

Supporting Information

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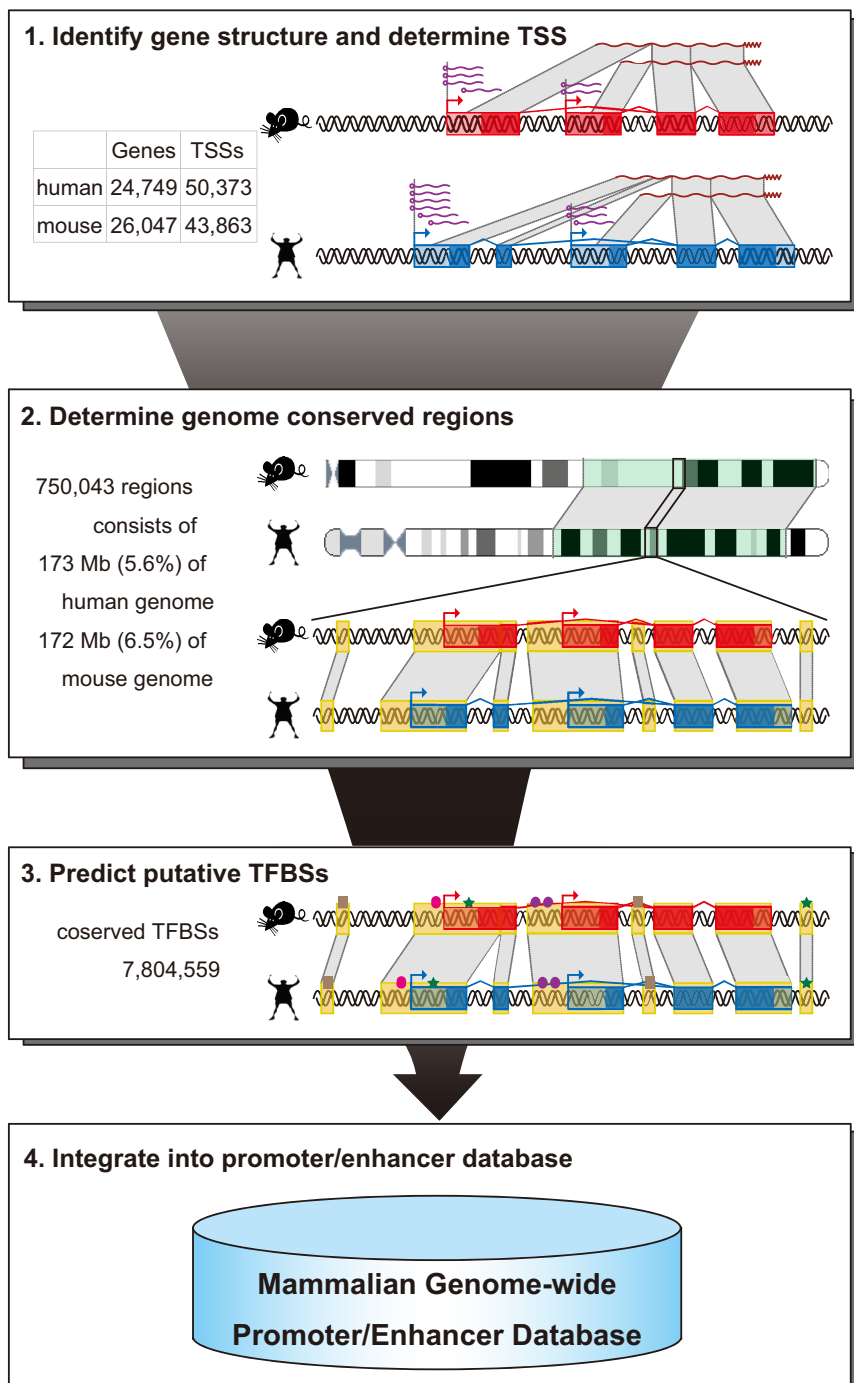


