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Supplemental Information

H19, a Long Non-coding RNA, Mediates

Transcription Factors and Target Genes through

Interference of MicroRNAs in Pan-Cancer

Aimin Li, Saurav Mallik, Haidan Luo, Peilin Jia, Dung-Fang Lee, and Zhongming Zhao

SUPPLEMENTARY FILES

Figure S1. H19 highly expressed across pan-cancer except for brain lower grade glioma (LGG), prostate adenocarcinoma (PRAD), and thyroid carcinoma (THCA).

Figure S2. TF-gene regulation was affected by H19 expression level.

 Table S1. Number of samples and genes across the 24 cancer types based on TCGA

 data.

Table S2. Eighty-eight H19-TF-gene regulation triplets identified in at least two cancer

 types.

Table S3. 173 of 186 (93%) TF-gene pairs had direct or indirect evidence to support their relation to cancer (Table S3). The remaining 13 TF-gene pairs might be potential candidates for cancer research.

Table S4. The list of 29 H19 target miRNAs with evidence in literature.

Table S5. Regulation of 29 miRNAs in eight triplets. In the H19-ETS1-*TGFBR2* sheet, we list all the 29 miRNAs and their targets (TFs and genes). Some of the targets were predicted and then verified. In the H19-ETS1-*TGFBR2* table, TFs are marked in yellow if miRNAs target them, and genes are marked in red if miRNAs target them.

Table S6. Primers for qRT-PCR.







Figure S2. TF-gene regulation was affected by H19 expression level.

BRCA, AHR-HSPB1 H19 lowly expressed, p-value=3.27e-03

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AHR, log2(FPKM)

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HSPB1, log2(FPKM)

BRCA, AHR-HSPB1 H19 highly expressed, p-value=2.3e-17



AHR, log2(FPKM)



BRCA, AHR–SOS1 H19 lowly expressed, p-value=6.07e–13

BRCA, AHR-SOS1 H19 highly expressed, p-value=6.4e-25



AHR, log2(FPKM)

AHR, log2(FPKM)

BRCA, AIP–RSF1 H19 lowly expressed, p-value=5.21e–05

BRCA, AIP-RSF1 H19 highly expressed, p-value=1.14e-12



AIP, log2(FPKM)





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AIP, log2(FPKM)

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CD40, log2(FPKM)

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BRCA, AKNA-CD40 H19 highly expressed, p-value=5.19e-37

AKNA, log2(FPKM)

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BRCA, CIITA-HLA-DRA H19 lowly expressed, p-value=1.4e-103

BRCA, CIITA-HLA-DRA H19 highly expressed, p-value=1.73e-62



CIITA, log2(FPKM)





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CIITA, log2(FPKM)



BRCA, CREBBP-CREB1 H19 lowly expressed, p-value=1.72e-35

BRCA, CREBBP-CREB1 H19 highly expressed, p-value=1.84e-58



CREBBP, log2(FPKM)

CREBBP, log2(FPKM)

BRCA, E2F1-GADD45B H19 lowly expressed, p-value=2.67e-02

E2F1, log2(FPKM)

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GADD45B, log2(FPKM)

BRCA, E2F1–GADD45B H19 highly expressed, p-value=2.45e–05



E2F1, log2(FPKM)



BRCA, E2F3–MAPK8 H19 lowly expressed, p-value=1.88e–04

BRCA, E2F3-MAPK8 H19 highly expressed, p-value=7.08e-18



E2F3, log2(FPKM)

E2F3, log2(FPKM)

BRCA, EGR1–SPRY1 H19 lowly expressed, p-value=1.81e–14

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BRCA, EGR1-SPRY1 H19 highly expressed, p-value=1.15e-35



EGR1, log2(FPKM)



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EGR1, log2(FPKM)



ETS1, log2(FPKM)

BRCA, EZH2-BRCA1 H19 highly expressed, p-value=1.46e-15



EZH2, log2(FPKM)

BRCA, EZH2–BRCA1 H19 lowly expressed, p-value=4.6e-02

BRCA, ETS1-TGFBR2 H19 highly expressed, p-value=2.09e-52



BRCA, ETS1-TGFBR2 H19 lowly expressed, p-value=1.69e-31



EZH2, log2(FPKM)



BRCA, EZH2–DACT3 H19 highly expressed, p-value=1.4e–20



EZH2, log2(FPKM)

BRCA, EZH2–DACT3 H19 lowly expressed, p-value=7.31e–02

EZH2, log2(FPKM)

BRCA, EZH2–SNAI2 H19 lowly expressed, p-value=8.49e–03

BRCA, EZH2-SNAI2 H19 highly expressed, p-value=7.22e-05



EZH2, log2(FPKM)



EZH2, log2(FPKM)



BRCA, FLI1–CTGF H19 lowly expressed, p-value=1.28e–06

BRCA, FLI1-CTGF H19 highly expressed, p-value=2.66e-15



FLI1, log2(FPKM)

FLI1, log2(FPKM)

BRCA, FLI1–TGFBR2 H19 lowly expressed, p-value=4.53e–58

BRCA, FLI1–TGFBR2 H19 highly expressed, p-value=8.37e–70



FLI1, log2(FPKM)





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FLI1, log2(FPKM)

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BRCA, FOSL2–BCL6 H19 lowly expressed, p-value=4.04e–03

BRCA, FOSL2–BCL6 H19 highly expressed, p-value=4.33e–12



FOSL2, log2(FPKM)

FOSL2, log2(FPKM)

BRCA, FOXO1–TXNIP H19 lowly expressed, p-value=1.27e–07

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FOXO1, log2(FPKM)

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TXNIP, log2(FPKM)

BRCA, FOXO1–TXNIP H19 highly expressed, p-value=8.73e–23



FOXO1, log2(FPKM)



BRCA, GATA2–VCAM1 H19 lowly expressed, p-value=5.08e–02

BRCA, GATA2-VCAM1 H19 highly expressed, p-value=7.39e-03



GATA2, log2(FPKM)

GATA2, log2(FPKM)

BRCA, GATA2–VWF H19 lowly expressed, p-value=4.84e–07





GATA2, log2(FPKM)



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GATA2, log2(FPKM)



BRCA, HDAC1–TXNIP H19 lowly expressed, p-value=1.36e–04

BRCA, HDAC1-TXNIP H19 highly expressed, p-value=2.64e-02



TXNIP, log2(FPKM)

HDAC1, log2(FPKM)

HDAC1, log2(FPKM)

BRCA, HDAC2-TWIST1 H19 lowly expressed, p-value=5.33e-02



HDAC2, log2(FPKM)

BRCA, HDAC2-TWIST1 H19 highly expressed, p-value=1.85e-02



HDAC2, log2(FPKM)



BRCA, HDGF-FAS H19 lowly expressed, p-value=9.91e-03

BRCA, HDGF–FAS H19 highly expressed, p-value=4e-05



HDGF, log2(FPKM)

HDGF, log2(FPKM)

BRCA, IKZF1-BIRC5 H19 lowly expressed, p-value=8.57e-04

IKZF1, log2(FPKM)

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BRCA, IKZF1-BIRC5 H19 highly expressed, p-value=5.21e-03



IKZF1, log2(FPKM)





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BIRC5, log2(FPKM)

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FAS, log2(FPKM)



BRCA, KAT2B-SMAD4 H19 lowly expressed, p-value=2.47e-08

BRCA, KAT2B–SMAD4 H19 highly expressed, p-value=4.89e–21



KAT2B, log2(FPKM)

KAT2B, log2(FPKM)

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KAT2B, log2(FPKM)

BRCA, KAT2B–ZEB1 H19 lowly expressed, p-value=2.12e–17

ZEB1, log2(FPKM)

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BRCA, KAT2B–ZEB1 H19 highly expressed, p–value=2.62e–27



KAT2B, log2(FPKM)



BRCA, KLF4–IL6 H19 lowly expressed, p-value=3.98e-05

BRCA, KLF4–IL6 H19 highly expressed, p-value=4.75e-21



KLF4, log2(FPKM)

KLF4, log2(FPKM)

BRCA, KLF6–TXNIP H19 lowly expressed, p-value=6.11e–03

BRCA, KLF6-TXNIP H19 highly expressed, p-value=1.77e-14



KLF6, log2(FPKM)



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TXNIP, log2(FPKM)

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KLF6, log2(FPKM)



MYBL2, log2(FPKM)

BRCA, MYBL2–COL1A1 H19 highly expressed, p-value=2.74e–10



MYBL2, log2(FPKM)

BRCA, NFKB1–CHUK H19 lowly expressed, p-value=6.26e-05

BRCA, NFKB1-CHUK H19 highly expressed, p-value=4.84e-18



NFKB1, log2(FPKM)



NFKB1, log2(FPKM)



BRCA, NFKB1–MIF H19 lowly expressed, p-value=4.42e–05

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MIF, log2(FPKM)

BRCA, NFKB1-MIF H19 highly expressed, p-value=8.42e-13

NFKB1, log2(FPKM)

NFKB1, log2(FPKM)

BRCA, NFYB–EDF1 H19 lowly expressed, p-value=5.55e–06

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NFYB, log2(FPKM)

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EDF1, log2(FPKM)





NFYB, log2(FPKM)



BRCA, NFYB-HMGCS1 H19 lowly expressed, p-value=1.39e-03

BRCA, NFYB-HMGCS1 H19 highly expressed, p-value=4.1e-11



NFYB, log2(FPKM)

NFYB, log2(FPKM)

BRCA, NFYB-SP3 H19 lowly expressed, p-value=1.45e-09

BRCA, NFYB-SP3 H19 highly expressed, p-value=3.48e-30



NFYB, log2(FPKM)



