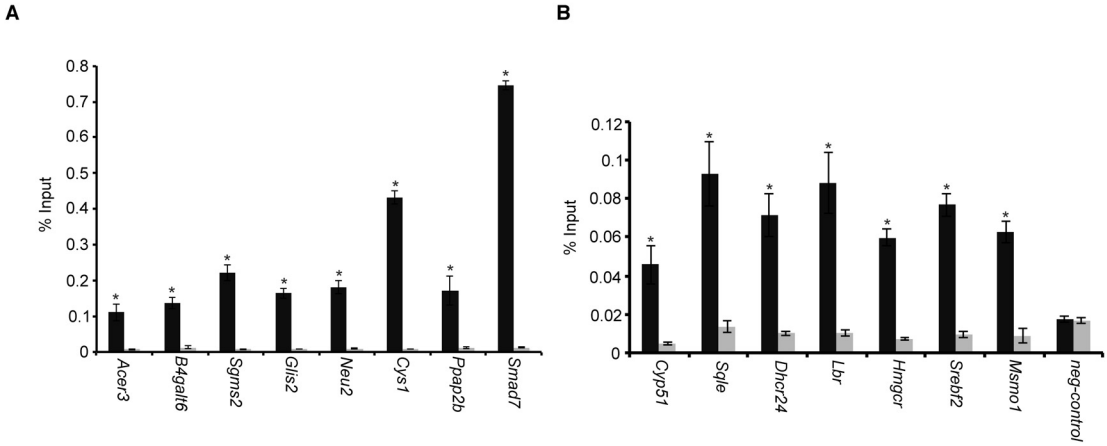
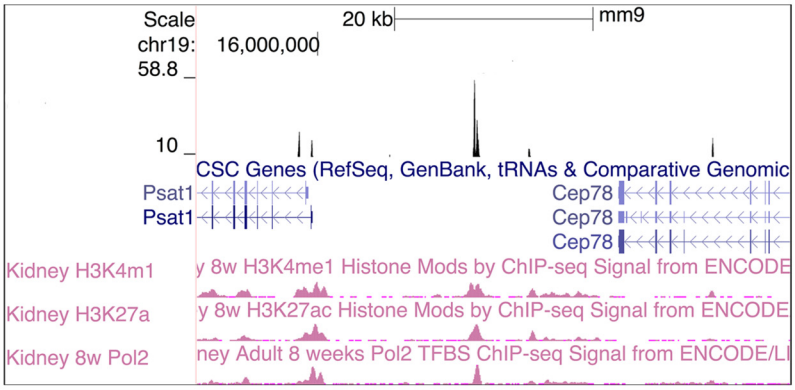
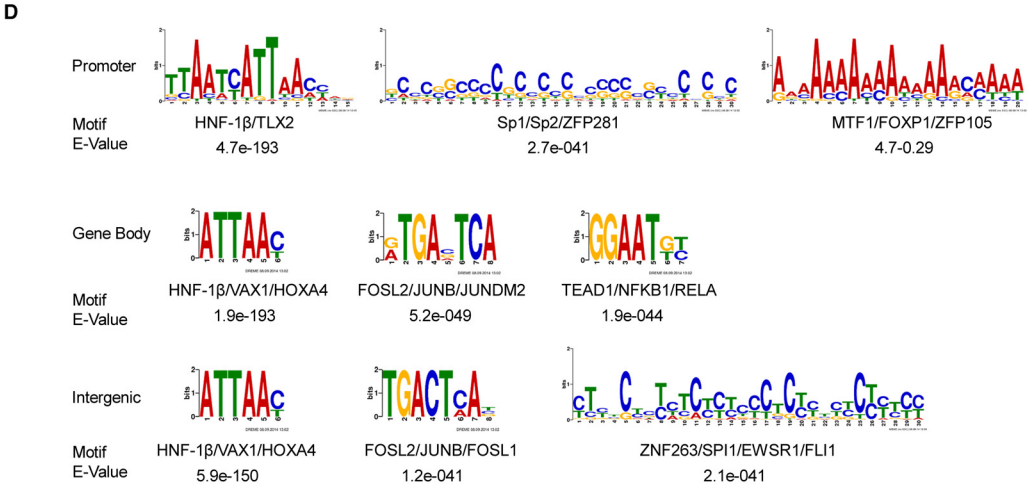
SUPPLEMENTARY FIGURES