Fig. S1. Construction of the mammalian promoter/enhancer database. Mammalian full-length cDNA and EST sequences were mapped onto mammalian genome sequences to identify 24,749 human genes with 50,373 TSSs and 26,047 mouse genes with 43,863 TSSs. These mammalian genes were then compared to identify 16,268 human-mouse orthologs (65.7% of human genes and 62.5% of mouse genes). The positional information of adjacent orthologs was used to determine 434 human-mouse syntenic regions, which contained 750,043 human-mouse conserved genomic regions. The 862 consensus TFBSs from TRANSFAC were then mapped on these conserved genomic regions to identify the 7,804,559 sites conserved between human and mouse in non-coding regions. Human-rat comparisons were performed using the same procedure. Finally, visualization of putative promoter/enhancer and TFBSs data, and curation of current genes were integrated into a free and publicly accessible website (Mammalian Promoter/Enhancer Database; <http://promoter.cdb.riken.jp/>).

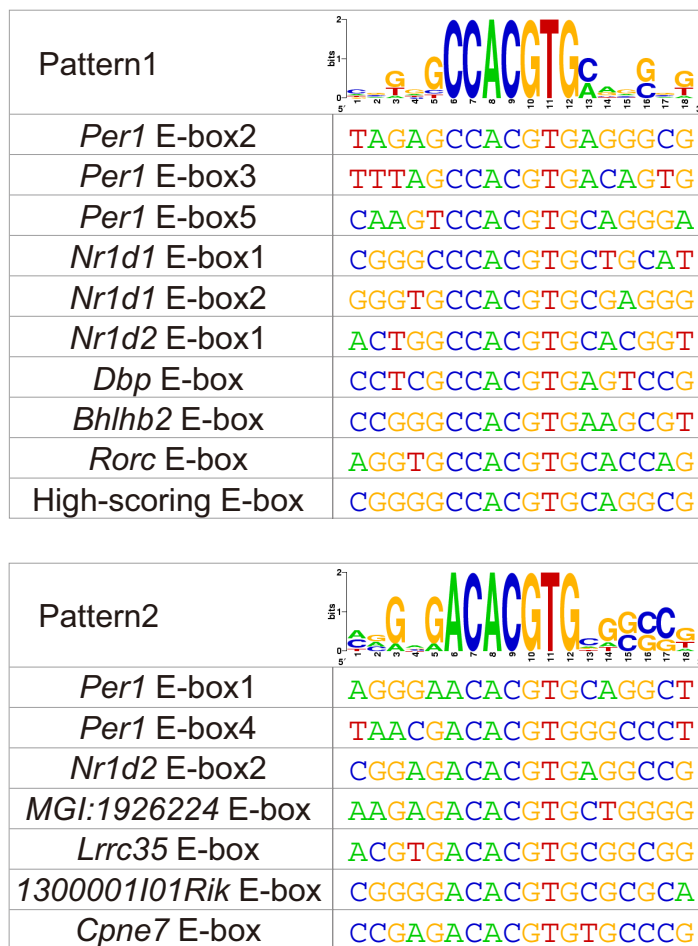


Fig. S4. Two patterns revealed in the adjacent sequence of high-amplitude E-boxes. High-amplitude E-box sequences classified into two patterns were shown. Information contents of the relative frequency of each nucleic acid at the position of the pattern were shown by sequence logos.

Other Supporting Information Files

[SI Appendix](#)