NFYB, log2(FPKM)



BRCA, NR3C1-CALD1 H19 lowly expressed, p-value=1.01e-02

BRCA, NR3C1-CALD1 H19 highly expressed, p-value=4.54e-19



NR3C1, log2(FPKM)

NR3C1, log2(FPKM)

BRCA, PARP1–FBN1 H19 lowly expressed, p-value=3.92e–02

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PARP1, log2(FPKM)

BRCA, PARP1-FBN1 H19 highly expressed, p-value=3.94e-02



PARP1, log2(FPKM)





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BRCA, PARP1–FN1 H19 lowly expressed, p-value=4.25e–02

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BRCA, PARP1-FN1 H19 highly expressed, p-value=2.29e-03

BRCA, POU2AF1–TK1 H19 lowly expressed, p-value=2.88e–04

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POU2AF1, log2(FPKM)

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TK1, log2(FPKM)

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BRCA, POU2AF1–TK1 H19 highly expressed, p-value=2.1e–03



POU2AF1, log2(FPKM)



BRCA, PPARA-KLF11 H19 lowly expressed, p-value=6.81e-15

BRCA, PPARA-KLF11 H19 highly expressed, p-value=5.66e-38



PPARA, log2(FPKM)

PPARA, log2(FPKM)

BRCA, RB1–WRN H19 lowly expressed, p-value=3.09e–05

BRCA, RB1–WRN H19 highly expressed, p-value=9.54e-15



RB1, log2(FPKM)

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RB1, log2(FPKM)

WRN, log2(FPKM)



RUNX2, log2(FPKM)

BRCA, RUNX2–MMP2 H19 highly expressed, p-value=1.18e–52



RUNX2, log2(FPKM)

BRCA, SNAI2–MET H19 lowly expressed, p-value=1.32e–12





SNAI2, log2(FPKM)





SNAI2, log2(FPKM)



SOX18, log2(FPKM)

BRCA, SOX18-CLDN5 H19 highly expressed, p-value=3.05e-59



SOX18, log2(FPKM)

BRCA, SP1-ADAM17 H19 lowly expressed, p-value=2.81e-09

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BRCA, SP1–ADAM17 H19 highly expressed, p–value=5.76e–27



SP1, log2(FPKM)



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SP1, log2(FPKM)

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BRCA, SP1–ATM H19 lowly expressed, p-value=1.56e-18

BRCA, SP1–ATM H19 highly expressed, p-value=1.96e–34



ATM, log2(FPKM)

SP1, log2(FPKM)

SP1, log2(FPKM)

BRCA, SP1–HRAS H19 lowly expressed, p-value=1.61e–10

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SP1, log2(FPKM)

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HRAS, log2(FPKM)

BRCA, SP1-HRAS H19 highly expressed, p-value=1.06e-32



SP1, log2(FPKM)



BRCA, SP1-HSPB1 H19 highly expressed, p-value=2.61e-12



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BRCA, SP1–HSPB1 H19 lowly expressed, p–value=6.68e–02

SP1, log2(FPKM)

BRCA, SP1–SIGIRR H19 lowly expressed, p–value=6.2e–02

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SIGIRR, log2(FPKM)

BRCA, SP1–SIGIRR H19 highly expressed, p-value=1.8e–10





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SP1, log2(FPKM)



BRCA, SP1–TGFBR2 H19 lowly expressed, p–value=1.03e–08

BRCA, SP1-TGFBR2 H19 highly expressed, p-value=1.05e-21



SP1, log2(FPKM)

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BRCA, SP1–UTRN H19 lowly expressed, p-value=7.05e–24





SP1, log2(FPKM)



SP1, log2(FPKM)



BRCA, SPI1–CD40 H19 lowly expressed, p-value=1.04e–50

BRCA, SPI1-CD40 H19 highly expressed, p-value=9.71e-40



BRCA, SPI1–IL18 H19 lowly expressed, p-value=2.57e-43

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BRCA, SPI1-IL18 H19 highly expressed, p-value=8.64e-17



SPI1, log2(FPKM)





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SPI1, log2(FPKM)

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BRCA, SPI1–NCF2 H19 highly expressed, p-value=3.34e-28



SPI1, log2(FPKM)

BRCA, SPI1–NCF2 H19 lowly expressed, p-value=3.8e–56

SPI1, log2(FPKM)

BRCA, STAT1-CD40 H19 lowly expressed, p-value=2.66e-21

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STAT1, log2(FPKM)

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CD40, log2(FPKM)

BRCA, STAT1-CD40 H19 highly expressed, p-value=1.71e-06



STAT1, log2(FPKM)



BRCA, STAT1-FCGR1A H19 lowly expressed, p-value=1.52e-23



BRCA, STAT1–SERPING1 H19 lowly expressed, p–value=7.07e–23

BRCA, STAT1-SERPING1 H19 highly expressed, p-value=4.85e-06



STAT1, log2(FPKM)

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STAT1, log2(FPKM)

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SERPING1, log2(FPKM)



STAT1, log2(FPKM)

BRCA, STAT1-TYMP H19 highly expressed, p-value=2.96e-02



STAT1, log2(FPKM)

BRCA, STAT3-AKAP12 H19 lowly expressed, p-value=2.81e-06

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STAT3, log2(FPKM)

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AKAP12, log2(FPKM)

BRCA, STAT3-AKAP12 H19 highly expressed, p-value=1.31e-16



STAT3, log2(FPKM)



BRCA, STAT3–IKBKE H19 lowly expressed, p-value=5.74e-02

BRCA, STAT3-IKBKE H19 highly expressed, p-value=2.46e-02



STAT3, log2(FPKM)

STAT3, log2(FPKM)

BRCA, STAT3-KLF11 H19 lowly expressed, p-value=1.52e-03



STAT3, log2(FPKM)

BRCA, STAT3-KLF11 H19 highly expressed, p-value=1.75e-14



STAT3, log2(FPKM)



BRCA, STAT3-NDUFA13 H19 lowly expressed, p-value=3.61e-08

BRCA, STAT3-NDUFA13 H19 highly expressed, p-value=4.08e-18



STAT3, log2(FPKM)

STAT3, log2(FPKM)

BRCA, STAT3-TYK2 H19 lowly expressed, p-value=2.83e-05



STAT3, log2(FPKM)

BRCA, STAT3-TYK2 H19 highly expressed, p-value=1.84e-13



STAT3, log2(FPKM)

Table S1. Number of Samples and Genes

		Cancer		Sample	S	After Filtr	FKPM ation	TF-gene Interactions			
No	Cancer Type Abbreviation	Cancer Type Name	Total Number of Samples	# Primary Tumor Samples	# Matched Controls	# Other Samples	# Genes	Number of TFs	# Pairs (TF- gene)	# TFs	# Genes
1	BLCA	Bladder urothelial carcinoma	426	407	19	0	11481	683	7723	607	2103
2	BRCA	Breast invasive carcinoma	1212	1092	113	7	11867	694	8181	625	2198
3	CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	309	304	3	2	11508	709	8057	634	2161
4	COAD	Colon adenocarcinoma	331	288	41	2	11537	700	8123	631	2187
5	ESCA	Esophageal carcinoma	195	181	13	1	11727	723	8277	655	2205
6	GBM	Glioblastoma multiforme	171	153	5	13	12279	717	7755	636	2156
7	HNSC	carcinoma	564	518	44	2	11406	691	7866	621	2140
8	KIRC	Kidney renal clear cell carcinoma	91	66	25	0	11881	697	7889	628	2172
9	KIRP	Kidney renal papillary cell carcinoma	321	288	32	1	11599	667	7130	591	2030
10	LGG	Brain lower grade glioma	523	509	0	14	12104	. 678	6837	589	1996
11	LIHC	Liver hepatocellular carcinoma	421	369	50	2	10577	622	6988	546	1964
12	LUAD	Lung adenocarcinoma	574	513	59	2	12065	695	8223	621	2233
13	LUSC	Lung squamous cell carcinoma	548	498	50	0	12002	720	8444	653	2281
14	OV	Ovarian serous cystadenocarcinoma	427	419	0	8	11838	699	8030	622	2159
15	PAAD	Pancreatic adenocarcinoma	183	178	4	1	12346	722	8758	651	2369
16	PCPG	Paraganglioma	185	177	3	5	11520	660	6438	562	1896
17	PRAD	Prostate adenocarcinoma	548	495	52	1	11785	700	7889	624	2170
18	SARC	Sarcoma	264	258	2	4	11343	690	7353	602	2053
19	SKCM	Skin cutaneous melanoma	470	102	1	367	11028	667	7055	585	1982
20	STAD	Stomach adenocarcinoma	450	414	36	0	11792	726	8460	648	2252
21	TGCT	Testicular germ cell tumors	154	148	0	6	12184	. 701	8042	620	2202
22	THCA	Thyroid carcinoma	571	504	59	8	11693	666	7284	587	2020
23	THYM	Thymoma	571	504	59	8	11757	680	7270	602	2055
24	UCEC	Uterine corpus endometrial carcinoma	204	180	23	1	11718	698	8092	625	2152