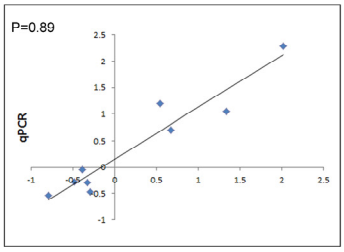




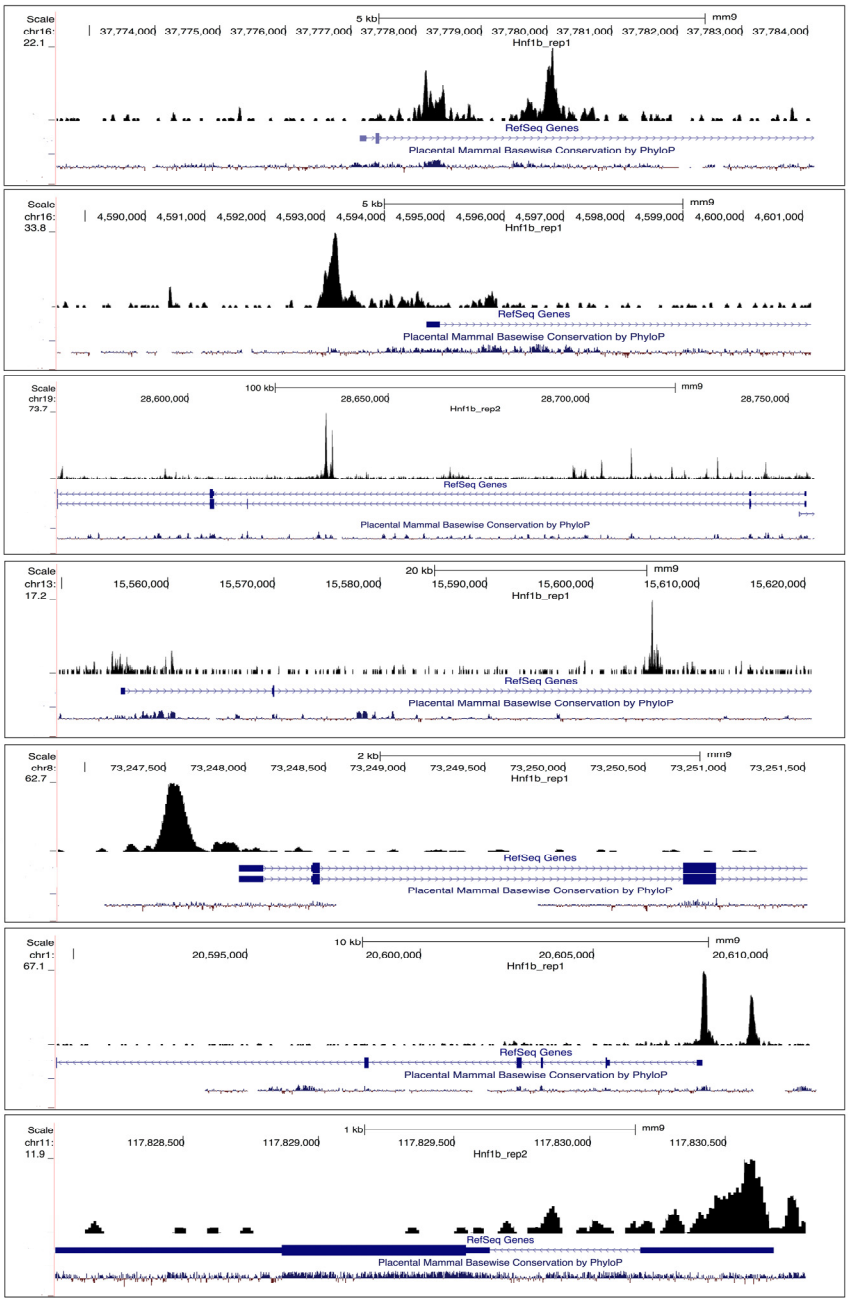
SUPPLEMENTARY FIGURE 1. A) Quantitative ChIP-qPCR verifying binding of HNF-1β near representative gene targets identified by ChIP-seq in mIMCD3 cells. Enrichment of HNF-1β and IgG binding was calculated according to the percent input method. Data represent means of three independent experiments. * indicates significant enrichment of HNF-1β compared to control IgG ($p<0.05$). B) Quantitative ChIP-qPCR showing binding of HNF-1β near genes involved in cholesterol synthesis in uninduced 53A cells. Negative control shows amplification of an intergenic region not bound by HNF-1β**.** Enrichment was calculated relative to input. Data shown are mean±SE of three independent experiments. * indicates $p<0.05$. C) Representative ChIP-seq showing binding of HNF-1β (black peaks) to genomic sites located between the *Psat1* and *Cep78* genes (blue). HNF-1β binding sites correspond to histone marks of active enhancers (pink). Data were visualized using the UCSC Genome Browser. D) MEME software was used to predict *de novo* motifs that are statistically overrepresented within a 200-bp region centered on the genomic coordinates where HNF-1β is bound. Analysis was carried out on peaks from three different regions: promoters, gene bodies, and intergenic domains.