Table S1. Functional RREs from known clock-controlled genes used in this study

Gene	GeneID	Element	Organism	chr	Start	End	Sequence	Evidence	Affymetrix Probe ID
<i>Elov15</i>	68801	RRE	Mouse	9	78317303	78317325	Mouse TCTTGTAAATGGGTCAATGGCGT 	ref. 1, ref. 2	93496_at
			Human	6	53273932	53273910	Human TTGTGCAAAGTAGGTCAATGCCGT		
<i>BC004004</i>	80748	RRE	Mouse	17	27851244	27851266	Mouse AGTCTGAATATAGGTCAATGTGA 	ref. 1, ref. 2	95517_i_at
			Human	6	36927126	36927148	Human TTTGGGAATCTAGGTCAATTCTGA		
<i>Macf1</i>	11426	RRE	Mouse	4	121994185	121994207	Mouse CCCTGAAAAGTAGGTCAATGCCCT 	ref. 2	98402_at
			Human	1	39277738	39277716	Human CCCTGAAAAGTAGGTCAATGCCCT		
<i>Atf5</i>	107503	RRE	Mouse	7	32213618	32213640	Mouse CAAGTAAACTGGGTCAATCGAAGG 	ref. 1, ref. 2	103006_at
			Human	19	55118372	55118350	Human GGAGGGTAACTGGGTCAATCGCAGG		
<i>Col4a1</i>	12826	RRE1	Mouse	8	11309356	11309378	Mouse GGCAGGAAAATGGGTCAATGCCTG 	ref. 1, ref. 2	101093_at
			Human	13	109748860	109748882	Human AGCAGGAAAATGGGTCAATGATG		
<i>Col4a1</i>	12826	RRE2	Mouse	8	11337102	11337124	Mouse TCAGCCAAACTAGGTCAAAACCT 	ref. 1, ref. 2	101093_at
			Human	13	109781193	109781215	Human TCAGCCAAAATAGGTCAAAACAG		
<i>D19Ert721e</i>	225896	RRE	Mouse	19	7972840	7972862	Mouse AGGAAGAAAATAGGTCAATGATG 	ref. 1, ref. 2	97240_g_at, 97241_at
			Human	11	62201916	62201894	Human AAGAAGAAATAGGTCAATGATC		
References									
1. Ueda HR, <i>et al.</i> (2002) A transcription factor response element for gene expression during circadian night. <i>Nature</i> 418:534-539.									
2. Panda S, <i>et al.</i> (2002) Coordinated transcription of key pathways in the mouse by the circadian clock. <i>Cell</i> 109:307-320.									

Element information on the gene symbol ('Gene'), NCBI GeneID ('GeneID'), element type ('Element'), the position ('Start' and 'End') on a chromosome ('chr') of mouse and human ('Organism') and the sequence alignment of human-mouse RREs ('Sequence') are indicated. Experimental evidence on clock-controlled genes ('Evidence') and Affymetrix probe ID detecting circadian expression of the genes ('Affymetrix Probe ID') are also indicated. The canonical consensus sequences for the RRE ([A/T]A[A/T]NT[A/G]GGTCA) is indicated in red. The function of these mouse RREs sequences in the context of a luciferase reporter was experimentally determined in **Fig. S2**.

Table S2. Functional clock-controlled elements used as train HMMs

Gene	GeneID	Element	Organism	chr	Start	End	Score of HMMER	Sequence	Evidence
<i>Per1</i>	18626	E-box 1	Mouse	11	68707450	68707433	15.39	AGGGAA CACGT GCAGGCT	ref. 1
<i>Per1</i>	18626	E-box 2	Mouse	11	68707634	68707617	17.87	TAGAGCC CACGT GAGGGCG	ref. 1
<i>Per1</i>	18626	E-box 3	Mouse	11	68710224	68710241	11.48	TTTAGCC CACGT GACAGTG	ref. 1
<i>Per1</i>	18626	E-box 4	Mouse	11	68710970	68710987	12.10	TAACGA CACGT GGGCCCT	ref. 1
<i>Per1</i>	18626	E-box 5	Mouse	11	68711333	68711350	13.45	CAAGTC CACGT GCAGGGA	ref. 2
<i>Nr1d1</i>	217166	E-box 1	Mouse	11	98445288	98445271	14.71	CGGGCC CACGT GCTGCAT	ref. 2
<i>Nr1d1</i>	217166	E-box 2	Mouse	11	98445008	98444991	15.77	GGGTGC CACGT GCGAGGG	ref. 2
<i>Nr1d2</i>	353187	E-box 1	Mouse	14	14904545	14904528	16.38	ACTGGC CACGT GCACGGT	ref. 2
<i>Nr1d2</i>	353187	E-box 2	Mouse	14	14904442	14904425	17.71	CGGAGA CACGT GAGGCCG	ref. 2
<i>Dbp</i>	13170	E-box	Mouse	7	33110149	33110166	15.23	CCTCGC CACGT GAGTCCG	ref. 2
<i>Bhlhb2</i>	20893	E-box	Mouse	6	109049680	109049697	18.55	CCGGGC CACGT GAAGCGT	ref. 2
<i>Rorc</i>	19885	E-box	Mouse	3	94357502	94357519	16.45	AGGTGC CACGT GCACCAG	ref. 2
<i>Per1</i>	18626	D-box	Mouse	11	68711473	68711496	17.30	GCCTGGCAT TTATGCAA CCCGCCTC	ref. 2
<i>Per2</i>	18627	D-box	Mouse	1	91377818	91377795	16.48	TGTGCGTCT TTATGTAA AGAGAGCG	ref. 2
<i>Per3</i>	18628	D-box 1	Mouse	4	148930820	148930797	18.62	CCCGCGGT TTATGTAA GGTACTCG	ref. 2
<i>Per3</i>	18628	D-box 2	Mouse	4	148930773	148930750	16.10	GCCCGCGGT TTATGTAA CCCCGCC	ref. 2
<i>Nr1d1</i>	217166	D-box	Mouse	11	98445195	98445218	19.41	GGAGCTCAT TTATGTAA CGAGGCCG	ref. 2

