Supplemental Material

Table S1. Genomic coordinates of HREs relative to the TSS

HRE	Sequence	Distance from TSS
1 1)	CCAGGTCC	- 350 / - 357
2	GTGTG**TGC**	- 367 / - 374
3	GTGTG**TGC**	- 823 / - 830
4 + 5 2)	GC**ACGTGC**	- 846 / - 853
6	AGACA**TGC**	- 883 / - 890
7	**GCA**CCTGG	- 1091 / - 1098
8	AC**ACG**CCT	- 1245 / - 1252
9	**GCA**GGTGG	- 1262 / - 1269
10	CCATG**TGC**	- 1393 / - 1400
11	**GCA**CATGG	- 1452 / - 1459
12	**GCA**CTTCT	- 1459 / - 1466
13	**GCA**CACAC	- 1670 / - 1677
14	**GCA**TGTCTG	- 1691 / - 1699
15	**GCA**GGTCC	- 1759 / - 1766
16	CCACC**TGC**	- 1778 / - 1785
17	**GCA**CCTCC	- 1838 / - 1845
18 1)	GGAAGTGG	- 2523 / - 2530
19	**GCA**AGTAT	- 2838 / - 2845
20	GTGCGTGC	- 2998 / - 3005
21 1)	GGACATGG	- 3092 / - 3099
22	**GCA**AGTGG	- 3191 / - 3198
23 1)	GGACCTGG	- 3314 / - 3321
24	CCAGG**TGC**	- 3339 / - 3346
25	GGACG**TGC**	- 3425 / - 3432
26	**GCA**CATCT	- 3517 / - 3524
27	AC**ACG**CCC	- 3551 / - 3558
28	**GCA**CGTAG	- 3563 / - 3570
29	GGATG**TGC**	- 3615 / - 3622

Bold characters indicate the conserved core of the HRE. Underlined HREs were identified as necessary to induce DEPP under hypoxic conditions. 1) Identified by JASPAR database as HRE but lacking the CGT (sense) or ACG (antisense) core. 2) HRE 4+5 are found at the same location, but on opposite strands

Table S2. Primer used to amplify human DEPP promoter

Forward (5′-3′)	Reverse (5′-3′)	Lenght
1) acgg GGTACC GTTGAGGAGCCCCTCGATGATCA	1) acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	3759 bp

1) Extra nucleotides shown in small letters, cloning restriction sites underlined.

Table S3. Sequence of the 3759 kb regulatory region (5′ → 3′)