A

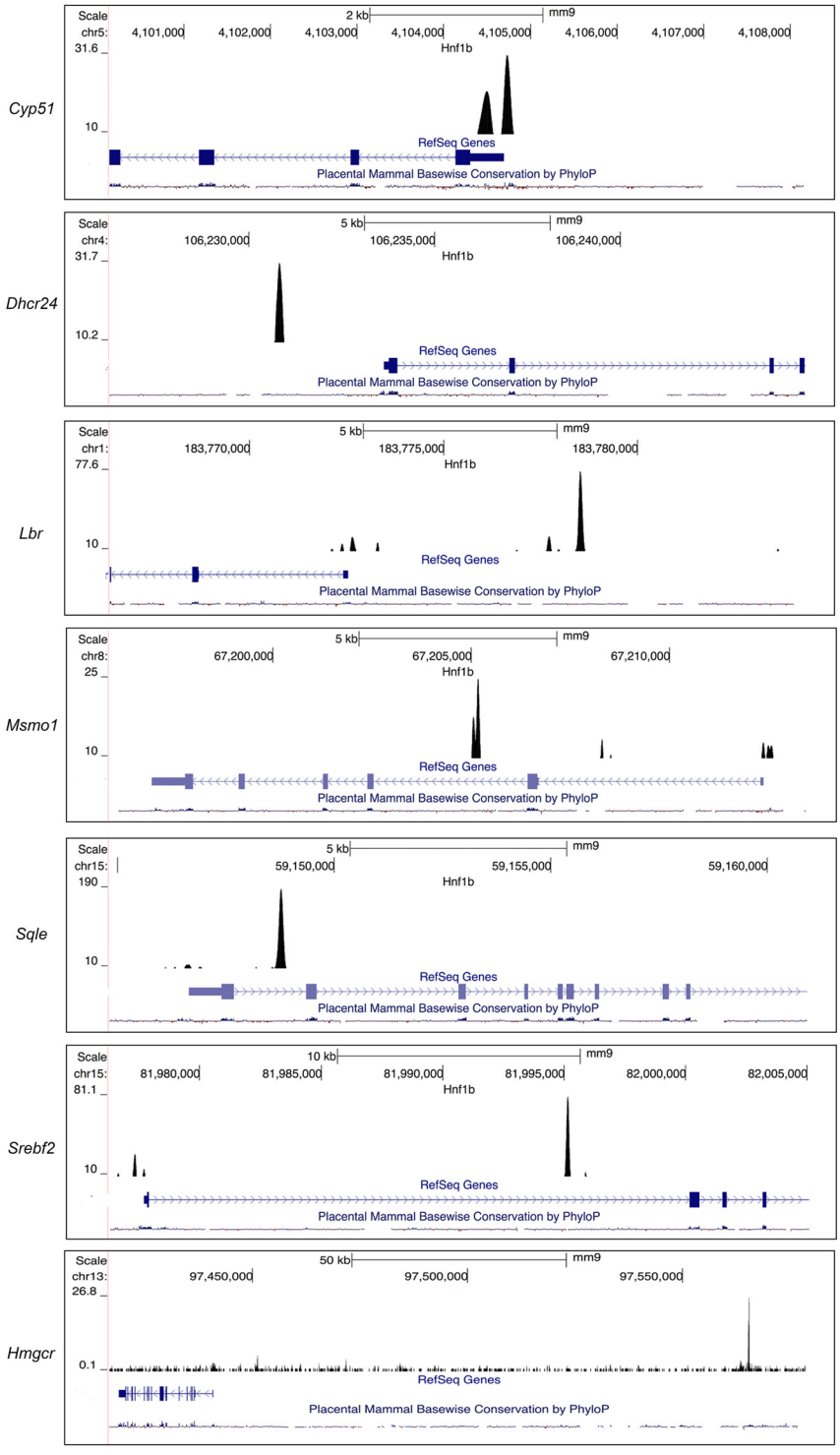
Gene Symbol	Common name	Log2 (microarray)	Log2 (qPCR)
Fstl1	Follistatin-related protein 1	-0.69	-1.8
Glis2	Glis family zinc finger 2	-0.56	-1.28
Glis3	Glis family zinc finger 3	-0.6	-0.68
Gli3	Gli family zinc finger 3	0.55	1.37
Pde4c	Phosphodiesterase 4C-cAMP specific	-0.77	-4.12
Pkhd1	Polycystic kidney and hepatic disease 1	-1.47	-2.88
Socs3	Suppressor of cytokine signaling 3	0.72	2.23



