

Supplemental Figure legends

Fig.S1. Hepatic miRs potentially regulated by FXR.

Total RNA was isolated from livers from three male wild type mice or FXR null mice using the mirVana™ miRNA isolation kit (Ambion, Austin, TX, USA). Micro RNA microarray studies including labeling, hybridization, image scanning, and data analysis were carried out according to the manufacturer's instruction. MiR-34a was detected as the most up-regulated microRNA in livers of FXR null mice.

Fig. S2. SHP interacts with p53 in cells. Cos-1 cells were transfected with expression plasmids as indicated and 36 hr later, cell extracts were prepared and p53 was immunoprecipitated from cell extracts and presence of flag-SHP in the immunoprecipitates was detected with western analysis.

Fig.S3. Ad-siSHP efficiently decreased protein levels in HepG2 cells. HepG2 cells were co-infected with Ad-flag-SHP along with either control Ad-empty or Ad-siSHP and 2 days later, cells were collected and flag-SHP levels were detected by western analyses.

Fig.S4. HNF-4 increases miR-34a promoter activity. HepG2 cells were cotransfected with plasmids as indicated and treated with respective ligands for LXR, CAR, PXR, and FXR overnight and collected for reporter assays.

Fig.S5. HNF-4 increases miR-34a promoter activity in a p53-independent manner. HepG2 cells were cotransfected with plasmids as indicated and collected for reporter assays.

Fig.S6. HNF-4 plays a role in the recruitment of SHP to the miR-34a promoter. (A) HepG2 cells were transfected with the indicated siRNA and 2 days later, endogenous HNF-4 levels were detected (B), or cells were treated with GW4064 and collected for ChIP assays (C). (D) Band intensities were quantified from two independent ChIP assays and the average relative occupancies of SHP and HNF-4 are shown.

Fig. S7. Infection of HepG2 cells with Ad-miR-34a increased mature miR-34a levels. HepG2 cells were infected with increasing amounts of Ad-miR-34a and 2 days after infection, cells were collected for q-RTPCR to measure miR-34a levels. Statistical significance was determined by the Student's t test (SEM, n=3) and ** indicates $p < 0.01$.

Fig. S8. Efficient down-regulation of miR-34a levels by anti-miR34a. (A) Cos-1 cells were infected with Ad-miR-34a and then treated with anti-miR-34a or control scrambled RNA and 2 days later, miR-34a levels were detected by q-RTPCR. (B) Cos-1 cells were treated with anti-miR34a or control scrambled RNA and 2 days later, miR-34a levels were detected by q-RTPCR.

Fig. S9. Transfection of plasmids expressing miR-34a decreased SIRT1 protein levels but not SIRT1 mRNA levels. HepG2 cells were transfected with either control pCDH vector or pCDH-miR-34a and 2 days later, miR-34a levels, SIRT1 mRNA, and protein levels were detected by q-RTPCR and western analysis, respectively. Statistical significance was measured using the Student's t test. ***, *, and NS indicate $p < 0.001$, $p < 0.05$, and statistically not significant, respectively, SEM (n=3).

Fig. S10. Elevated hepatic miR-34a levels in mice infected with Ad-miR-34a. Normal mice were tail vein injected with Ad-miR-34a or control Ad-empty as described in Methods and 5 days later, infection efficiency was monitored by western analysis to measure GFP and control Tubulin levels (A). Hepatic miR-34a levels were also measured using q-RTPCR (B).

Fig. S11. Effects of GW4064 on the expression of *Shp* and *p53* in obese mouse liver

Mice fed high fat western-style diet (WD) for 20 weeks were daily treated with GW4064 for 5 days and livers were collected for q-RTPCR (A, B) and western analysis (C). (C) The p53 protein levels and β -actin as a loading control were measured by western analysis.

Fig. S12. Treatment with resveratrol for 1 week substantially decreases miR-34a levels in diet-induced obese mice. (A) Experimental outline. (B) Mice fed WD chow were injected with Ad-flag-SIRT1 and 1 week later, hepatic miR-34a levels were measured. Statistical significance was determined by the Student's t test (SEM, n=3) and * indicates $p < 0.05$. (C) Mice fed high fat chow for 20 weeks were daily treated with resveratrol via oral gavages and livers were collected to measure miR-34a levels. Statistical significance was determined by the Student's t test (SEM, n=3) and * indicates $p < 0.05$.