<i>Nr1d2</i>	353187	D-box	Mouse	14	14904456	14904479	17.41	AGCTCGCATTTATGTAA TGCTGCGT	ref. 2
<i>Rora</i>	19883	D-box 1	Mouse	9	69195245	69195222	11.78	AAGCTGTTTATGTAA TAGCTTTG	ref. 2
<i>Rora</i>	19883	D-box 2	Mouse	9	68926158	68926135	16.84	CACTGCTGTTATGTAA CCAAACGT	ref. 2
<i>Rora</i>	19883	D-box 3	Mouse	9	68894279	68894302	17.42	CGAGCGGGTTATGTAA CAGGGTTA	ref. 2
<i>Rorb</i>	225998	D-box	Mouse	19	18304970	18304993	14.84	TCCAGTTC TATGTAA TGAATATA	ref. 2
<i>Arntl</i>	11865	RRE	Mouse	7	100478066	100478088	19.72	AGGCAGAAAGTAGGTCA GGGACG	ref. 2
<i>Npas2</i>	18143	RRE	Mouse	1	39516271	39516293	14.66	GAAAAATATGTAGGTCA GTGGAA	ref. 2
<i>Nfil3</i>	114519	RRE 1	Rat	17	18094293	18094271	15.64	AGTGTGTTAGTAGGTCA GTTCCG	ref. 2
<i>Nfil3</i>	18030	RRE 2	Mouse	13	52011542	52011520	21.79	ACAGAAAAGTGGGTCA GTTTGT	ref. 2
<i>Clock</i>	12753	RRE	Mouse	5	75037420	75037442	15.91	AGGAATAAAGTGGGTCA CAAGGC	ref. 2
<i>Cry1</i>	12952	RRE 1	Mouse	10	84829678	84829656	20.81	GACTAGAAAGTAGGTCA TTGTGA	ref. 2
<i>Cry1</i>	12952	RRE 2	Mouse	10	84829601	84829623	16.47	GTTTCTAAAGTAGGTCA TCGCTA	ref. 2
<i>Rorc</i>	19885	RRE	Mouse	3	94352279	94352301	19.40	GGAATAAAGTGGGTCA TCTTGT	ref. 2
<i>Elov15</i>	68801	RRE	Mouse	9	78317303	78317325	17.19	TCTTGTAAATTGGGTCA TGGCGT	This study
<i>BC004004</i>	80748	RRE	Mouse	17	27851266	27851244	17.53	AGTCTGAATATAGGTCA ATGTGA	This study
<i>Macf1</i>	11426	RRE 2	Mouse	4	121994185	121994207	20.05	CCCTGAAAAGTAGGTCA GTGCCT	This study
<i>Atf5</i>	107503	RRE	Mouse	7	32213618	32213640	14.65	CAAGTAAAAGTGGGTCA CGAAGG	This study
<i>Col4a1</i>	12826	RRE 1	Mouse	8	11309378	11309356	19.92	GGCAGGAAAATGGGTCA GTGCTG	This study
<i>Col4a1</i>	12826	RRE 2	Mouse	8	11337124	11337102	14.10	TCAGCCAAACTAGGTCA AAAACCT	This study
<i>D19Erd721e</i>	225896	RRE	Mouse	19	7972862	7972840	18.30	AGGAAGAAAATAGGTCA GACATG	This study

<p>References</p> <ol style="list-style-type: none"> Hida A, <i>et al.</i> (2000) The human and mouse Period1 genes: five well-conserved E-boxes additively contribute to the enhancement of mPer1 transcription. <i>Genomics</i> 65:224-233. Ueda HR, <i>et al.</i> (2005) System-level identification of transcriptional circuits underlying mammalian circadian clocks. <i>Nat Genet</i> 37:187-192. 						