B



SUPPLEMENTARY FIGURE 2. A) Left panel: Changes in expression of representative HNF-1β target genes in cells expressing mutant HNF-1β measured by microarray analysis and qRT-PCR. Right panel: Correlation between microarray analysis and qRT-PCR. Pearson coefficient=0.89. B) ChIP-seq showing peaks of HNF-1β binding relative to the indicated genes in chromatin from mIMCD3 cells. Each panel shows genomic coordinates and size bar (top), HNF-1β binding peaks (black), gene exons and direction of transcription (blue), and evolutionary sequence conservation (bottom). Data were visualized using the UCSC Genome Browser (1).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4,103,000
4,104,000
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4,107,000
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31.6
Hnf1b
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RefSeq Genes
Placental Mammal Basewise Conservation by PhyloP
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Hnf1b
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RefSeq Genes
Placental Mammal Basewise Conservation by PhyloP
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mm9
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183,780,000
77.6
Hnf1b
10
RefSeq Genes
Placental Mammal Basewise Conservation by PhyloP
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mm9
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Hnf1b
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RefSeq Genes
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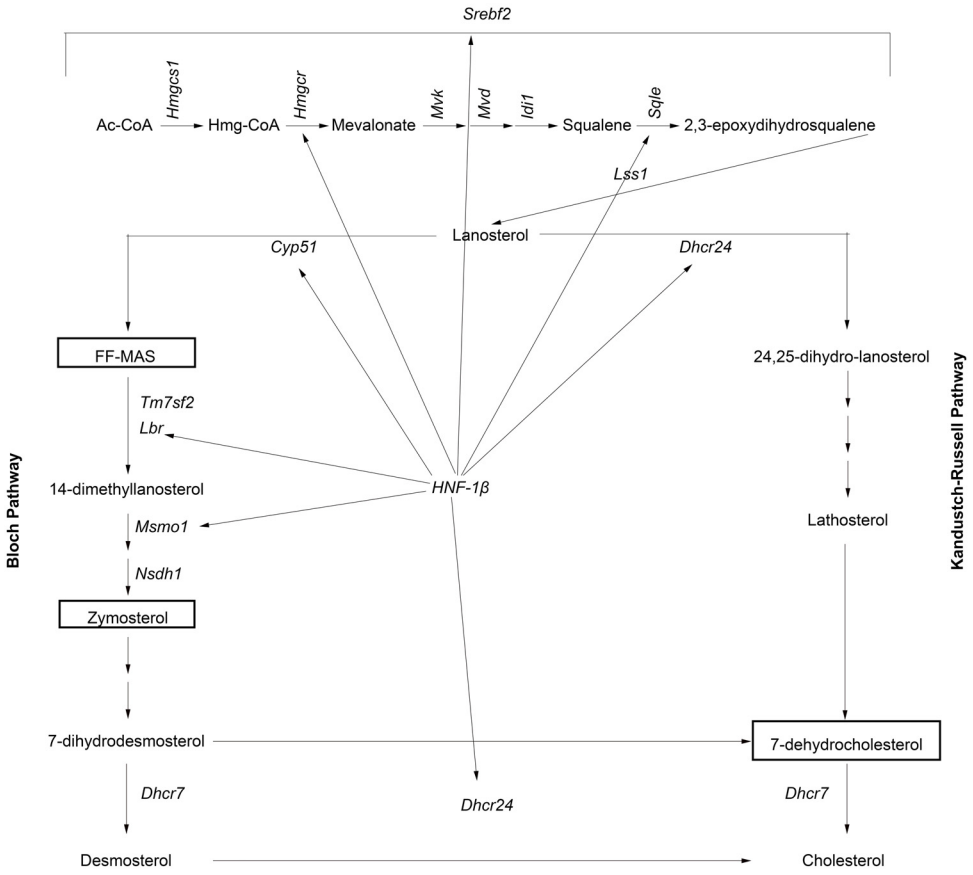
0.1
RefSeq Genes
Placental Mammal Basewise Conservation by PhyloP

SUPPLEMENTARY FIGURE 3. ChIP-seq showing peaks of HNF-1β binding (black) relative to genes involved in cholesterol synthesis (blue). Data were visualized using the UCSC Genome Browser (1). Genomic coordinates are shown at the top, and plots of evolutionary sequence conservation are shown at the bottom of each panel.



SUPPLEMENTARY FIGURE 4. Schematic diagram of the cholesterol synthesis pathway. Cholesterol intermediates that are down-regulated in cells expressing the HNF-1βΔC mutant are indicated by rectangles. Genes that are directly regulated by HNF-1β are indicated by arrows.

SUPPLEMENTARY TABLES

Sample	Uniquely Mapped Reads	Nonredundant fraction (NRF)	NSC	RSC	FRiP	Genomic coverage
HNF-1β_Rep1	12,742,595	0.986	1.46	1.06	6.5%	26%
HNF-1β_Rep2	12,491,746	0.986	1.58	1.13	6.8%	
IgG_Rep1	14,262,672	0.994				27%
IgG_Rep2	8,664,621	0.993				

SUPPLEMENTARY TABLE 1. Quality control analysis of the ChIP-seq samples. The ChIP-seq data for both HNF-1β and IgG fulfilled the criteria of the ENCODE consortium (>20 million total reads from two replicate samples, FRiP enrichment >1%, NSC ≥1.05, RSC≥0.8, and NRF ≥0.8). NSC, normalized strand coefficient; RSC, relative strand coefficient; FRiP, fraction of reads in peaks.