Trinlet	BRCA	COAD	HNSC	KIRC	LGG	LUAD	ΡΔΔΒ	STAD	тест	тнса	# of cancer	H19 lowley	H19 highly
	DRCA	COAD	muse	MINU	LUU	LUAD	IAAD	BIAD	1001	шся	types	expressed	expressed
H19_AHR_HSPB1	5.05									2.98	2	-1	-1-1
H19_AIP_RSF1	2.97									2.77	2	-1	
H19_EZH2_DACT3	5.87							4.90			2	4	
H19_NFKB1_MIF	2.47						3.33				2	-	
H19_NFYB_EDF1	5.59									2.28	2	4	
H19_SP1_HRAS	4.02									4.98	2	4	
H19_SP1_HSPB1	3.50									2.54	2	-1	
H19_SP1_SIGIRR	3.15				_					2.16	2	-1	
H19_SP3_EDF1		_		5.92						4.91	2	H	-1-1
H19_STAT3_NDUFA13	2.54									2.93	2	H	-1-1
H19_STAT3_TYK2	2.57							_		3.18	2	H	-1-1
H19_AHR_CCNG2	2.99						2.38				2	\rightarrow	$\rightarrow \rightarrow$
H19_AHR_SOS1	3.91						2.73			2.94	3	\rightarrow	$\rightarrow \rightarrow$
H19_CREBBP_CREB1	3.13					3.94					2	\rightarrow	$\rightarrow \rightarrow$
H19_E2F3_MAPK8	4.49									3.59	2	\rightarrow	$\rightarrow \rightarrow$
H19_EGR1_SPRY1	3.44				3.38						2	\rightarrow	$\rightarrow \rightarrow$
H19_ERG_EPB41L3							2.22			2.84	2	\rightarrow	$\rightarrow \rightarrow$
H19_ETS1_TGFBR2	9.19			4.21				-			2	\rightarrow	$\rightarrow \rightarrow$
H19_EZH2_BRCA1	3.70				4.87						2	\rightarrow	$\rightarrow \rightarrow$
H19_FLI1_CTGF	2.51	3.53									2	\rightarrow	$\rightarrow \rightarrow$
H19_FLI1_TGFBR2	6.02		4.14								2	\rightarrow	$\rightarrow \rightarrow$
H19_FOSL2_BCL6	3.02	6.40									2	\rightarrow	$\rightarrow \rightarrow$
H19_FOXM1_CCNB1					3.83				3.39		2	\rightarrow	$\rightarrow \rightarrow$
H19_FOXO1_TXNIP	2.93			3.12							2	\rightarrow	$\rightarrow \rightarrow$
H19_GATA2_VWF	3.20			8.26							2	\rightarrow	$\rightarrow \rightarrow$
H19_HNRNPK_EIF4E					-	2.92				5.33	2	\rightarrow	$\rightarrow \rightarrow$
H19_KAT2B_SMAD4	5.05						-			2.19	2	\rightarrow	$\rightarrow \rightarrow$
H19_KAT2B_ZEB1	2.66						2.78				2	\rightarrow	$\rightarrow \rightarrow$
H19_KLF4_IL6	4.16							-		3.96	2	\rightarrow	$\rightarrow \rightarrow$
H19_KLF6_TXNIP	3.26					2.66					2	\rightarrow	$\rightarrow \rightarrow$
H19_NFKB1_CHUK	3.60						-			5.56	2	\rightarrow	$\rightarrow \rightarrow$

Table S2. Regression of H19's regulation on TF-gene pairs
Triplet	BRCA	COAD	HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT	THCA	# of cancer types	H19 lowley expressed	H19 highly expressed
H19_NFYB_HMGCS1	2.37									3.79	2	\rightarrow	$\rightarrow \rightarrow$
H19_NFYB_SP3	7.48									2.79	2	\rightarrow	$\rightarrow \rightarrow$
H19_NR3C1_CALD1	5.86									2.72	2	\rightarrow	$\rightarrow \rightarrow$
H19_PPARA_KLF11	6.41									3.46	2	\rightarrow	$\rightarrow \rightarrow$
H19_RB1_WRN	2.40									2.86	2	\rightarrow	$\rightarrow \rightarrow$
H19_RUNX2_MMP2	3.20									2.81	2	\rightarrow	$\rightarrow \rightarrow$
H19_SOX18_CLDN5	9.50					3.07					2	\rightarrow	$\rightarrow \rightarrow$
H19_SP1_ADAM17	3.71									5.66	2	\rightarrow	$\rightarrow \rightarrow$
H19_SP1_ATM	3.51									5.70	2	\rightarrow	$\rightarrow \rightarrow$
H19_SP1_TGFBR2	2.91									4.08	2	\rightarrow	$\rightarrow \rightarrow$
H19_SP1_UTRN	4.22									3.01	2	\rightarrow	$\rightarrow \rightarrow$
H19_STAT3_AKAP12	2.67									3.59	2	\rightarrow	$\rightarrow \rightarrow$
H19_STAT3_KLF11	3.53									3.41	2	\rightarrow	$\rightarrow \rightarrow$
H19_TWIST2_SRPX		•				3.97	3.33				2	\rightarrow	$\rightarrow \rightarrow$
H19_AHR_CYP1B1									2.45	7.59	2	$\rightarrow \rightarrow$	\rightarrow
H19_AKNA_CD40	2.68						3.30				2	$\rightarrow \rightarrow$	\rightarrow
H19_CIITA_HLA-DRA	3.73									3.68	2	$\rightarrow \rightarrow$	\rightarrow
H19_IRF8_CD68							4.43			5.10	2	$\rightarrow \rightarrow$	\rightarrow
H19_SNAI2_MET	2.58		5.20								2	$\rightarrow \rightarrow$	\rightarrow
H19_SPI1_ACP5							2.42			4.55	2	$\rightarrow \rightarrow$	\rightarrow
H19_SPI1_CD40	3.07							3.39			2	$\rightarrow \rightarrow$	\rightarrow
H19_SPI1_IL18	3.75									3.14	2	$\rightarrow \rightarrow$	\rightarrow
H19_SPI1_NCF2	3.67						2.63				2	$\rightarrow \rightarrow$	\rightarrow
H19_STAT1_CD40	4.37							_		3.12	2	$\rightarrow \rightarrow$	\rightarrow
H19_STAT1_FCGR1A	4.69									2.73	2	$\rightarrow \rightarrow$	\rightarrow
H19_STAT1_SERPING1	4.06									4.74	2	$\rightarrow \rightarrow$	\rightarrow
H19_STAT1_TYMP	3.88					3.72					2	$\rightarrow \rightarrow$	\rightarrow
H19_GATA2_VCAM1	2.95			6.16							2	-	\rightarrow
H19_NFKB1_NCAM1							3.51			3.86	2	-	\rightarrow
H19_SP1_ME1						4.42				5.08	2	-	\rightarrow
H19_TP53_IGFBP3					4.07		_			3.41	2	-	\rightarrow
H19_CTCF_IPO13						3.15				3.26	2	\rightarrow	-
H19_E2F1_GADD45B	5.75	3.86					_				2	\rightarrow	-

Triplet	BRCA	COAD	HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT	THCA	# of cancer	H19 lowley	H19 highly
H10 E2E1 MVC							3 64			6 27	cypes 2		
$\mathbf{H}_{\mathbf{L}}^{\mathbf{L}} = \mathbf{L}_{\mathbf{L}}^{\mathbf{L}} = \mathbf{L}_{\mathbf$							3.04	4 20		0.27	2		י
H19_EZH2_CHIA	C 0.4	1 5 5					5.52	4.20			2	~	-
HI9_EZH2_SNAI2	0.04	4.55				0.64			0.10		2	7	-
HI9_FOXOI_HYOUI	1.00					2.64			9.10		2	\rightarrow	-1
H19_HDAC1_TXNIP	4.88					4.11					2	\rightarrow	-1
H19_HDAC2_TWIST1	2.77	3.76									2	\rightarrow	-1
H19_HDGF_FAS	6.14						7.27				2	\rightarrow	4
H19_IKZF1_BIRC5	4.72						3.70				2	\rightarrow	H
H19_MYB_COL1A1		4.33						4.66			2	\rightarrow	4
H19_MYBL2_COL1A1	11.03	4.48						6.07			3	\rightarrow	4
H19_MYC_E2F1							4.03			5.84	2	\rightarrow	H
H19_NFKB2_HIF1A						3.54	3.57				2	\rightarrow	4
H19_PARP1_FBN1	2.70								5.57		2	\rightarrow	4
H19_PARP1_FN1	3.53	3.08									2	\rightarrow	H
H19_POU2AF1_TK1	5.63						7.38		_		2	\rightarrow	H
H19_POU2F1_VWF						7.74		5.91			2	\rightarrow	H
H19_RELA_BGN							3.90			3.75	2	\rightarrow	H
H19_RUNX1_SYMPK		5.54				7.74				5.65	3	\rightarrow	H
H19_SOX9_CD3E			-	4.64			5.49				2	\rightarrow	4
H19_SP1_ABCA2						8.08				4.60	2	\rightarrow	H
H19_SP1_FLNA						5.20				5.60	2	\rightarrow	4
H19_STAT3_DNMT1						4.92				3.38	2	\rightarrow	4
H19_STAT3_IKBKE	2.59							6.50			2	\rightarrow	4
H19_USF1_FMR1							3.09			2.91	2	\rightarrow	H

Notes: The values are transformed as $-\log 10$ (p-value). Pattern: \rightarrow activation, \dashv repression.