Element information on the gene symbol ('Gene'), NCBI GeneID ('GeneID'), element type ('Element'), the position ('Start' and 'End') on a chromosome ('chr') of mouse and rat ('Organism') and the sequence ('Sequence') are indicated. Experimental evidence on functional clock-controlled elements ('Evidence') and match score of HMMER search performed using the constructed HMMs ('Score of HMMER') is also indicated. Canonical consensus sequences for the E-box (CACGTG), D-box (TTATG[T/C]AA) and RRE ([A/T]A[A/T]NT[A/G]GGTCA) are indicated in red. Information contents of the relative frequency of each nucleic acid at the position of the pattern for each element were shown by sequence logos.

9	<i>Jag2</i>	16450	E-box	0.024	Mouse	12	107682267	107682284	15.64	Mouse	CCTGGCCACGTGGGCGCG
					Human	14	104704954	104704971	15.64	Human	CCTGGCCACGTGGGCGCG
10	<i>Rps19</i>	20085	E-box	0.024	Mouse	7	13623927	13623944	15.62	Mouse	CGCGGCCACGTGCGAGCG
					Human	19	47056319	47056336	15.62	Human	CGCGGCCACGTGCGAGCG
-	<i>Per3</i>	18628	D-box	0	Mouse	4	148930797	148930820	18.62	Mouse	CCCGCGCGTTATGTAAGGTACTCG
					Human	1	7778455	7778432	21.11	Human	CCCGCGCGTTATGTAACGCGCCCC
1	<i>Gria2</i>	14800	D-box	0.051	Mouse	3	81194005	81193982	17.31	Mouse	CGGGGCTGTTACATAATGCCACC
					Human	4	158501155	158501178	17.63	Human	CGGGGCTGTTACATAACGCCACC
2	<i>Spry4</i>	24066	D-box	0.122	Mouse	18	39043332	39043309	16.38	Mouse	AGGTGCGTTTACATAACGCCGGGC
					Human	5	141683774	141683751	16.80	Human	AGGTGCGTTTACATAACACCAGGC
3	<i>Etv4</i>	18612	D-box	0.181	Mouse	11	101455967	101455990	17.09	Mouse	CACACGTC TTATGTAACCCAGTTC
					Human	17	38978809	38978832	15.20	Human	ACACGTC TTATGTAACCGAGCCC
4	<i>Pogz</i>	229584	D-box	0.181	Mouse	3	94832639	94832662	16.89	Mouse	CCCCTGTGTTATGTAATCCCCTC
					Human	1	148244037	148244014	15.15	Human	CCCTTGTGTTATGTAATCTCTGCT
5	<i>Fmn2</i>	54418	D-box	0.209	Mouse	1	174628879	174628902	14.89	Mouse	ACCGCGCATTTATGCAAAGCGGCAG
					Human	1	236581260	236581283	16.89	Human	GCCGCGCATTTATGCAAAGCGGCGG
6	<i>Plcb1</i>	18795	D-box	0.325	Mouse	2	134535724	134535747	15.25	Mouse	GGGGCGCGTTATGCAATGGGGCGC
					Human	20	8061473	8061496	15.25	Human	GGGGCGCGTTATGCAATGGGGCGCA
7	<i>Irf2bp1</i>	272359	D-box	0.363	Mouse	7	10526613	10526636	16.21	Mouse	CCCGCGCGTTATGTAACCTTCCCT
					Human	19	51081280	51081257	13.67	Human	CAGGCGTGTTATGTAACCTTCCCT
8	<i>Slc22a20</i>	381203	D-box	0.363	Mouse	19	5775101	5775078	14.95	Mouse	CTGCCTTTTACATAAGGCCTGGG
					Human	11	64737873	64737896	14.81	Human	CGGCCTCTTACATAAAGCCGGGG
9	<i>Trim8</i>	93679	D-box	0.387	Mouse	19	45844359	45844336	14.62	Mouse	GACACTCATTACATAAACAGCAGC
										Human	GACACTCATTACATAAACAGCAGC