Fig. S1

No.	Probe_ID	WT	FKO Signal	log2 (Sample B / Sample A)
1	hsa-miR-34a	152.09	657.51	1.96
2	hsa-miR-802	102.10	337.40	1.83
3	hsa-miR-31	2,498.25	702.22	-1.80
4	mmu-miR-31	2,542.73	731.32	-1.79
5	mmu-miR-680	294.77	1,085.93	1.75
6	mmu-miR-802	168.17	532.44	1.66
7	hsa-miR-765	113.55	283.87	1.32
8	mmu-miR-350	132.85	280.70	1.29
9	rno-miR-327	363.97	844.04	1.20
10	mmu-miR-720	1,642.94	786.83	-1.11
11	hsa-miR-132	253.00	475.47	1.02
12	hsa-miR-101	3,705.58	6,774.51	0.87
13	mmu-miR-805	2,320.66	1,285.14	-0.84
14	hsa-miR-199a*	1,481.11	2,605.64	0.76
15	hsa-miR-92b	3,675.29	2,191.78	-0.76
16	hsa-miR-92	8,414.39	5,092.44	-0.73
17	mmu-miR-101b	8,205.21	13,217.66	0.71
18	mmu-miR-705	6,584.73	10,823.16	0.70
19	hsa-miR-29b	1,455.01	2,386.44	0.68
20	hsa-miR-451	5,370.74	8,367.27	0.62
21	hsa-miR-146a	3,271.53	2,179.68	-0.58
22	hsa-miR-320	1,875.52	1,247.94	-0.58
23	mmu-miR-451	9,499.99	14,182.79	0.58
24	hsa-miR-342	1,427.13	2,048.71	0.56
25	mmu-miR-689	4,627.53	6,271.70	0.47
26	mmu-miR-455-3p	1,792.37	1,307.13	-0.46
27	hsa-let-7e	10,821.34	8,205.68	-0.40
28	hsa-miR-23a	16,310.85	21,178.03	0.38
29	hsa-miR-20a	3,167.34	2,449.28	-0.37
30	mmu-miR-690	8,416.92	10,620.65	0.35
31	hsa-miR-143	3,331.26	4,239.07	0.33
32	hsa-let-7b	28,723.88	23,366.55	-0.30
33	hsa-miR-30d	8,592.47	7,019.51	-0.28
34	hsa-miR-23b	19,533.76	23,560.40	0.27
35	hsa-miR-26b	20,672.56	17,117.25	-0.27
36	hsa-miR-126	27,462.15	31,723.38	0.27
37	hsa-let-7d	25,409.90	21,342.10	-0.25

38	hsa-let-7g	24,535.02	20,567.75	-0.24
39	hsa-let-7c	31,308.60	26,929.03	-0.22
40	hsa-miR-26a	34,984.38	30,296.13	-0.21
41	hsa-miR-22	11,514.32	13,274.10	0.21
42	hsa-miR-30c	27,565.16	23,664.68	-0.20
43	hsa-let-7f	32,985.82	28,770.88	-0.20
44	hsa-miR-30b	24,971.24	21,945.68	-0.19
45	hsa-miR-148a	18,596.24	16,448.05	-0.18
46	mmu-let-7f	32,242.35	28,794.99	-0.17
47	mmu-let-7a	36,566.09	32,758.77	-0.16
48	hsa-miR-638	14,132.91	15,765.84	0.16
49	hsa-miR-29a	30,075.72	32,669.76	0.13
50	hsa-miR-21	40,857.04	44,811.48	0.13
51	hsa-let-7a	35,436.66	32,241.90	-0.12
52	hsa-miR-122a	53,939.03	57,349.05	0.09

