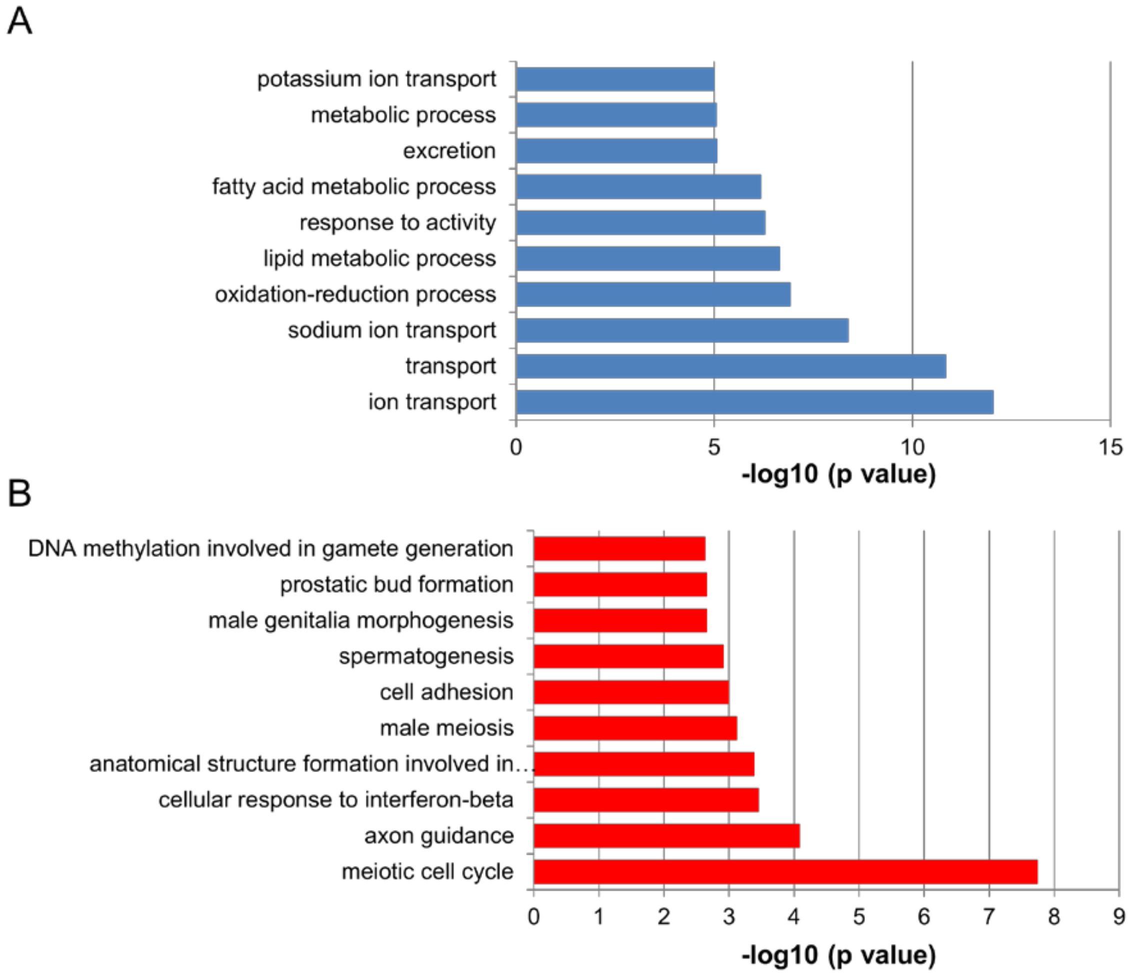
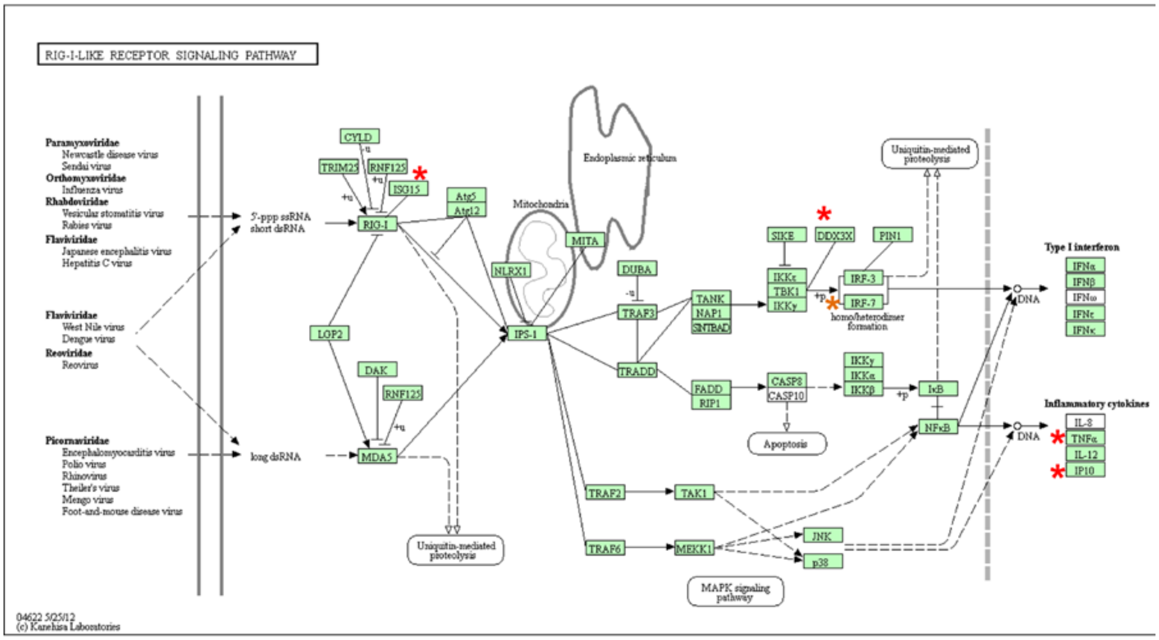
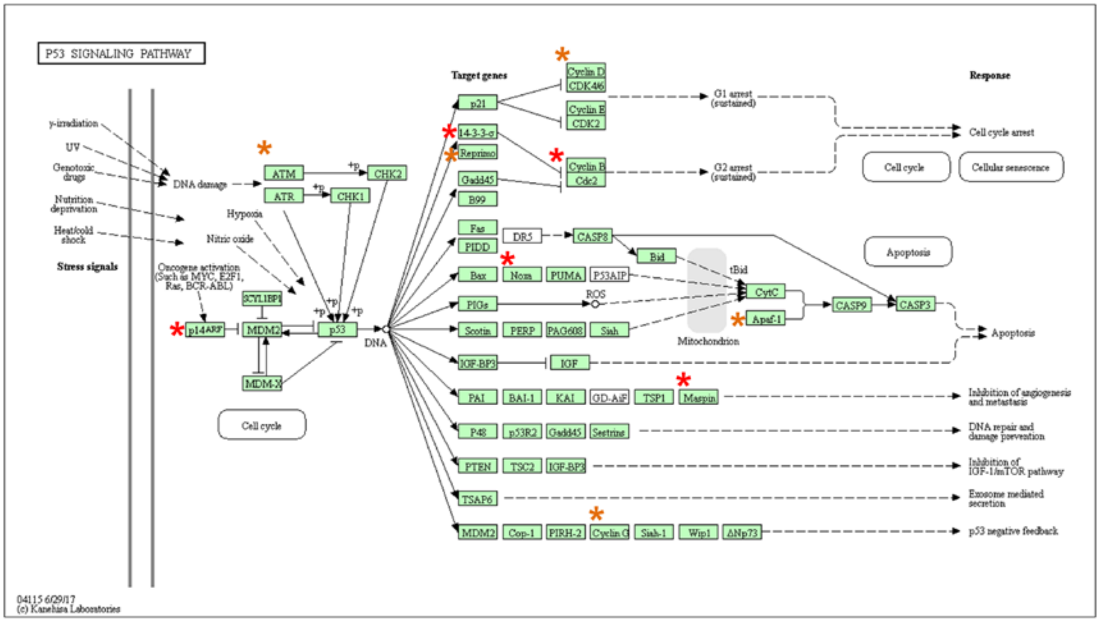