					Human	10	104395331	104395308	14.62		
10	<i>Tspan7</i>	21912	D-box	0.388	Mouse	X	8817583	8817560	13.68	Mouse	AGAGGGTCTTACATAAGCCAGGGG
					Human	X	38177725	38177702	15.27	Human	AGAGGGTCTTACATAAGCCAGGGG
-	<i>Arntl</i>	11865	RRE	0.066	Mouse	7	100478066	100478088	20.38	Mouse	AGGCAGAAAGTAGGTCAGGGACG
					Human	11	13255933	13255955	20.38	Human	AGGCAGAAAGTAGGTCAGGGACG
1	<i>Atp1b2</i>	11932	RRE	0.066	Mouse	11	69217609	69217631	20.61	Mouse	GCGGAGAAAGTAGGTCAGTCCG
					Human	17	7495878	7495856	19.61	Human	GCGGAGAAAGTAGGTCAGTCCG
2	<i>Spsb3</i>	79043	RRE	0.083	Mouse	17	23484948	23484970	18.81	Mouse	GAACGGAAAGTGGGTCAGCGCCG
					Human	16	1772556	1772534	19.64	Human	GGGCGGAAAGTGGGTCAGGGCCG
3	<i>Zfp318</i>	57908	RRE	0.104	Mouse	17	44564473	44564495	19.35	Mouse	GAGAGAAAGTGGGTCATTGAGA
					Human	6	43417992	43417970	18.25	Human	AAGAGAAAGTGGGTCATTGAGC
4	<i>Mgea5</i>	76055	RRE	0.112	Mouse	19	45123691	45123713	17.41	Mouse	ATCTCCAAAGTAGGTCAGTGTCT
					Human	10	103568543	103568565	20.12	Human	CCATAGAAAGTAGGTCAGTTCTT
5	<i>Lasp1</i>	16796	RRE	0.139	Mouse	11	97476169	97476191	16.54	Mouse	TTCGTGAAAGTGGGTCATGGTCT
					Human	17	34284865	34284887	19.34	Human	TGTGAGAAAGTGGGTCATGGTCT
6	<i>Ryr1</i>	20190	RRE	0.148	Mouse	7	18096374	18096352	17.94	Mouse	AGGCTCTGACCTATTTAAATTCT
					Human	19	43616749	43616771	17.45	Human	AGACTCTGACCTATTTAAATTCT
7	<i>Adam12</i>	11489	RRE	0.148	Mouse	7	121856769	121856791	15.44	Mouse	TACTTAAAGTAGGTCAGAAAAA
					Human	10	128077170	128077148	19.88	Human	AACTTGAAAGTAGGTCAGTAAGA
8	<i>A730009L09Rik</i>	402727	RRE	0.168	Mouse	16	84900535	84900513	16.17	Mouse	TCTTAA TGACCCAATTTCTAAAT
					Human	21	25632353	25632331	18.49	Human	TCTTAA TGACCCAATTTCTAAAT
9	<i>Myo1b</i>	17912	RRE	0.179	Mouse	1	52270010	52269988	18.02	Mouse	TGGTGCTGACCACTTTCTCTTT
										Human	GGATATGACCTACTTTCCCTT

