

Supplemental Table S1. Target genes common to E2F and AHR

GENE	PROPERTIES
APAF1-Apaf1	Guo Z, Yikang S, Yoshida H, Mak TW, Zacksenhaus E.; Inactivation of the retinoblastoma tumor suppressor induces apoptosis protease-activating factor-1 dependent and independent apoptotic pathways during embryogenesis. <i>Cancer Res.</i> 2001 Dec 1;61(23):8395-400. Apaf-1 plays a critical role in apoptosis in a subset of tissues and that both E2F1:p53:Apaf-1-dependent and -independent apoptotic pathways operate downstream of Rb.
CDCA7-Cdca7	Cell division cycle associated 7. This gene was identified as a c-Myc responsive gene, and behaves as a direct c-Myc target gene. Overexpression of this gene is found to enhance the transformation of lymphoblastoid cells, and it complements a transformation-defective Myc Box II mutant, suggesting its involvement in c-Myc-mediated cell transformation.
RAM2-BC006933	Cell division cycle associated 7-like. Transcription factor RAM2.
CDT1-Ris2	Cdt1 function is negatively regulated by the Cdk phosphorylation independent of geminin binding. Sugimoto N, Tatsumi Y, Tsurumi T, Matsukage A, Kiyono T, Nishitani H, Fujita M. Cdt1 phosphorylation by cyclin A-dependent kinases negatively regulates its function without affecting geminin binding. <i>J Biol Chem.</i> 2004 May 7;279(19):19691-7. Cdt1, together with origin recognition complex and CDC6 proteins, constitutes the machinery that loads the minichromosome maintenance complex, a candidate replicative helicase, onto chromatin during the G(1) phase. a Skp2-independent pathway that requires the N-terminal 32 residues of Cdt1 is critical for the degradation of Cdt1 in S phase- this degradation is necessary for the optimum progression of cells through S phase. human CDT1 is essential for DNA
CKS1B-Cks1	Cks1b (suc1) interacts with Cdc2. Cdkn1b (p27) interacts with Cks1b (suc1). CKS1B protein binds to the catalytic subunit of the cyclin dependent kinases and is essential for their biological function.
DNMT1-Dnmt1	DNA (cytosine-5-)-methyltransferase 1 has a role in the establishment and regulation of tissue-specific patterns of methylated cytosine residues. Aberrant methylation patterns are associated with certain human tumors and developmental abnormalities. Direct role of Dnmt1 in the restoration of epigenetic information during DNA repair. DNMT1 plays a key role in methylation maintenance. DNA methylation is tightly coupled to replication through physical interaction of DNMT1 and core components of the replication machinery. reduction in DNMT1 triggers intra-S-phase arrest of DNA replication proposed to protect the genome from extensive DNA demethylation.
EZH2-Ezh2	This gene encodes a member of the Polycomb-group (PcG) family. PcG family members form multimeric protein complexes, which are involved in maintaining the transcriptional repressive state of genes over successive cell generations. The findings of this study indicate that EZH2 mRNA expression was upregulated in human HCC and may play an important role in tumour progression, especially by facilitating portal vein invasion.
HMGN1-Hmgn1	HMGN1, a nuclear protein that binds to nucleosomes and reduces the compaction of the chromatin fiber, modulates histone posttranslational modifications. Chromosomal protein HMG14 and its close analog HMG17 (MIM 163910) bind to the inner side of the nucleosomal DNA, potentially altering the interaction between the DNA and the histone octamer. The 2 proteins may be involved in the process that maintains transcribable genes in a unique chromatin conformation. Their ubiquitous distribution and relative abundance, as well as the high evolutionary conservation of the DNA-binding domain of the HMG14 family of proteins, suggest that they may be involved in an important cellular function.