Gene	Forward primer (5'-3')	Reverse primer (5'-3')
Srebf2	gcagcaacgggaccattct	ccccatgactaagtccttcaact
Cyp51	gacaggaggcaacttgctttc	gtggacttttcgctccagc
Dhcr24	ctctgggtgcgagtgaagg	ttcccggacctgtttctggat
Fdft1	atggagttcgtcaagtgtctagg	cgtgccgtatgtccccatc
Hmgcr	agcttgcccgaattgtatgtg	tctgttgtgaaccatgtgacttc
Hmgcs1	aactggtgcagaaatctctagc	ggttgaatagctcagaactagcc
Idi1	accagccatcttgatgaaaaaca	cagcaactattggtgaaacaacc
Lss	tcgtgggggaccctataaaac	cgtcctccgcttgataataagtc
Msmo1	aaacaaaagtgttggcgtgttc	aagcattcttaaagggctcctg
Mvd	atggcctcagaaaagcctcag	tggtcgtttttagctggtcct
Mvk	ggtgtggtcggaacttccc	ccttgagcgggttggagac
Nsdhl	aaggtgtaagcacagttttcca	gcaggtttcaatgacagtcttgg
Sqle	ataagaaatgcggggatgtcac	atatccgagaaggcagcgaac
Lbr	atgccaagtaggaagtttgttga	gatttgttgtcgtggctcaga
Gli3	aacaattcctggaacgctgt	tcccagcacgacactgtaga
Fstl1	cacggcgaggaggaaccta	tcttgccattactgccacaca
Glis3	tgtggcatgaatctccaccg	tgatgggagggatatgttgacc
Glis2	gacgagcccctcgacctaa	agctctcgatgcaaagcatga
Pde4c	agctttgacctcgaaaatggg	gtccgaacggtacaggaagg
Socs3	gcaagctgcaggagagcggatt	aagaagtggcgctggtccga
Pkhd1	aagtcaagggccatcacatc	atgtttctggtcaacagccc
Gli3	gaagaaacgcaatcactatgcag	gtcccacggtaagggagaga
Pcsk9	ttgccccatgtggagtacatt	gggagcggtcttcctctgt
Srebf1	tgacccggctattccgtga	ctgggctgagcaatacagttc
18S	gtaacccgttgaaccccatt	ccatccaatcggtagtagcg

SUPPLEMENTARY TABLE 2. Primers used for quantitative RT-PCR

Gene	Forward (5'-3')	Reverse (5'-3')
Acer3	gtgctcggcaaggtttct	tgctgtttcctttcttccttct
Cys1	gcgagattcctacttcttgttaga	tcagcctggtgcttgtatg
Glis2	gcctcagactctagtgatgttc	ggatttaggaagaggtcggttc
Smad7	ctccttgaccttgggagttac	agccgcgatgcagattat
Dhcr24	gttagcttgcaaaatgctgg	ggaaatgaaatcttcttgagcc
Lbr	caggtaaaggtgggaggtga	agttggagagtgcctggcta
Neu2	accttgcctcttaacccattg	acaaagaacgcggccaa
Pcsk9	ttgcagcccaattaggattt	gtgaaggtggaagccttctg
Sqle	cgtcgctggtactcaggga	aagcctgaagcagtccca
Srebf2	gtgtaggcatgtgaatgtgctg	aatccccagcactcatacaaa
Cyp51a	acgaggtcccgcgtgctta	gctctgctgacgccacatag
B4galt6	ggtcattatttaactccgctcac	aagacaatataactctgagcacatc
Ppap2b	ctggcactcacttcagtgtt	agctgctgtccttggtaga
Sgms2	tgcttaacccagacccttc	gtagaattccgctcgctctc
Msmo	tctggaaaggcaccactacc	aacatttccaaggtgcttcg
Hmgcr	ttcggttttcctctctggttt	gcgagaaaattcttgccaaa
Neg-cont	ggacaattcaaccgaggaaa	tgaactggtttggtgtgctc

SUPPLEMENTARY TABLE 3. Primers used for ChIP-qPCR