11	<i>C330011F03</i>	328837	low-score E-box	--	Mouse	17	49541248	49541231	3.08	Mouse	GTTTCC CACGTG TTTGGC
					Human	3	17954468	17954451	3.08	Human	GTTTCC CACGTG TTTGGC
12	<i>Prkce</i>	18754	low-score E-box	-	Mouse	17	85008129	85008146	3.20	Mouse	ATATAA CACGTG CTAAAA
					Human	2	46068028	46068045	3.20	Human	ATATAA CACGTG CTAAAA
13	<i>Map3k9</i>	338372	low-score E-box	-	Mouse	12	77032273	77032290	2.44	Mouse	GACAAA CACGTG TGCGTC
					Human	14	70276648	70276665	4.03	Human	GACAAA CACGTG TATGCA
14	<i>Zfx1b</i>	24136	low-score E-box	-	Mouse	2	45057246	45057229	3.29	Mouse	GTATTA CACGTG AAAAGC
					Human	2	145095987	145095970	3.29	Human	GTATTA CACGTG AAAAGC
15	<i>Ppfibp2</i>	19024	low-score E-box	-	Mouse	7	94860226	94860243	4.93	Mouse	GTTTCC CACGTG TGTCCC
					Human	11	7489362	7489379	1.76	Human	GTTTCC CACGTG TTTGTC

The element information including the gene symbol ('Gene'), NCBI GeneID ('GeneID'), element type ('Element'), the position ('Start' and 'End') on a chromosome ('chr') of mouse and human ('Organism'), the sequence alignments of human and mouse ('Sequence') and the match score of HMMER search ('Score of HMMER') are indicated. The estimated accuracy of the HMM-based prediction is indicated as false discovery rate ('FDR'). The mouse elements were used for experimental validation. The element type 'low-score E-box' indicate evolutionary conserved 15 most low-score E-boxes with the core consensus sequence 'CACGTG' in non-coding regions. The function of these element sequences in the context of a luciferase reporter was experimentally determined in **SI Fig. S3**.

Table S4. Similarity between DNA binding domains of DNA binding activators and repressors

Element	Gene	Alignment	Accession	Domain position	Domain name	Type	Homology
E-box	<i>Arntl</i>	-KNAREAHSQIEKRRRDKMNSFIDELASLVPTCNAM--SRKLDKLTVLRMAVQHMKTLR----	NP_031515.1	71-126	HLH	Activator	Identity 30%, Similarity 57% to <i>Bhlhb2</i>
	<i>Clock</i>	DKAKRVSRNKSEKKRRDQFNVLIKELGSMPLGN-----ARKMDKSTVLQKSIDFLRKHKE---	NP_031741.1	32-86		Activator	Identity 22%, Similarity 55% to <i>Bhlhb2</i>
	<i>Bhlhb2</i>	KETYKLPRLIEKKRRDRINECIAQLKDLLPEHLKLTTLGHLEKAVVLELTLKHVKALTNLID	NP_035628.1	50-112		Repressor	-
		: : .: **:***::* * :* .::* ::* .** . ::::					
D-box	<i>Dbp</i>	KDEKYWSRRYKNNEAAKRSRDARRLKENQISVRAAFLEKENALLRQEVVAVRQE	NP_058670.1	254-307	bZIP_2	Activator	Identity 44%, Similarity 69% to <i>Nfil3</i>
	<i>Nfil3</i>	KDAMYWEKRRKNNEAAKRSREKRRLNDLVLENKLIALGEENATLKAELLSLK--	NP_059069.1	72-123		Repressor	-
		** **_* *****:***:: :. : * :*** * : *:::					
RRRE	<i>Rora</i>	IPCKICGDKSSGIHYGVITCEGCKGFFRSQQSNATYS-CPRQKNCLIDRTSRNRCQHCRLLQKCLAVGMSRDVAVKFG	NP_038674.1	71-146	zf-C4	Activator	Identity 65%, Similarity 81% to <i>Nr1d1</i>
	<i>Nr1d1</i>	-LCKVCGDVASGFHYGVHACEGCKGFFRSIQQNIQYKRCLKNENCSIVRINRNRCQQCRFKKCLSVGMSRDVAVRFG	NP_663409.2	132-207		Repressor	
		::* :**::*** :***** * . * * . * :::** * * .*****:** :::***:*****:**					

The gene symbol ('Gene') of DNA binding activators and repressors, target element ('Element'), alignment ('Alignment') of DNA binding domain, accession No. ('Accession') of protein sequence, position of DNA binding domain ('Domain position') at the protein sequence and name of the DNA binding domain ('Domain name') are indicated. Homology ('Homology') between DNA binding domains of DNA binding activators and repressors is also indicated.