No	TF/Gene	BRCA	COAD HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT	THCA
1	AHR	[1]					[2]			
	CCNG2	[3]					[4]			
2	AHR								[5]	[6]
	CYP1B1								[7]	[8]
3	AHR	[1]								[6]
	HSPB1	[9]								[10]
4	AHR	[1]					[2]			[6]
	SOS1	[11]					[12]			[13]
5	AIP	[14]								[15]
	RSF1	[16]								[17]
6	AKNA	[18]					[19]			
	CD40	[20]					[21]			
7	CIITA	[22]								[23]
	HLA-DRA	[24]								[25]
8	CREBBP	[26]				[27]				
	CREB1	[28]				[29]				
9	CTCF					[30]				[31]
	IPO13					?				?
10	E2F1	[32]	[33]							
	GADD45B	[34]	[35]							
11	E2F1						[36]			[37]
	MYC						[38]			[39]
12	E2F3	[40]								[41]
	MAPK8	[42]								[43]
13	EGR1	[44]			[45]					
	SPRY1	[46]			[47]					
14	ERG						[48]			[49]
	EPB41L3						[50]			[51]
15	ETS1	[52]		[53]						
	TGFBR2	[54]		[55]						
16	EZH2	[56]			[57]					
	BRCA1	[58]			[59]					
17	EZH2						[60]	[61]		
	CIITA						[62]	[63]		
18	EZH2	[56]						[61]		
	DACT3	[64]						?		
19	EZH2	[56]	[65]							
	SNAI2	[66]	[67]							
20	FLI1	[68]	[69]							
	CTGF	[70]	[71]							

Table S3. TF-gene pairs modulated by H19 and their evidences that related to specific cancers.

No	TF/Gene	BRCA	COAD	HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT	THC
21	FLI1	[68]		[72]							
	TGFBR2	[52]		[73]							
22	FOSL2	[74]	[75]								
	BCL6	[76]	[77]								
23	FOXM1	[78]				[79]				[80]	
	CCNB1	[81]				[82]				[83]	
24	FOXO1	[84]					[85]			[86]	
	HYOU1	[87]					[88]			?	
25	FOXO1	[84]			[89]						
	TXNIP	[90]			[91]						
26	GATA2	[92]			[93]						
	VCAM1	[94]			[93]						
27	GATA2	[92]			[93]						
	VWF	[95]			[96]						
28	HDAC1	[97]					[98]				
	TXNIP	[90]					[99]				
29	HDAC2	[100]	[101]								
	TWIST1	[102]	[103]								
30	HDGF	[104]						[105]			
	FAS	[106]						[107]			
31	HNRNPK						[108]				[109]
	EIF4E						[110]				[111]
32	IKZF1	[112]						[113]			
	BIRC5	[114]						[115]			
33	IRF8							[116]			[117]
	CD68							[118]			[119]
34	KAT2B	[120]									[121]
	SMAD4	[122]									[123]
35	KAT2B	[120]						[124]			
	ZEB1	[125]						[126]			
36	KLF4	[127]									[128]
	IL6	[129]									[130]
37	KLF6	[131]					[132]				
	TXNIP	[90]					[99]				
38	MYB		[133]						[134]		
	COL1A1		[135]						[136]		
39	MYBL2	[137]	[35]						[138]		
	COL1A1	[139]	[135]						[136]		
40	MYC							[38]			[39]
	E2F1							[36]			[37]

No	TF/Gene	BRCA	COAD	HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT	THCA
41	NFKB1	[140]									[141]
	CHUK	[142]									?
42	NFKB1	[143]						[144]			
	MIF							[145]			
43	NFKB1							[144]			[141]
	NCAM1							[146]			[147]
44	NFKB2						[148]	[149]			
	HIF1A						[150]	[151]			
45	NFYB	[152]									[153]
	EDF1	[154]									?
46	NFYB	[152]									[153]
	HMGCS1	[155]									[156]
47	NFYB	[152]									[153]
	SP3	[157]									[158]
48	NR3C1	[159]									[160]
	CALD1	[161]									[162]
49	PARP1	[163]								[164]	
	FBN1	[161]								[165]	
50	PARP1	[163]	[166]								
	FN1	[167]	[168]								
51	POU2AF1	[169]						[170]			
	TK1	[171]						[172]			
52	POU2F1						[173]		[174]		
	VWF						[175]		[176]		
53	PPARA	[177]									[178]
	KLF11	[179]									[180]
54	RB1	[181]									[182]
	WRN	[183]									[184]
55	RELA							[185]			[186]
	BGN							[187]			?
56	RUNX1		[188]				[189]				[190]
	SYMPK		[191]				[192]				?
57	RUNX2	[193]									[194]
	MMP2	[195]									[196]
58	SNAI2	[66]		[197]							
	MET	[198]		[199]							
59	SOX18	[200]					[201]				
	CLDN5	[202]					[203]				
60	SOX9				[204]			[205]			
	CD3E				[206]			[207]			

No	TF/Gene	BRCA	COAD 1	HNSC	KIRC	LGG	LUAD	PAAD	STAD	TGCT THCA
61	SP1						[208]			[209]
	ABCA2						[210]			[211]
62	SP1	[212]								[209]
	ADAM17	[213]								[214]
63	SP1	[212]								[209]
	ATM	[215]								[216]
64	SP1	[212]					[208]			[209]
	FLNA	[217]					[218]			[219]
65	SP1	[212]								[209]
	HRAS	[220]								[221]
66	SP1	[212]								[209]
	HSPB1	[9]								[222]
67	SP1	[212]					[208]			[209]
	ME1	[223]					[224]			?
68	SP1	[212]								[209]
	SIGIRR	[225]								?
69	SP1	[212]								[209]
	TGFBR2	[52]								[226]
70	SP1	[212]								[209]
	UTRN	[227]								[228]
71	SP3				[229]					[158]
	EDF1				?					?
72	SPI1							[187]		[230]
	ACP5							[231]		[232]
73	SPI1	[233]							[234]	
	CD40	[20]							[235]	
74	SPI1	[233]								[230]
	IL18	[236]								[237]
75	SPI1	[233]						[187]		
	NCF2	[238]						[239]		
76	STAT1	[240]								[241]
	CD40	[20]								[242]
77	STAT1	[240]								[241]
	FCGR1A	[243]								[244]
78	STAT1	[240]								[241]
	SERPING1	[245]								[246]
79	STAT1	[240]					[247]			
	TYMP	[248]					[249]			
80	STAT3	[250]								[251]
	AKAP12	[252]								[253]

No	TF/Gene	BRCA COAD HNSC	C KIRC	LGG	LUAD	PAAD	STAD	TGCT THCA
81	STAT3				[254]			[251]
	DNMT1				[255]			[256]
82	STAT3	[250]					[257]	
	IKBKE	[258]					[259]	
83	STAT3	[250]						[251]
	KLF11	[179]						[180]
84	STAT3	[250]						[251]
	NDUFA13	[260]						[261]
85	STAT3	[250]						[251]
	TYK2	[262]						[263]
86	TP53			[264]				[265]
	IGFBP3			[266]				[267]
87	TWIST2				[268]	[269]		
	SRPX				[270]	[271]		
88	USF1					?		[272]
	FMR1					[273]		[274]

Notes: '?' means having not found related evidences. There are 13 TFs/genes which have not evidences to support their relation to specific cancers. TF: Transcription Factor, BRCA: Breast invasive carcinoma, COAD: Colon adenocarcinoma, HNSC: Head and Neck squamous cell carcinoma, KIRC: Kidney renal clear cell carcinoma, LGG: Brain Lower Grade Glioma, LUAD: Lung adenocarcinoma, PAAD: Pancreatic adenocarcinoma, STAD: Stomach adenocarcinoma, TGCT: Testicular Germ Cell Tumors, THCA: Thyroid carcinoma.

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Table S4. miRNAs targeted by H19

miRNA	Description	Reference
let-7a	> The H19/let-7 double-negative feedback loop contributes to glucose	[1]
	metabolism in muscle cells.	[2]
	The imprinted H19 lncRNA antagonizes let-7 microRNAs.	[3]
	▶ H19 lncRNA alters stromal cell growth via IGF signaling in the	[4]
	endometrium of women with endometriosis.	
	Glycolysis gatekeeper PDK1 reprograms breast cancer stem cells under hypoxia.	
let-7b	➤ The imprinted H19 lncRNA antagonizes let-7 microRNAs.	[2]
	➢ Glycolysis gatekeeper PDK1 reprograms breast cancer stem cells	[4]
	under hypoxia.	[5]
	The lncRNA H19 mediates breast cancer cell plasticity during EMT and MET plasticity by differentially sponging miR-200b/c and let- 7b.	
let-7g	The imprinted H19 lncRNA antagonizes let-7 microRNAs.	[2]
	H19 lncRNA alters stromal cell growth via IGF signaling in the endometrium of women with endometriosis.	[3]
let-7i	H19/let-7/LIN28 reciprocal negative regulatory circuit promotes breast cancer stem cell maintenance.	[6]
miR-106a	miR-CLIP capture of a miRNA targetome uncovers a lincRNA H19- miR-106a interaction.	[7]
miR-130b-3p	H19 lncRNA regulates keratinocyte differentiation by targeting miR- 130b-3p.	[8]
miR-138-5p	 Decreased Expression of MiR-138-5p by LncRNA H19 in Cervical Cancer Promotes Tumor Proliferation. 	[9]
miR-139	> H19 lncRNA alters stromal cell growth via IGF signaling in the	[3]
	endometrium of women with endometriosis.	[10]
	Long Non-Coding RNA H19 Protects H9c2 Cells against Hypoxia- Induced Injury by Targeting MicroRNA-139.	
miR-141	H19 activates Wnt signaling and promotes osteoblast differentiation by functioning as a competing endogenous RNA.	[11]
miR-152-3p	 Long non-coding RNA H19 promotes the proliferation and invasion of breast cancer through upregulating DNMT1 expression by sponging miR 152 	[12]
$miR_{-152}5n$	Long non-coding PNA H10 promotes the proliferation and investor	[10]
шк-152-эр	of breast cancer through upregulating DNMT1 expression by sponging miR-152.	[12]
miR-17-5p	Long noncoding RNA H19 competitively binds miR-17-5p to	[13]
*	regulate YES1 expression in thyroid cancer.	[14]
	Long non-coding RNA H19 suppresses retinoblastoma progression	