Supplemental Figures

Fig. S2

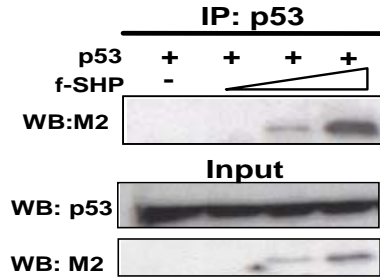


Fig. S3

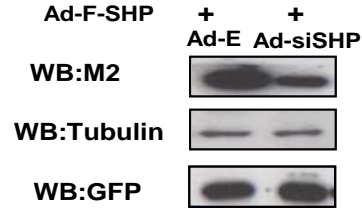


Fig. S4

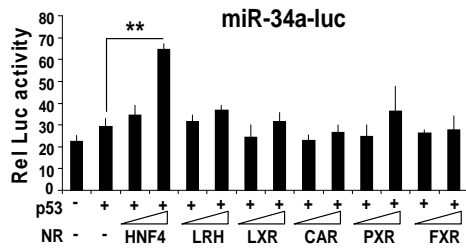


Fig. S5

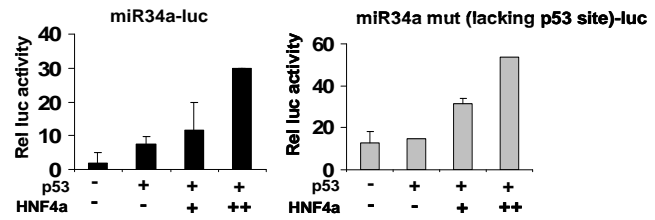


Fig. S6

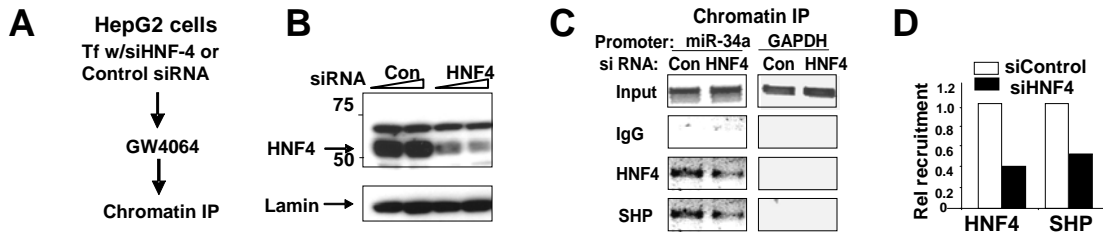


Fig. S7

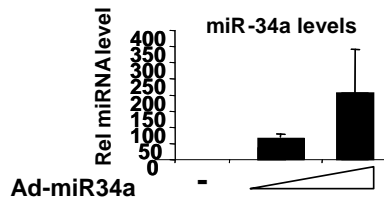
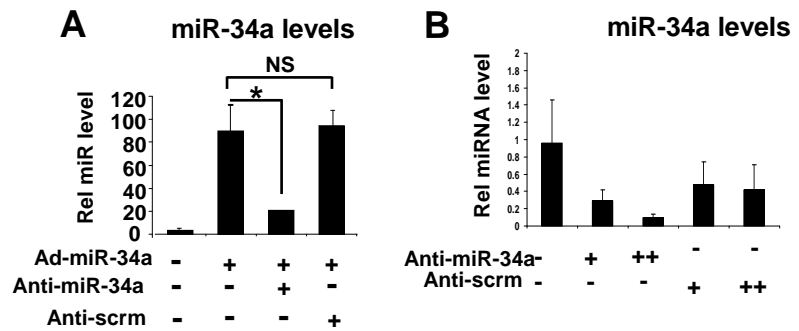


Fig. S8



Supplemental Figures

Fig. S9

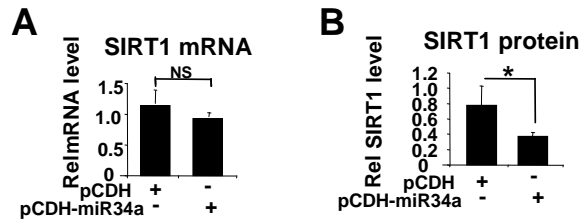


Fig. S10

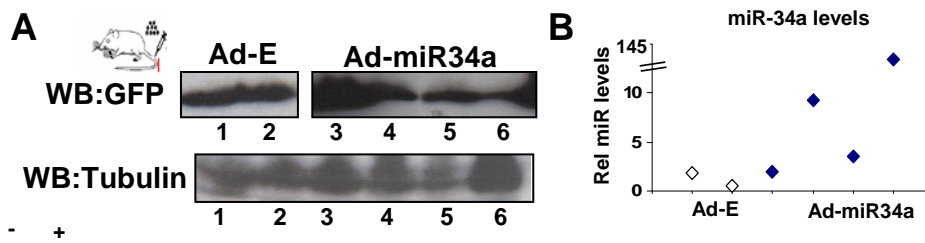


Fig. S11

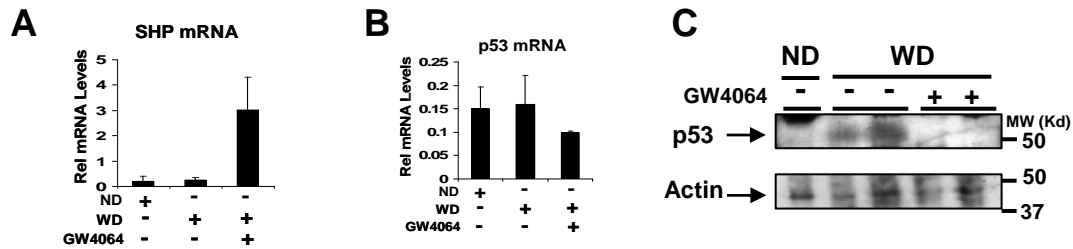


Fig. S12