HNRPR-Hnrpr	This gene belongs to the subfamily of ubiquitously expressed heterogeneous nuclear ribonucleoproteins (hnRNPs). The hnRNPs are RNA binding proteins and they complex with heterogeneous nuclear RNA (hnRNA). These proteins are associated with pre-mRNAs in the nucleus and appear to influence pre-mRNA processing and other aspects of mRNA metabolism and transport.
IGF2R-Igf2r	CD222 is a 250kDa transmembrane protein with a short cytoplasmic tail containing an internalization signal. CD222 was originally identified as a receptor for IGFII and M6P-containing proteins (e.g. lysosomal hydrolases). CD222 is also a receptor for TGFbeta latency associated peptide (LAP), proliferin and may bind several molecules independently of M6P, including plasminogen, CD87 or retinoic acid. It is involved in activation of latent TGFbeta
MCM3-Mcm3	The protein encoded by this gene is one of the highly conserved mini-chromosome maintenance proteins (MCM) that are involved in the initiation of eukaryotic genome replication. The hexameric protein complex formed by MCM proteins is a key component of the pre-replication complex (pre_RC) and may be involved in the formation of replication forks and in the
NASP-Nasp	In the cytoplasm linker histones are bound to a complex containing NASP and HSP90 whose ATPase activity is stimulated by binding NASP. Overexpression affects progression through cell cycle. This gene encodes a H1 histone binding protein that is involved in transporting histones into the nucleus of dividing cells.
NES-Nes	Nestin-expressing cells, marked by GFP fluorescence in nestin-GFP transgenic mice, appear in the permanent upper hair follicle immediately below the sebaceous glands. Nestin expression is recognized under all conditions of vascular development. Nestin expression in tumor endothelium is enhanced by the first intron. Detection of nestin-positive keratinocytes in the basal layer of cultured epidermis
PLTP-Pltp	plasma. The encoded protein transfers phospholipids from triglyceride-rich lipoproteins to high density lipoprotein (HDL). In addition to regulating the size of HDL particles, this protein may be involved in cholesterol metabolism. The phospholipid transfer protein gene is a liver X receptor target expressed by macrophages in atherosclerotic lesions. Pltp is regulated by liver X receptors in mice. PLTP regulates the bioavailability of vitamin E in atherogenic lipoproteins and suggest a novel strategy for achieving more effective concentrations of anti-oxidants in lipoproteins, independent of dietary supplementation.
TFDP1-Tfdp1	cell cycle. E2F factors bind to DNA as homodimers or heterodimers in association with dimerization partner DP1. TFDP1 may be the first example of a family of related transcription factors. DP-1alpha is a novel isoform of DP-1 that acts as a
TMPO-Tmpo	Thymopoietin. Data suggest that hypophosphorylated Rb is anchored in the nucleus by the interaction of pocket C with LAP2alpha (Tmpo)-lamin A/C complexes

Supplemental Table S2

Canonical E2F and AHR binding sites in the -5000 to +1 bp promoter regions of cell cycle-regulated genes