		via counteracting miR-17-92 cluster.	
miR-181d-3p		Hypoxia induces H19 expression through direct and indirect Hif-1 α activity, promoting oncogenic effects in glioblastoma.	[15]
miR-181d-5p		Hypoxia induces H19 expression through direct and indirect Hif-1 α	[15]
miR-18a	۶	Long non-coding RNA H19 suppresses retinoblastoma progression	[14]
		via counteracting miR-17-92 cluster.	
miR-194-5p		Long noncoding RNA H19 contributes to gallbladder cancer cell proliferation by modulated miR-194-5p targeting AKT2.	[16]
miR-196a	۶	The lncRNA H19 Mediates Pulmonary Fibrosis by Regulating the miR-196a/COL1A1 Axis.	[17]
miR-19a	۶	Long non-coding RNA H19 suppresses retinoblastoma progression via counteracting miR-17-92 cluster.	[14]
miR-19b-1	۶	Long non-coding RNA H19 suppresses retinoblastoma progression via counteracting miR-17-92 cluster	[14]
miR-200b		The lncRNA H19 mediates breast cancer cell plasticity during EMT	[5]
		and MET plasticity by differentially sponging miR-200b/c and let- 7b.	
miR-200c		The lncRNA H19 mediates breast cancer cell plasticity during EMT and MET plasticity by differentially sponging miR-200b/c and let-	[5]
		7b.	
miR-20a		Long non-coding RNA H19 suppresses retinoblastoma progression	[14]
miP 22	Ν	H10 activates Wat signaling and promotes astachlast differentiation	[11]
IIIIK-22		by functioning as a competing endogenous RNA.	[11]
miR-29a		Long non-coding RNA H19 regulates glioma angiogenesis and the biological behavior of glioma-associated endothelial cells by inhibiting microRNA-29a.	[18]
miR-29b		Long noncoding RNA H19 accelerates tenogenic differentiation and promotes tendon healing through targeting miR-29b-3p and activating TGE-61 signaling	[19]
miR-342-3p	4	Long non-coding RNA H19 regulates FOXM1 expression by competitively binding endogenous miR-342-3p in gallbladder	[20]
miR-630		cancer. Long noncoding RNA H19 regulates EZH2 expression by interacting with miR-630 and promotes cell invasion in nasopharyngeal	[21]
:D 074	~	carcinoma.	[22]
m1K-8/4	*	AQP3 expression by sponging miR-874 in the intestinal barrier.	[22]
miR-92a-1		Long non-coding RNA H19 suppresses retinoblastoma progression via counteracting miR-17-92 cluster.	[14]

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Table S5. Regulation of 29 miRNAs in eight triplets.

miRNAs	miR-106a	miR_130b_	3nmiR_138_5	n miR-139	miR_141	miR_152_3r	miR_152_5
Prodicted to	mate	IIIIX-1300	5µmk-158-5	p mik-139	IIIIK-141	1111X-152-5) mik-152-5
of miRNAs	gets						
TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3
	PPARA	STAT3	RELA				KLF4
	RB1	~~~~~	SP1				
	SP1						
	STAT3						
	KAT2B						
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1
	E2F1	TGFBR2		ZEB1		FBN1	FMR1
	HIF1A					FMR1	SOS1
	SMAD4					SOS1	
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						
of miknas TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9				
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

H19-ETS1-TGFBR2

Notes: In the H19-ETS1-TGFBR2 sheet, we list all the 29 miRNAs and their targets (TFs and genes). Some of the targets were predicted and then verified. In the H19-ETS1-TGFBR2 table, TFs are marked in yellow if miRNAs target them, and genes are marked in red if miRNAs target them.

miRNAs	miR-17	miR-181d-3p	miR-181d-5p	miR-18a	miR-194-5p	miR-196a	miR-19a
Predicted targets							

of miRNAs

TFs	RUNX1	RUNX1	RUNX1	E2F3	ERG	
	E2F1	KLF6	KLF6	FLI1	FLI1	
	RB1	ETS1	NR3C1	SP3		
	STAT3	NR3C1	POU2F1			
	KAT2B	KAT2B				
Genes	CALD1	ATM	ATM	ACP5	FAS	FMR1
	CCNG2	SOS1	CTGF	FMR1	COL1A1	IL18
	E2F1	VCAM1	HIF1A	SP3	MAPK8	
	HIF1A	EPB41L3	HMGCS1	RSF1	ZEB1	
	MMP2		MAPK8			
	SOS1					
	TGFBR2					
	KLF11					
	TXNIP					

Validated targets

of miRNAs

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs	miR-19b-1	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b
Predicted targets							

of miRNAs

TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8			
		SOS1			
		TGFBR2			
		KLF11			
		TXNIP			

Validated targets

of miRNAs

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
				DNMT1			

miRNAs	miR-342-3p	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g
Predicted targets							

of miRNAs

TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN

Validated targets

of miRNAs

TFs	FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
	E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
			STAT3	KAT2B	MYC	EZH2	
			E2F3	MYBL2	NFKB1	MYC	
				NFKB1	PARP1	SOX9	
				STAT3	SP1	SP1	
				HDAC2	STAT3		
				KLF4			
				IKZF1			
Genes	DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
	E2F1			CCNB1	HRAS	CCNB1	FN1
				EPB41L3	E2F1	EPB41L3	
				FLNA	IL6	FLNA	
				HMGCS1		HIF1A	
				SMAD4		HMGCS1	
				TGFBR2		MYC	
				TYMP		UTRN	
				MAPK8		HRAS	
				DNMT1			

miRNAs let-7i Predicted targets of miRNAs

TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

Validated targets of miRNAs

TFs	
Genes	
H19-FLI1-TGFBR2

miRNAs	miR-106a	miR-130b-3p	miR-138-5p	miR-139	miR-141	miR-152-3p	miR-152-5p	miR-17
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Predicted targets

of miRNAs

TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6	RUNX1
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3	E2F1
	PPARA	STAT3	RELA				KLF4	RB1
	RB1		SP1					STAT3
	SP1							KAT2B
	STAT3							
	KAT2B							
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1	CALD1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1	CCNG2
	E2F1	TGFBR2		ZEB1		FBN1	FMR1	E2F1
	HIF1A					FMR1	SOS1	HIF1A
	SMAD4					SOS1		MMP2
	MMP2							SOS1
	MAPK8							TGFBR2
	SOS1							KLF11
	TGFBR2							TXNIP
	KLF11							
	TXNIP							

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	E2F1
	MYB	E2F1	NFKB1		PPARA		E2F3
	RB1	NR3C1	SNAI2		HDGF		KAT2B
	RUNX1	PPARA	SOX9				MYC
	STAT3	RB1	TWIST2				RB1
		STAT3					RUNX1
							STAT3
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	E2F1
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	MMP2
	TGFBR2	SMAD4			KLF11		MYC
	ATM	TGFBR2			ZEB1		SMAD4
	HIF1A	ZEB1					TGFBR2
		FMR1					HIF1A
		MMP2					DNMT1
							IGFBP3

miRNAs miR-181d-3 miR-181d-5 miR-18a	miR-194-5p miR-196a	miR-19a	miR-19b-1	miR-200b
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TFs	RUNX1	RUNX1	E2F3	ERG		KLF6
	KLF6	KLF6	FLI1	FLI1		SP3
	ETS1	NR3C1	SP3			
	NR3C1	POU2F1				
	KAT2B					
Genes	ATM	ATM	ACP5	FAS	FMR1	NCF2
	SOS1	CTGF	FMR1	COL1A1	IL18	MAPK8
	VCAM1	HIF1A	SP3	MAPK8		SP3
	EPB41L3	HMGCS1	RSF1	ZEB1		
		MAPK8				

TFs		NR3C1	FOXM1	FOXO1	KAT2B	KAT2B	E2F3
		RUNX1				NR3C1	ETS1
							MYB
							SP1
							EZH2
Genes	HRAS	CTGF		FLNA	CTGF	CTGF	CREB1
		EDF1		TGFBR2	SMAD4	FMR1	FN1
		ATM			TGFBR2	ATM	KLF11
		HIF1A			DNMT1	HMGCS1	ZEB1
		HMGCS1				SMAD4	DNMT1
		SMAD4				TGFBR2	
		TGFBR2				DNMT1	
		DNMT1					

miRNAs	miR-200c	miR-20a	miR-22	miR-29a	miR-29b	miR-342-3p	miR-630	miR-874

TFs	E2F1	FOXO1	ETS1	MYBL2	E2F3	KLF6	POU2F1
	E2F3	HNRNPK	KAT2B			EZH2	STAT3
	EZH2						
	PPARA						
	RB1						
	STAT3						
	KAT2B						
Genes	CALD1	CD68		DNMT1	DNMT1		FBN1
	CCNG2	SOS1		FBN1	ZEB1		FMR1
	E2F1	UTRN		EDF1			SIGIRR
	HIF1A	VCAM1					
	SMAD4	WRN					
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						