GTTGAGGAGCCCCTCGATGATCAGAGTCCCTTCTTCCTGTGGGGGTCCACACATCAGCCCTTCCC
CCAGAGCAGCTGCCTACCTTCCCTGTGCCCCCTAGGGATGGGATGCTCTGAACACTCAGGCCTT
GCACATCCCTCCTCCTGAGTGGCCCCATCCCCTCAGGAAGGACCATCAGCCACTACGTGCCCTG
GGGCGTGTGACCAGGCCCTGTGGGAGGGAGCCTGAGATGTGCTCAGCTCATGCCTGGCCAGGG
GCACAGCGCAGAACACAGTGGCTGAGTCAGGTGTCCCACAGGAAGCCAGCTGCTGGCCGGCA
GGCACGTCCACACCGCGGTGAAGAAGTGGTTCCAGGGACGCACAGCCTGTCTGCTCATGCCAA
GCAGGGGACCTCTCTGCCCACACTGCACCTGGGAGGGGGTCCTGCGCCACCAGGTCCTATGGC
CACCAGGCCCGGCAGGGTCCCACACCCACCAGAGCAGAAGTGGGCACTCTCTGTCCTAGCTGT
GTCTCAGCCTCACCCTTCTCCCGGTGCCTTCCAACAGCAGCAGCGTCCACTTGCCAGGGCTGAC
AAAGGGTCTTGCTTTTCTCACCACTGCTTAGACATCACTAGCCCTATATCCCATACCAGAATTTC
TACAACAGCCTTCATCCCATGTCCCCAACCTCCCTCGGTTTCCCTAGGTCTGCAGGTGACATGGC
TTCTCTCCTGCTGCCAACCTGGGGCCCTAATCAACAGAGTCCTCTGCACGCACCTTGCTAGTAGT
GCTGGTTGGCACCCCTTGGGCCCTTGATTCAGTGCCTCTGACCTATTCCAGGCCTCTGTCTCTGC
GAGACCACCCCAGGCCTCTGTGCCAATCCCGGTCACTCTGTGTGTAAGCCTGGCCAAGCTGAGT
CATTTGCCAGAATACTTGCCAGCAACCTCGGCTGCCCTCTACCCAGAGCCGCAGTCTCGAAACT
ACACACTCCTAATGTGCTCTGACACTAGTCTTCCCACAATTAACTTTGAATATCATTCTCTCATT
GCCATCTCAACCAACATTTAATTTTATTATTTATGTTTTATTGTGATAAGGACATTTAACATAAG
AACTACCCTCTAAACAAACTGTTCAGTGCACAATACTGTATTGTTCACTGTAGGCACAACGTTG
TCCAGCCCATATCCAGGACTTACTCATCTTGCATAGCTGAAACATTATATCAGCTGCACAGCAA
CTCTCCACTTCCTCCTCCCCTGCCCCAGTCCCTGCAACCACCATTTTCACTCTCTGCCTCTATGAG
CCTATTTTAGATTCCTTATATAAGGGAATCATGCAGTATTTCTGACCCATATTTTAGATTCACAA
ATCCCATTTCTCTCTCCTCGTTGGCACTAAAAGCCCTGTGAGAACAGGGACGCCATGGAAACTT
CTTTGTATCCCTGGCAGCACTCAGGAAGACCCTGCACAATGTGGATTTCATGGTAACTTAGAAA
TGGGGTTTCTAGGTTCAAACATCCTGCCATCCACAGAGAAAATAGTGTATCCAAAGGTTATCAA
ATATACACACAGCTTCCAGATATGACCTTGCACTATCTGCTAAAAAGGAAAACAAACAAGCAG
AAACCAGAGCTGTTTTTGATACTCACTGGTGCTCTACAAGCACAGATGTGTCACTGAGCTTCCT
ATGAAGGAGAGGCCAGCATGGATCTATGGAGTTCAAAGGTCTATGGGGGGTTCTGTTCTTGCCT
CTTGGTCTCGGGTGCCTCTCAGTGGAGAGAGCTTGTGGGGATGGCTCACTCATGGAGACCCACT
GCCCTCCAGCCCCACCCTGGACGCCAGGCAGAGGAAGATGGAGCAGACACAGCCCTGGCCAC
GAGGGGCTCGGGCTTGGACACAGAAGGAGATGCAATGGAGCTTCTTGGAGGAGGTGCTTGTGC
ACTGCACCCTGGAAGACGAGTGAAGGGGGACGGGGAGGAAAGCTGAGCAGGTGGCCCTGACC
TCAGGACCTGCCTGGACAAGGTCGGGGGCTTGGCTGTACTGGGGACAGGCTGGCTCTCCATGA
CTCAGGCCAGACATGCCTACACAGGTGATGTGTGTGCCCCCAACATAGCCGCCCACTGTTCACC
CTCCCCCAGCTTGGCCGCATCTGAATGGAGGGAAAGCCCCGTCAGCCAGCAGCGAATTCTCCG
CCTCCCTCCCTCTTTTGGTCTCTTGACTAATCTGCTCATTGCTAATAAATTCAAAGAAGAGCCAG
CGAACTAGACAAAGGGTCTACAAAAGATATAAGAGCTTGGGCAAGGTGAGAAGTGCCATGTG
CCACTGAAATCCTGGTCACTGTCTCAGGCACTCCCTGCCCCGATGCCTTTGTGCACATGGAGTTC
CCACCTAGAATTCAAGAACTTGGGACTGCCGGTCCCTCTTGCTTGCCTAGGGAGTCTGGGGTCT
GCCCAGTACTCAGAGCTCAGGCTTGGGCTAACTCTCAAGACTCCTCTTTCTCCCCCACCTGCAG
CACAGGCAGGCGTGTTCCAGGTGGGGCTGTGGCTGGGGCAGAGGATCTGTGGCCTGTCTGGGG
AGTGCAGGAGCTTCCCAGGGGCTGCCTCTCTCATCCTTGGCAGCCTCCTTTGCTGGCATGGTCAC
TCCTGGACAGATGCAGTGGCTTTCTAATGTTGCCCAGGTGCTCCTTGGCAGCCCCCCAGCCCCA
GCCCCAGCCCAGTCCCAGCAGCTGCAGCGATCCTTTGAAGCAGAAGCCAGACTGCAGTGCCCT
TGTTCAAACCCTGCAGTCTTCCCCTCCCTCCTAGAGGGAAACACAGCATCCACCCCAAGGTCCA
CTGACCCCCTCCTACATGGGCCAGTCTGCAGGCCCCTTGCTGTGCCCTGAGCATGTCTGTCCGGC
GCGCCCTCACCACAGGGGCTTTGCACGTGCTGCCCCTGCCACCTGGAATGTGCATTTTCCCATTT
TTTTCAGGTTTCTGCTCCAATATCTGCTCTTAGGGAAGACACCCCTGACCACTGTACCTGTGGCG
GCAGCCCACCACAGCATGCCACTGCGCTGCTTTCCTTCAGGCAGTTCTTGCTGTTGCCTGAATCA
CAGCACCCATTCATCTCTGGCTTGATCTCCTCCCTTACTAGAATATGAGCTCCAGGGGGCCACA
CCTTTGTCCGCTGCTACGTTTGCTGTGCTTAGTGCATTCACAGCACACACTAGCACCTCATATCT
GGTGAACAAGTAAACAAACAAATCCTCCGAAAGCACCCCATCTGGGGTGTAAGAAGACCAGG
GTCAGACCCCGCAGACCGCCCTTGGTCCCTTGCGAGCAGGGTGTGTCTCTCCTAGGAGCAGGCC