Gene Name	Accession Number		Mouse			Human	
	Mouse	Human	Binding Site	Position	Sequence	Position	Sequence
Dnmt1	NM_010066	NM_001379	AHR	-3554	CACGCC	-2363	CACGCC
				-2961	GGCGTG	-1886	GGCGTG
				-1514	TGCGTG	-1133	GGCGTG
E2F				-3065	TTTGGGGC	-2980	TTTGACAC
				+16	TTCCGCGC	+179	TTCCGCGC
Apaf1	NM_009684	NM_013229	AHR	-1985	CATGCA	-2813	CAAGCA
				-207	CGCGCA	-309	CGCGCA
E2F				-467	TTTCCTGC	-681	CTTCCCGC
				-424	TTGGGCC	-635	TTGGGCC
				-208	GCGCGCAG	-310	GCGCGCAG
Tfdp1	NM_009361	NM_007111	AHR	-221	CACGCG	-230	CACGCG
				-215	CACGCG	-224	CACGCG
				-39	CACGCG	-34	CACGCG
E2F				-161	GCGGGAGA	-153	GCGGGAGA
				-121	GCGCCGAA	-116	GCGCCGAA
				-112	GCGCGAAA	-107	GCGCGAAA
Cdt1	NM_026014	NM_030928	AHR	-2804	CGCGTG	-2197	CGCGTG
				-241	CACGCC	-161	CACGCC
				-268	CACGCG	-220	CACGCG
				-478	TGCGTG	-406	AGCGTG
E2F				-1293	GCTGCAAA	-1193	TTTCTCGC
				-323	GCGCCAAG	-201	GCGCTAAA
				-15	CCGCGAAA	-16	TTTGGCGG
Cdca7	NM_025866	NM_031942	AHR	-249	CGCGCA	-202	CGCGCA
			E2F	-270	TTTCGCGC	-224	TTTCGCGC
				-60	GCGGGAAA	-13	GCGGGAAA
Cks1	NM_016904	NM_001826	AHR	-1587	CACGAG	-1972	CACGCC
			E2F	-4717	CTTCCCAC	-4586	CCGCCACC
				-3046	AAGCCAAA	-3190	ATGCCAAA
				-2957	TTTAGCAT	-3125	TTTTTCAC
Ezh2	NM_007971	NM_004456	AHR	-172	CACGCG	-152	CACGCG
				-61	CGCTTG	-22	CGCTTG
E2F				-394	ATTCCC GC	-393	GTTCCC GC
				-390	CCGCCAAG	-389	CCGCCAAG
				-361	GTTCCC GC	-349	GTTCCC GC
Nasp	NM_016777	NM_172164	AHR	-133	CAAGCG	-551	CAAGCG
			E2F	-593	TTTCCAGC	-1458	TTTCACTC
				-130	GCGCGATA	-549	GCGCGGTA
Hmgn1	NM_008251	NM_004965	AHR	-297	CACGTG	-1196	TGCCTG
				-274	CGCGCA	-225	CCC GTG
E2F				-275	GCGCGCAG	-1779	GAGCAAAA
				-249	GCTTCAAA	-1690	CTGCCAAA
Mcm3	NM_008563	NM_002388	AHR	-4349	CACGCT	-3865	CACGCC
				-3865	GGCGTG	-3478	GGCGTG
E2F				-14	TTTGGCGC	-132	TTTCCC GC
				-10	GCGCCAAG	-108	GCGGAAAA
Pltp	NM_011125	NM_006227	AHR	-89	GGCTTG	-175	GGCTTG
			E2F	-19	GCCCCCAA	-94	GCCCCCAA
Cdca7-like	BC006933	NM_018719	E2F	-1768	CTGAGAAA	-1722	CAGCCAAA
				-154	GCTACACA	-257	GCTCCACT

Supplemental Table S3. PCR primer sets to amplify discrete domains of the mouse *Apaf1* promoter