TFs	MYB	E2F1	PPARA	KLF4	SP1	FOSL2	SNAI2	PARP1
	ETS1	E2F3		AHR	STAT3	E2F1	FOXM1	HDAC1
	SP1	MYC		MYC	SP1			STAT3
	E2F3	RB1			STAT3			E2F3
	FOXO1	RUNX1			MYC			
	E2F3	STAT3						
Genes	FLNA	CCNB1	HIF1A	MMP2	COL1A1	DNMT1	SNAI2	
	FN1	E2F1		DNMT1	DNMT1	E2F1		
	KLF11	FLNA		FBN1	MMP2			
	ZEB1	HIF1A		MYC	FBN1			
	NCAM1	MYC			MYC			
	CYP1B1	SMAD4						
		TGFBR2						
		DNMT1						

miRNAs	miR-92a-1	let-7a	let-7b	let-7g	let-7i
Predicted targets					

of miRNAs

TFs		EZH2	EZH2	EZH2	EZH2
		POU2F1	POU2F1	POU2F1	POU2F1
		RB1	RB1	RB1	RB1
		TP53	TP53	TP53	TP53
Genes	COL1A1	FAS	FAS	FAS	FAS
	DACT3	COL1A1	COL1A1	COL1A1	CHUK
		IL6	IL6	IL6	COL1A1
		MAPK8	MAPK8	MAPK8	IL6
		UTRN	UTRN	UTRN	MAPK8
					UTRN

Validated targets

TFs	HDAC1	E2F1	CTCF	MYC
	HDGF	EZH2	E2F3	
	KAT2B	MYC	EZH2	
	MYBL2	NFKB1	MYC	
	NFKB1	PARP1	SOX9	
	STAT3	SP1	SP1	
	HDAC2	STAT3		
	KLF4			
	IKZF1			
Genes	ATM	MYC	BIRC5	MYC
	CCNB1	HRAS	CCNB1	FN1
	EPB41L3	E2F1	EPB41L3	
	FLNA	IL6	FLNA	
	HMGCS1		HIF1A	
	SMAD4		HMGCS1	
	TGFBR2		MYC	
	TYMP		UTRN	
	MAPK8		HRAS	
	DNMT1			

H19-FOXO1-TXNIP

miRNAs	miR-106a	miR-130b-3p	miR-138-5p	miR-139	miR-141	miR-152-3p	miR-152-5p

Predicted targets of miRNAs

TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3
	PPARA	STAT3	RELA				KLF4
	RB1		SP1				
	SP1						
	STAT3						
	KAT2B						
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1
	E2F1	TGFBR2		ZEB1		FBN1	FMR1
	HIF1A					FMR1	SOS1
	SMAD4					SOS1	
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9				
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

TFs	RUNX1	RUNX1	RUNX1	E2F3	ERG	
	E2F1	KLF6	KLF6	FLI1	FLI1	
	RB1	ETS1	NR3C1	SP3		
	STAT3	NR3C1	POU2F1			
	KAT2B	KAT2B				
Genes	CALD1	ATM	ATM	ACP5	FAS	FMR1
	CCNG2	SOS1	CTGF	FMR1	COL1A1	IL18
	E2F1	VCAM1	HIF1A	SP3	MAPK8	
	HIF1A	EPB41L3	HMGCS1	RSF1	ZEB1	
	MMP2		MAPK8			
	SOS1					
	TGFBR2					
	KLF11					
	TXNIP					

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs	miR-19b-1	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b
D 11 4 1 4							

TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8			
		SOS1			
		TGFBR2			
		KLF11			
		TXNIP			

Validated targets

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
				DNMT1			

miRNAs	miR-342-3p	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g

01 11111 (115							
TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN

Validated targets

TFs	FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
	E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
			STAT3	KAT2B	MYC	EZH2	
			E2F3	MYBL2	NFKB1	MYC	
				NFKB1	PARP1	SOX9	
				STAT3	SP1	SP1	
				HDAC2	STAT3		
				KLF4			
				IKZF1			
Genes	DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
	E2F1			CCNB1	HRAS	CCNB1	FN1
				EPB41L3	E2F1	EPB41L3	
				FLNA	IL6	FLNA	
				HMGCS1		HIF1A	
				SMAD4		HMGCS1	
				TGFBR2		MYC	
				TYMP		UTRN	
				MAPK8		HRAS	
				DNMT1			

miRNAs	let-7i
Predicted targets	
of miRNAs	
TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

TFs	
a	
Genes	

H19-KLF6-TXNIP miR-130b-3p miR-138-5p miR-139 miRNAs miR-106a miR-141 miR-152-3p miR-152-5p Predicted targets of miRNAs

TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3
	PPARA	STAT3	RELA				KLF4
	RB1		SP1				
	SP1						
	STAT3						
	KAT2B						
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1
	E2F1	TGFBR2		ZEB1		FBN1	FMR1
	HIF1A					FMR1	SOS1
	SMAD4					SOS1	
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9		KLF6????		
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

miRNAs miR-17 miR-181d-3p miR-181d-5p miR-18a	miR-194-5p miR-196a miR-19a
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RUNX1	RU	JNX1	RUNX1	E2F3	ERG	
E2F1	KL	.F6	KLF6	FLI1	FLI1	
RB1	ET	S1	NR3C1	SP3		
STAT3	NR	R3C1	POU2F1			
KAT2B	KA	T2B				
CALD1	AT	Ъ	ATM	ACP5	FAS	FMR1
CCNG2	SO	S1	CTGF	FMR1	COL1A1	IL18
E2F1	VC	CAM1	HIF1A	SP3	MAPK8	
HIF1A	EP	B41L3	HMGCS1	RSF1	ZEB1	
MMP2			MAPK8			
SOS1						
TGFBR2						
KLF11						
TXNIP						
	RUNX1 E2F1 RB1 STAT3 KAT2B Image: CALD1 CCNG2 E2F1 HIF1A MMP2 SOS1 TGFBR2 KLF11 TXNIP Image: Comparison of the second	RUNX1 RU E2F1 KI RB1 ET STAT3 NR KAT2B KA Image: Solution of the second seco	RUNX1 RUNX1 E2F1 KLF6 RB1 ETS1 STAT3 NR3C1 KAT2B KAT2B KAT2B KAT2B CALD1 ATM CCNG2 SOS1 E2F1 VCAM1 HIF1A EPB41L3 MMP2 SOS1 TGFBR2 KLF11 TXNIP I	RUNX1RUNX1RUNX1RUNX1E2F1KLF6KLF6RB1ETS1NR3C1STAT3NR3C1POU2F1KAT2BKAT2BIIIIIICALD1ATMATMCCNG2SOS1CTGFE2F1VCAM1HIF1AHIF1AEPB41L3HMGCS1MMP2IIKLF11IITXNIPIII	RUNX1RUNX1RUNX1E2F3E2F1KLF6KLF6FLI1RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BAAABAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAABAAAAAAAAAAAAAAAAAAAAAA <td>RUNX1RUNX1RUNX1E2F3ERGE2F1KLF6KLF6FL11FL11RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BKAT2BKAT2BCALD1ATMATMACP5CCNG2SOS1CTGFFMR1COL1A1EPB41L3HMGCS1RSF1ZEF1VCAM1HIF1AZEB1MMP2MAPK8SOS1TGFBR2KLF11ATMACMTXNIPImage: Construction of the state of the state</td>	RUNX1RUNX1RUNX1E2F3ERGE2F1KLF6KLF6FL11FL11RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BKAT2BKAT2BCALD1ATMATMACP5CCNG2SOS1CTGFFMR1COL1A1EPB41L3HMGCS1RSF1ZEF1VCAM1HIF1AZEB1MMP2MAPK8SOS1TGFBR2KLF11ATMACMTXNIPImage: Construction of the state

Validated targets

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs	miR-19b-1	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b
D H i i i							

TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8			
		SOS1			
		TGFBR2	2		
		KLF11			
		TXNIP			

Validated targets

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
	DNMT1			TGFBR2 DNMT1			
	DNMT1			TGFBR2 DNMT1			

miRNAs	miR-342-3p	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g

TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN

Validated targets

TFs	FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
	E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
			STAT3	KAT2B	MYC	EZH2	
			E2F3	MYBL2	NFKB1	MYC	
				NFKB1	PARP1	SOX9	
				STAT3	SP1	SP1	
				HDAC2	STAT3		
				KLF4			
				IKZF1			
Genes	DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
	E2F1			CCNB1	HRAS	CCNB1	FN1
				EPB41L3	E2F1	EPB41L3	
				FLNA	IL6	FLNA	
				HMGCS1		HIF1A	
				SMAD4		HMGCS1	
				TGFBR2		MYC	
				TYMP		UTRN	
				MAPK8		HRAS	
				DNMT1			

miRNAs	let-7i

TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

Validated targets

H19-PPARA-KLF11

	miRNAs	miR-106a	miR-130b-3p	miR-138-5p	miR-139	miR-141	miR-152-3p	miR-152-5p	
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Predicted targets of miRNAs

TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3
	PPARA	STAT3	RELA				KLF4
	RB1		SP1				
	SP1						
	STAT3						
	KAT2B						
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1
	E2F1	TGFBR2		ZEB1		FBN1	FMR1
	HIF1A					FMR1	SOS1
	SMAD4					SOS1	
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9				
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

miRNAs miR-17 miR-181d-3pmiR-181d-5pmiR-18a miR-194-5pmiR-196a miR-19a
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RUNX1		RUNX1	RUNX1	E2F3	ERG	
E2F1		KLF6	KLF6	FLI1	FLI1	
RB1		ETS1	NR3C1	SP3		
STAT3		NR3C1	POU2F1			
KAT2B		KAT2B				
CALD1		ATM	ATM	ACP5	FAS	FMR1
CCNG2		SOS1	CTGF	FMR1	COL1A1	IL18
E2F1		VCAM1	HIF1A	SP3	MAPK8	
HIF1A		EPB41L3	HMGCS1	RSF1	ZEB1	
MMP2			MAPK8			
SOS1						
TGFBR2						
KLF11						
TXNIP						
	RUNX1 E2F1 RB1 STAT3 KAT2B CALD1 CCNG2 E2F1 HIF1A MMP2 SOS1 TGFBR2 KLF11 TXNIP	RUNX1 E2F1 RB1 STAT3 KAT2B Image: CALD1 CALD1 CCNG2 E2F1 HIF1A MMP2 SOS1 TGFBR2 KLF11 TXNIP Image: Comparison of the system	RUNX1 RUNX1 E2F1 KLF6 RB1 ETS1 STAT3 NR3C1 KAT2B KAT2B Image: State of the state	RUNX1RUNX1RUNX1RUNX1E2F1KLF6KLF6RB1ETS1NR3C1STAT3NR3C1POU2F1KAT2BKAT2B	RUNX1RUNX1RUNX1E2F3E2F1KLF6KLF6FLI1RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BII <td>RUNX1RUNX1RUNX1E2F3ERGE2F1KLF6KLF6FL11FL11RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BAAABAAAAAAAAAAAAAAAAA<td< td=""></td<></td>	RUNX1RUNX1RUNX1E2F3ERGE2F1KLF6KLF6FL11FL11RB1ETS1NR3C1SP3STAT3NR3C1POU2F1KAT2BKAT2BAAABAAAAAAAAAAAAAAAAA <td< td=""></td<>

Validated targets

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs miR-19b-1 miR-200b miR-200c miR-20a miR-22 miR-29a miR-29b

TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8	3		
		SOS1			
		TGFBR	2		
		KLF11			
		TXNIP			

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
				DNMT1			

miRNAs	miR-342-3p	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g

TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN

TFs	FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
	E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
			STAT3	KAT2B	MYC	EZH2	
			E2F3	MYBL2	NFKB1	MYC	
				NFKB1	PARP1	SOX9	
				STAT3	SP1	SP1	
				HDAC2	STAT3		
				KLF4			
				IKZF1			
Genes	DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
	E2F1			CCNB1	HRAS	CCNB1	FN1
				EPB41L3	E2F1	EPB41L3	
				FLNA	IL6	FLNA	
				HMGCS1		HIF1A	
				SMAD4		HMGCS1	
				TGFBR2		MYC	
				TYMP		UTRN	
				MAPK8		HRAS	
				DNMT1			

miRNAs	let-7i
Predicted targets	
of miRNAs	
TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

TFs	
Genes	

miRNAs	miR-106a	miR-130b-3p	miR-138-5p	miR-139	miR-141	miR-152-3p	miR-152-5p
Predicted targets							
of miRNAs							
TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3
	PPARA	STAT3	RELA				KLF4
	RB1		SP1				
	SP1						
	STAT3						
	KAT2B						
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1
	E2F1	TGFBR2		ZEB1		FBN1	FMR1
	HIF1A					FMR1	SOS1
	SMAD4					SOS1	
	MMP2						
	MAPK8						
	SOS1						
	TGFBR2						
	KLF11						
	TXNIP						

H19-SP1-TGFBR2

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9				
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

	miRNAs mi	iR-17 miR-181d-3p	miR-181d-5p miR-18a	miR-194-5p	miR-196a	miR-19a
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TFs	RUNX1	RUNX1	RUNX1	E2F3	ERG	
	E2F1	KLF6	KLF6	FLI1	FLI1	
	RB1	ETS1	NR3C1	SP3		
	STAT3	NR3C1	POU2F1			
	KAT2B	KAT2B				
Genes	CALD1	ATM	ATM	ACP5	FAS	FMR1
	CCNG2	SOS1	CTGF	FMR1	COL1A1	IL18
	E2F1	VCAM1	HIF1A	SP3	MAPK8	
	HIF1A	EPB41L3	HMGCS1	RSF1	ZEB1	
	MMP2		MAPK8			
	SOS1					
	TGFBR2					
	KLF11					
	TXNIP					

Validated targets

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs	miR-19b-1	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b

Predicted targets

of	miRNAs	
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TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8			
		SOS1			
		TGFBR2			
		KLF11			
		TXNIP			

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
				DNMT1			

miRNAs miR-342-3p miR-630 miR-874 miR-92a-1 let-7a let-7b let-7g	
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Predicted targets

of miRNAs	
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TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN

TFs	FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
	E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
			STAT3	KAT2B	MYC	EZH2	
			E2F3	MYBL2	NFKB1	MYC	
				NFKB1	PARP1	SOX9	
				STAT3	SP1	SP1	
				HDAC2	STAT3		
				KLF4			
				IKZF1			
Genes	DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
	E2F1			CCNB1	HRAS	CCNB1	FN1
				EPB41L3	E2F1	EPB41L3	
				FLNA	IL6	FLNA	
				HMGCS1		HIF1A	
				SMAD4		HMGCS1	
				TGFBR2		MYC	
				TYMP		UTRN	
				MAPK8		HRAS	
				DNMT1			

miRNAs	let-7i
Predicted targets	
of miRNAs	
TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

TFs	
Genes	

H19-STAT3-KLF11

miRNAs	miR-106a	miR-130b-3p	miR-138-5p	miR-139	miR-141	miR-152-3p	miR-152-5p	miR-17	
									2

Predicted targets of miRNAs

TFs	RUNX1	FOSL2	EZH2	ETS1	CREBBP	KLF6	KLF6	RUNX1
	E2F1	MYB	POU2F1		POU2F1	KLF4	E2F3	E2F1
	PPARA	STAT3	RELA				KLF4	RB1
	RB1		SP1					STAT3
	SP1							KAT2B
	STAT3							
	KAT2B							
Genes	CALD1	FMR1	HIF1A	FMR1	FMR1	CHUK	DNMT1	CALD1
	CCNG2	MET	KLF11	MAPK8		DNMT1	FBN1	CCNG2
	E2F1	TGFBR2		ZEB1		FBN1	FMR1	E2F1
	HIF1A					FMR1	SOS1	HIF1A
	SMAD4					SOS1		MMP2
	MMP2							SOS1
	MAPK8							TGFBR2
	SOS1							KLF11
	TGFBR2							TXNIP
	KLF11							
	TXNIP							

Validated targets

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	E2F1
	MYB	E2F1	NFKB1		PPARA		E2F3
	RB1	NR3C1	SNAI2		HDGF		KAT2B
	RUNX1	PPARA	SOX9				MYC
	STAT3	RB1	TWIST2				RB1
		STAT3					RUNX1
							STAT3
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	E2F1
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	MMP2
	TGFBR2	SMAD4			KLF11		MYC
	ATM	TGFBR2			ZEB1		SMAD4
	HIF1A	ZEB1					TGFBR2
		FMR1					HIF1A
		MMP2					DNMT1
							IGFBP3

TFs	RUNX1	RUNX1	E2F3	ERG		
	KLF6	KLF6	FLI1	FLI1		
	ETS1	NR3C1	SP3			
	NR3C1	POU2F1				
	KAT2B					
Genes	ATM	ATM	ACP5	FAS	FMR1	
	SOS1	CTGF	FMR1	COL1A1	IL18	
	VCAM1	HIF1A	SP3	MAPK8		
	EPB41L3	HMGCS1	RSF1	ZEB1		
		MAPK8				

TFs		NR3C1	FOXM1	FOXO1	KAT2B	KAT2B
		RUNX1				NR3C1
Genes	HRAS	CTGF		FLNA	CTGF	CTGF
		EDF1		TGFBR2	SMAD4	FMR1
		ATM			TGFBR2	ATM
		HIF1A			DNMT1	HMGCS1
		HMGCS1				SMAD4
		SMAD4				TGFBR2
		TGFBR2				DNMT1
		DNMT1				

	miRNAs	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b	miR-342-3p
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TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2	E2F3
	SP3	E2F3	HNRNPK	KAT2B		
		EZH2				
		PPARA				
		RB1				
		STAT3				
		KAT2B				
Genes	NCF2	CALD1	CD68		DNMT1	DNMT1
	MAPK8	CCNG2	SOS1		FBN1	ZEB1
	SP3	E2F1	UTRN		EDF1	
		HIF1A	VCAM1			
		SMAD4	WRN			
		MMP2				
		MAPK8				
		SOS1				
		TGFBR2				
		KLF11				
		TXNIP				

TFs	E2F3	MYB	E2F1	PPARA	KLF4	SP1	FOSL2
	ETS1	ETS1	E2F3		AHR	STAT3	E2F1
	MYB	SP1	MYC		MYC	SP1	
	SP1	E2F3	RB1			STAT3	
	EZH2	FOXO1	RUNX1			MYC	
		E2F3	STAT3				
Genes	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1	DNMT1
	FN1	FN1	E2F1		DNMT1	DNMT1	E2F1
	KLF11	KLF11	FLNA		FBN1	MMP2	
	ZEB1	ZEB1	HIF1A		MYC	FBN1	
	DNMT1	NCAM1	MYC			MYC	
		CYP1B1	SMAD4				
			TGFBR2				
			DNMT1				

miRNAs	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g	let-7i

Predicted targets

of	miRNAs	

TFs	KLF6	POU2F1		EZH2	EZH2	EZH2	EZH2
	EZH2	STAT3		POU2F1	POU2F1	POU2F1	POU2F1
				RB1	RB1	RB1	RB1
				TP53	TP53	TP53	TP53
Genes		FBN1	COL1A1	FAS	FAS	FAS	FAS
		FMR1	DACT3	COL1A1	COL1A1	COL1A1	CHUK
		SIGIRR		IL6	IL6	IL6	COL1A1
				MAPK8	MAPK8	MAPK8	IL6
				UTRN	UTRN	UTRN	MAPK8
							UTRN