Figure S10. Functional annotation analysis (DAVID). Functional annotation analysis of down- **(A)** and down-regulated genes **(B)** in between *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice.

RIG-I-like receptor signaling pathway



p53 signaling pathway



Adjusted p value < 0.05 * Fold change >2 *Fold change >1.5

Figure S11. KEGG pathways for RIG-I-like receptor signaling pathway and P53 signaling pathway. Differentially expressed genes in between *Dnmt1*$^{f/f}$ and *Six2*^{Cre} *Dnmt1*$^{f/f}$ mice are marked by asterisks.

Target gene	Strand	Sequence
Dnmt1	F	ATAAGAAACGCAGAGTTGTAGACAC
	R	GGTTCCCGCTGTTACCTC
Dnmt3a	F	CAGCTGCTTACGCCCCACCC
	R	CACCAGCCGCTCCCTTGTGC
Dnmt3b	F	GAACCATTGTTGGAATTGGG
	R	CATGTGCAGTGCCAGTTTTT
Tet1	F	CAAATGACAGCACAACCGCAGCT
	R	CTGCCCTTGCTGAAGGTGCCTC
Tet2	F	CCACGCCCACCAAGGCTGAG
	R	GGCCGGTGTGTCCAGCAGAC
Tet3	F	TGGAGCCTGGACACACAGTA
	R	TGTGTTGGTTGTAGAGGGCA
Nephrin	F	CCATGGGGAGCTGAAGAATA
	R	CCGAGTCCAAACCAAGATGT
Aqp1	F	AAGTGGCAAGGAAGGGACAG
	R	GGAAGGCTGTGTGTGTGAA
Aqp2	F	CGCTCCTTTTCGTCTTCTTT
	R	ACAGTCACAGCAGGGTTGAT
Six2	F	CACCTCCACAAGAATGAAAGCG
	R	CTCCGCCTCGATGTAGTGC
Cited1	F	AACCTTGGAGTGAAGGATCGC
	R	GTAGGAGAGCCTATTGGAGATGT
Umod	F	GGATGCTGCTGGTAATGATGG
	R	GAACACCGTCTCGCTTCTGT
Slc12a3	F	ACACGGCAGCACCTTATACAT
	R	GAGGAATGAATGCAGGTCAGC

Table S1. Primer sequences used in this study.

Table S2. List of differentially expressed genes between P0 kidneys of Dnmt1 knock-out mice and controls.

Please find it in the xls file.

Table S3. List of differentially expressed transposable elements between P0 kidneys of Dnmt1 knock-out mice and controls.

Please find it in the xls file.