RefSeq	GeneID and coordinates	Forward primer	Sequence	Tm	Reverse Primer	Sequence	Tm	Position (Relative to TSS)	Amplicon size
NM_009684	11783:-:90641224:90641573	For90641224	CAGCGGTGTTTGAGTGCTC	60.6	Rev90641224	ACACCCCTCTCACACCCTTC	61.4	22	100
Gene name	11783:-:90641574:90641923	For90641574	TCTTTCGGCTCTTCACTTCG	60.6	Rev90641574	CCCTCCAAGCCATCCTG	61.6	-328	69
Apaf1	11783:-:90641924:90642273	For90641924	GCAAACCTTGAGCGTGCACT	60	Rev90641924	CTCCTGTCGCTGCCCTCTAA	62.9	-678	93
Location	11783:-:90642274:90642623	For90642274	GCATTTATCGCTCAGCAACA	60	Rev90642274	GCTTTGCGGATGAGTTTGCT	62.7	-1028	100
10 48.0 cM	11783:-:90642624:90642973	For90642624	TTTCAAAGCTACAAATGTTGAG	55	Rev90642624	GTATGACACATACAACCCAGCT	56.6	-1378	97
	11783:-:90642974:90643323	For90642974	CTCAAGGACTCAGGGTGCA	58.8	Rev90642974	TGGATATCCTCCAGGGTAGAG	58.1	-1728	80
	11783:-:90643324:90643673	For90643324	ACTCAGTAATATCTTTCCCAA	52.5	Rev90643324	TGTGTTGGATTTGCTGTTTT	56.7	-2078	108
	11783:-:90643674:90644023	For90643674	AGTGGATTATGAGGCTTTGTCT	57	Rev90643674	CACCAGGGCTTAATACAAGTGG	60.8	-2428	83
	11783:-:90644024:90644373	For90644024	CACTTTGGAGAGACAAAGCTCA	59.7	Rev90644024	TTGTGCTTCATCTTAGGGATT	57.9	-2778	110
	11783:-:90644374:90644723	For90644374	AAGACAACAATGGAACAGTCTT	41.5	Rev90644374	ATATATTTGGAGTTATTTAA	41.5	-3128	98
	11783:-:90644724:90645073	For90644724	ACATATTTTGGAGTAAATAAG	55.5	Rev90644724	TGCAGGTTTAGAAGGGAGGC	61.6	-3478	89
	11783:-:90645074:90645423	For90645074	TTGTTAAAAGAGCTTTTGAGGA	56.1	Rev90645074	TACAGAGGGCAAGCACTTTC	58.1	-3828	63
	11783:-:90645424:90645773	For90645424	AAGATTATAGAGGGGGCTGG	58.6	Rev90645424	TCAGAGCTTTCTCTCATCCA	59.3	-4178	88
	11783:-:90645774:90646123	For90645774	CAGGAAGCAGTTATGGTCCA	58.7	Rev90645774	CAGTGTTCCCTTCAACATTAGG	58.6	-4528	102
	11783:-:90646124:90646473	For90646124	GGGAGCCCATTTGGTAACAA	62	Rev90646124	CCTGTGTATAGTGAAGAAGGC	58.9	-4878	108

Supplemental Table S4. Gene-specific primer sets for real-time PCR analysis of relative mRNA expression levels

Gene Name	Accession Number	Forward Primer (5'-3')	Reverse Primer (5'-3')	Product Size
β -actin	M12481	catccgtaaagacctctatgcc	acgcagctcagtaacagtcc	287
Cyp1a1	NM_009992	gtgtctggttactttgacaagtgg	aacatggacatgcaaggaca	199
Apaf1	NM_009684	tcagcaaacgagaggaaaag	cataggggggagaagtccacag	235
Cdca7	NM_025866	aagaggaggaggaagaggag	ggtcggattatatgcggaag	142
Cdca7-like	NM_146040	tgcttccgttccaaatacttc	cctcctcttcatcatcttcttc	202
Cks1	NM_016904	caaatacgacgacgaggag	tcagaaagatggcaggag	277
Dnmt1	NM_010066	ctgaccgcttctacttcttc	tccctttccccttcccttcc	111
Ezh2	NM_007971	aagacaccacctaaacgcc	accactccactccacattc	273
Hmgn1	NM_008251	agataaaaggaagaggggag	ttaaaaaatgggatgaggtggg	289
Mcm3	NM_008563	gcaggaagaatgaaaagagg	aggaagcaggaagtgagag	199
Nasp	NM_016777	atgctcctgctccttctacc	cccaacactccattctccattc	252
p73(common)	NM_011642	tcacagagacagagagccac	atgagcgcacttcccttcag	152
TAp73	NM_011642	tcttctcctcctccacctt	ccttgcaggtggaagacat	143
Pltp	NM_011125	agaccatcaccatcccagac	gccccatcatataagaaccag	203
Ris2 (Cdt1)	NM_026014	tccttgctggttcttctcatc	gccatccaacataccctactc	184
Tfdp1	NM_009361	ttagaggtggagaggcagag	ttgacaatgatgaagggaag	182