TFs	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC	
	FOXM1	HDAC1	HDGF	EZH2	E2F3		
		STAT3	KAT2B	MYC	EZH2		
		E2F3	MYBL2	NFKB1	MYC		
			NFKB1	PARP1	SOX9		
			STAT3	SP1	SP1		
			HDAC2	STAT3			
			KLF4				
			IKZF1				
Genes	SNAI2		ATM	MYC	BIRC5	MYC	
			CCNB1	HRAS	CCNB1	FN1	
			EPB41L3	E2F1	EPB41L3		
			FLNA	IL6	FLNA		
			HMGCS1		HIF1A		
			SMAD4		HMGCS1		
			TGFBR2		MYC		
			TYMP		UTRN		
			MAPK8		HRAS		
			DNMT1				

H19-NFYB-SP3 miR-106a miRNAs miR-130b-3p miR-138-5p miR-139 miR-141 miR-152-3p miR-152-5p **Predicted targets** of miRNAs TFs RUNX1 FOSL2 EZH2 ETS1 CREBBP KLF6 KLF6 E2F1 MYB POU2F1 POU2F1 KLF4 E2F3 PPARA STAT3 KLF4 RELA RB1 SP1 SP1 STAT3 KAT2B HIF1A Genes CALD1 FMR1 FMR1 FMR1 CHUK DNMT1 CCNG2 MET KLF11 MAPK8 DNMT1 FBN1 TGFBR2 ZEB1 E2F1 FBN1 FMR1 HIF1A FMR1 SOS1 SMAD4 SOS1 MMP2 MAPK8 SOS1 TGFBR2 KLF11

targets of

TXNIP

miRNAs

TFs	E2F1	AHR	EZH2	NFKB1	E2F3	KLF4	
	MYB	E2F1	NFKB1		PPARA		
	RB1	NR3C1	SNAI2		HDGF		
	RUNX1	PPARA	SOX9				
	STAT3	RB1	TWIST2				
		STAT3					
Genes	E2F1	E2F1	HIF1A	HRAS	ZEB1	DNMT1	
	FAS	KLF11	SNAI2	MET	EIF4E	ADAM17	
	TGFBR2	SMAD4			KLF11		
	ATM	TGFBR2			ZEB1		
	HIF1A	ZEB1					
		FMR1					
		MMP2					

miRNAs	miR-17	miR-181d-3p	miR-181d-5p	miR-18a	miR-194-5p	miR-196a	miR-19a
Predicted targets							

rge of miRNAs

TFs	RUNX1	RUNX1	RUNX1	E2F3	ERG	
	E2F1	KLF6	KLF6	FLI1	FLI1	
	RB1	ETS1	NR3C1	SP3		
	STAT3	NR3C1	POU2F1			
	KAT2B	KAT2B				
Genes	CALD1	ATM	ATM	ACP5	FAS	FMR1
	CCNG2	SOS1	CTGF	FMR1	COL1A1	IL18
	E2F1	VCAM1	HIF1A	SP3	MAPK8	
	HIF1A	EPB41L3	HMGCS1	RSF1	ZEB1	
	MMP2		MAPK8			
	SOS1					
	TGFBR2					
	KLF11					
	TXNIP					

targets of miRNAs

TFs	E2F1		NR3C1	FOXM1	FOXO1	KAT2B
	E2F3		RUNX1			
	KAT2B					
	MYC					
	RB1					
	RUNX1					
	STAT3					
Genes	E2F1	HRAS	CTGF		FLNA	CTGF
	MMP2		EDF1		TGFBR2	SMAD4
	MYC		ATM			TGFBR2
	SMAD4		HIF1A			DNMT1
	TGFBR2		HMGCS1			
	HIF1A		SMAD4			
	DNMT1		TGFBR2			
	IGFBP3		DNMT1			

miRNAs	miR-19b-1	miR-200b	miR-200c	miR-20a	miR-22	miR-29a	miR-29b
Predicted targets							

of miRNAs

TFs	KLF6	E2F1	FOXO1	ETS1	MYBL2
	SP3	E2F3	HNRNPK	KAT2B	
		EZH2			
		PPARA			
		RB1			
		STAT3			
		KAT2B			
Genes	NCF2	CALD1	CD68		DNMT1
	MAPK8	CCNG2	SOS1		FBN1
	SP3	E2F1	UTRN		EDF1
		HIF1A	VCAM1		
		SMAD4	WRN		
		MMP2			
		MAPK8			
		SOS1			
		TGFBR2			
		KLF11			
		TXNIP			

targets of miRNAs

TFs	KAT2B	E2F3	MYB	E2F1	PPARA	KLF4	SP1
	NR3C1	ETS1	ETS1	E2F3		AHR	STAT3
		MYB	SP1	MYC		MYC	SP1
		SP1	E2F3	RB1			STAT3
		EZH2	FOXO1	RUNX1			MYC
			E2F3	STAT3			
Genes	CTGF	CREB1	FLNA	CCNB1	HIF1A	MMP2	COL1A1
	FMR1	FN1	FN1	E2F1		DNMT1	DNMT1
	ATM	KLF11	KLF11	FLNA		FBN1	MMP2
	HMGCS1	ZEB1	ZEB1	HIF1A		MYC	FBN1
	SMAD4	DNMT1	NCAM1	MYC			MYC
	TGFBR2		CYP1B1	SMAD4			
	DNMT1			TGFBR2			
				DNMT1			

miRNAs	miR-342-3p	miR-630	miR-874	miR-92a-1	let-7a	let-7b	let-7g
Predicted tar	gets						
of miRNAs							
TFs	E2F3	KLF6	POU2F1		EZH2	EZH2	EZH2
		EZH2	STAT3		POU2F1	POU2F1	POU2F1
					RB1	RB1	RB1
					TP53	TP53	TP53
Genes	DNMT1		FBN1	COL1A1	FAS	FAS	FAS
	ZEB1		FMR1	DACT3	COL1A1	COL1A1	COL1A1
			SIGIRR		IL6	IL6	IL6
					MAPK8	MAPK8	MAPK8
					UTRN	UTRN	UTRN
targets of							
miRNAs					-		-

FOSL2	SNAI2	PARP1	HDAC1	E2F1	CTCF	MYC
E2F1	FOXM1	HDAC1	HDGF	EZH2	E2F3	
		STAT3	KAT2B	MYC	EZH2	
		E2F3	MYBL2	NFKB1	MYC	
			NFKB1	PARP1	SOX9	
			STAT3	SP1	SP1	
			HDAC2	STAT3		
			KLF4			
			IKZF1			
DNMT1	SNAI2		ATM	MYC	BIRC5	MYC
E2F1			CCNB1	HRAS	CCNB1	FN1
			EPB41L3	E2F1	EPB41L3	
			FLNA	IL6	FLNA	
			HMGCS1		HIF1A	
			SMAD4		HMGCS1	
			TGFBR2		MYC	
			TYMP		UTRN	
			MAPK8		HRAS	
			DNMT1			
	FOSL2 E2F1	FOSL2 SNAI2 E2F1 FOXM1 Image: Constraint of the system	FOSL2 SNAI2 PARP1 E2F1 FOXM1 HDAC1 STAT3 E2F3 - - -	FOSL2SNAI2PARP1HDAC1E2F1FOXM1HDAC1HDGFCSTAT3KAT2BCE2F3MYBL2MYBL2STAT3STAT3CSTAT3HDAC2CSTAT3HDAC2CSTAT3IKZF1CSTAT3STAT3DNMT1SNAI2ATME2F1CCNB1EPB41L3CSMAD4FLNASMAD4TGFBR2SMAPK8DNMT1	FOSL2SNAI2PARP1HDAC1E2F1E2F1FOXM1HDAC1HDGFEZH2E2F1FOXM1HDAC1HDGFEZH2Image: Constraint of the stress of t	FOSL2SNAI2PARP1HDAC1E2F1CTCFE2F1FOXM1HDAC1HDGFEZH2E2F3ISTAT3KAT2BMYCEZH2IE2F3MYBL2NFKB1MYCIISTAT3SP1SOX9IISTAT3SP1SP1IIIHDAC2STAT3IIIKLF4III

miRNAs let-7i Predicted targets of miRNAs

TFs	EZH2
	POU2F1
	RB1
	TP53
Genes	FAS
	CHUK
	COL1A1
	IL6
	MAPK8
	UTRN

targets of miRNAs

TFs	
Genes	

 Table S6. Primers for qRT-PCR experiment

Gene	Forward sequence	Reverse sequence
GAPDH	5'-CCACTCCTCCACCTTTGAC-3'	5'-ACCCTGTTGCTGTAGCCA-3'
H19	5'-GTGGACTTGGTGACGCTGTA-3'	5'-CACCATCCTCCTCCTGAGA-3'
SP1	5'-TGGCAGCAGTACCAATGGC-3'	5'-CCAGGTAGTCCTGTCAGAACTT-3'
ETS1	5'-GATAGTTGTGATCGCCTCACC-3'	5'-GTCCTCTGAGTCGAAGCTGTC-3'
STAT3	5'-ACCAGCAGTATAGCCGCTTC-3'	5'-GCCACAATCCGGGCAATCT-3'
TGFBR2	5'-GTAGCTCTGATGAGTGCAATGAC-3'	5'-CAGATATGGCAACTCCCAGTG-3'
KLF11	5'-GTTGCGGATAAGACCCCTCAC-3'	5'-TGGAATCTGTTACTTGGGGAGA-3'