TAGGGACCCAGCCTCAGCTGCCTCCAGACTGGGGTCCTGTGCTGCTGATTTTTCATCAAAGTTGC
CAAGGACCTGGCCCAACTTCACAGGAGTCATGATGGGGTGGTGTAACACAGAGTGGGAAACA
AGCTTTGGGGCAGGGGTGGCCCTGGGGCTACCTGTGAGGGCCCAGTGGAACCCCTCCCTCTCCC
AGTGCCCCTACTTGACCAGCAGTGAACCCACCCCTTTCCTGCCCTGCAGCGTAAACATTCCCCA
GCCTCCTACAGGCAGAAAAACACCTCCAAGCTGGCAGCTGGGCCAGGCCCCGCCCACCAAGCT
GTTTTCCTAAGACAGCCTTCCGAGTAGGCTATTTTTGGCCCTCGTGACAGTGATTGATAGCTGCT
GGGAAGGTATAAAAGCAGCTTGCCTGCGAAGGTTCTTCA**C**1)ACTGCTCAGG

1) TSS is bold and underlined. TSS is base 0 and the first base after the TSS is +1

Table S4. Primers used to generate BLOCKs

BLOCK		Forward (5′-3′)	Reverse (5′-3′)	Lenght
BLOCK 1 1)		acgg GGTACC AGCTCAGGCTTGGGCTAACT	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	1318
BLOCK 2 1)		acgg GGTACC TCTGACACTAGTCTTCC	acgcc GCTAGC AGTTAGCCCAAGCCT	1485
BLOCK 3 1)		acgg GGTACC GTTGAGGAGCCCCTCGATGATCA	acgcc GCTAGC TGTGGGAAGACTAGTGTCAGAGC	997
BLOCK 1 + 2 1)		acgg GGTACC TCTGACACTAGTCTTCC	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	2783
BLOCK 2 + 3 1)		acgg GGTACC GTTGAGGAGCCCCTCGATGATCA	acgcc GCTAGC AGTTAGCCCAAGCCT	2461
BLOCK 1 + 3 1)	Step 1	acgg GAGCTC AGCTCAGGCTTGGGCTAACT	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	1318
	Step 2	acgg GGTACC GTTGAGGAGCCCCTCGATGATCA	acgcc GAGCTC TGTGGGAAGACTAGTGTCAGAGC	997

1) Extra nucleotides shown in small letters, cloning restriction sites underlined.

Table S5. Primers used for 5′ end truncations

HREs in fragments	Forward (5′-3′)	Reverse (5′-3′)	Lenght
1 - 26 1)	acgg GGTACC GAGGGAGCCTGAGATGTGCT	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	3543
1 - 25 1)	acgg GGTACC CCTGGCCAGGGGCACAGCGC	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	3514
1 - 24 1)	acgg GGTACC TGAAGAAGTGGTTCCAGGGA	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	3423
1 - 19 1)	acgg GGTACC TGCTAGTAGTGCTGGTTGGC	acgcc GCTAGC CCTGAGCAGTGTGAAGAACCTTC	3003

1) Extra nucleotides shown in small letters, cloning restriction sites underlined.

Table S6. Primers used for site directed mutagenesis

HRE		consensus	Forward (5′-3′)	Reverse (5′-3′)
29	wt	GGATG**TGC**	AGGAGGGATGcatAAGGCCTGAGTGTTCAGAG	CCTGAGTGGCCCCATCCC
	mut	GGATG**CAT**		
28	wt	CT**ACG**TGC	ATCAGCCACTgtaTGCCCTGGGGC	GGTCCTTCCTGAGGGGAT
	mut	CT**GTA**TGC		
27	wt	GGG**CGT**GT	TGCCCTGGGGtacGTGACCAGGC	CGTAGTGGCTGATGGTCC
	mut	GGG**TAC**GT		
26	wt	AGATG**TGC**	GCCTGAGATGcatTCAGCTCATGCC	TCCCTCCCACAGGGCCTG
	mut	AGATG**CAT**		
25	wt	GG**ACGTGC**	CGCGGTGTGGgtacatCTGCCGGCCA	GTGAAGAAGTGGTTCCAGG
	mut	GG**GTACAT**		
20	wt	GTGCG**TGC**	GCAAGGTGCGcatAGAGGACTCTG	TAGTAGTGCTGGTTGGCA
	mut	GTGCG**CAT**		