

A

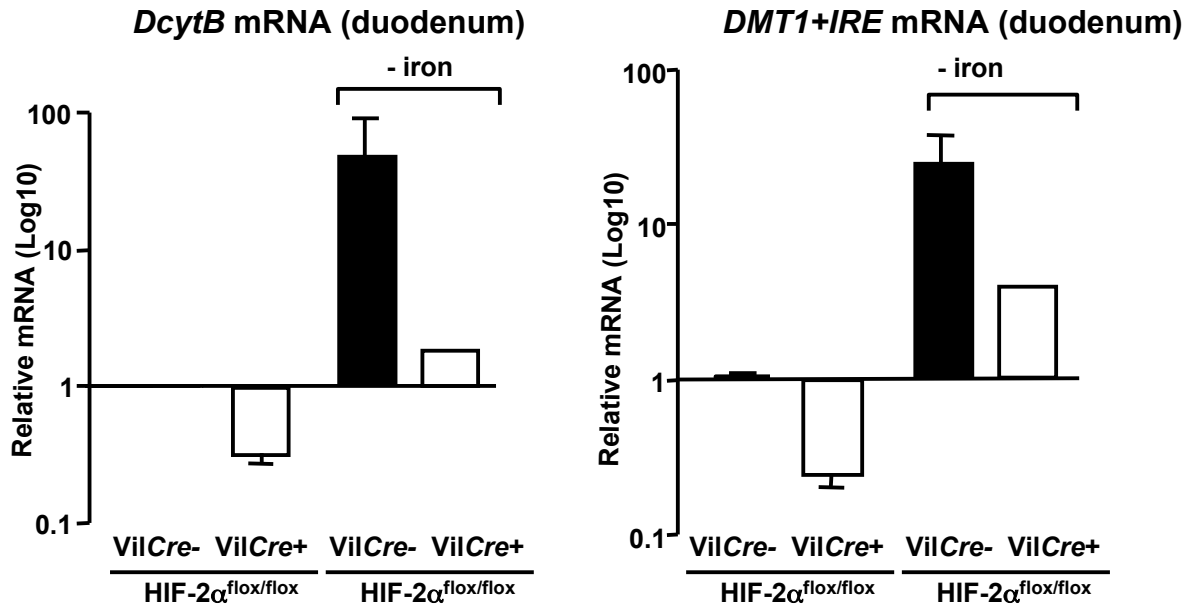
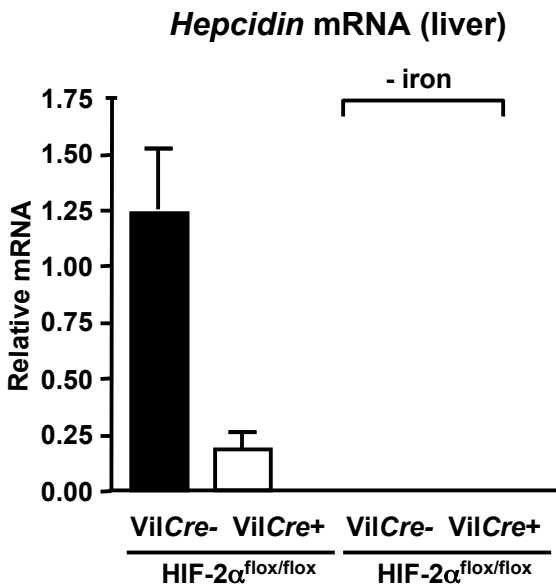
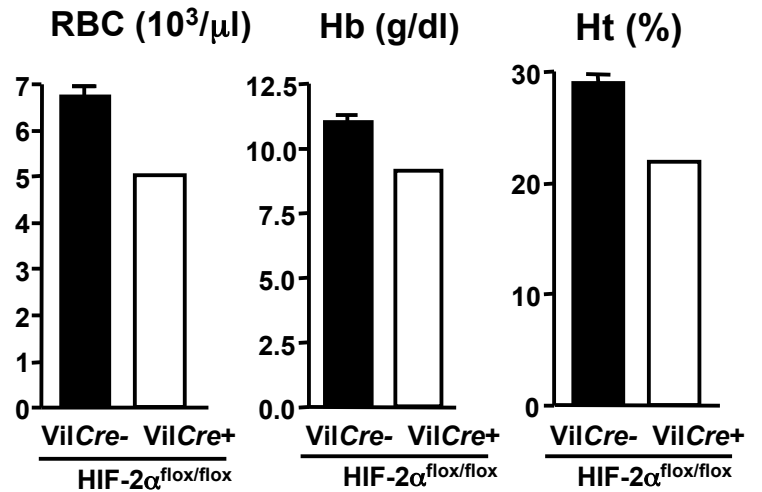
HRE-5
 -610 TTTTCCATCAGGCACCAAGTCCGGAGTTT**GCGTGG**CTCTGATGTCTGCTCGTGGATCACT
 -550 GATTGACCAGGCTGAAGCCAGAGGGTCTTTAGATCCCAGGGATAATAGAGCAGGCAGC
 -490 ATTTCCACC**CACGT**TCTGAGACTCCTCATAATTGCCTCAGTGCTG**CACGT**ACCTATATGG
 -430 AAAATACAAGTGCACCTGTGAGGCTTGGGGTTAATGGTTTCACT**CACGT**CTCAGAGGAGC
 -370 AGAGTCCTAGTGCACCTGTGGAGCCTGAACCAGCTGCACTCCAAGAGGAGCAGAGAAGGG
 -310 AAGCAATTTCTTACTCCACCCCTTTCAACCACTGGCACTCACAGGCTTGCCACCTACTCT
 -250 TGCTCCTGCCAAATGGTACAGAGATGAAATCTTAGAATAAAAATTTTGAACCTCAATAAAT
 -190 TGTTAATTAATATCTAGGAGTGGCAGATATATAATGCTTCTCTTTTCACGACAGGTCAAA
 -130 GATGAAATCTGATTAGGCTTTGGAGGG**GCGTGG**TTTGCTCTTGAAATTCCTTGCTCGTCT
 -70 TTAGAAAGCTGTGTTGCTTAGAGCACCCAAAAGTGCCCTTTATCTAACTGAGGGAGGCGC
 +1
 -10 ACTTGTCTTCATATATAGAGGCAGGAGCTGGCATTGGGAAAAGTCAAACCTAGTTCTGCACC
ATGAGGAAGAAGCAGCTGAAGACGGAGGCAGCTCCACACTGTGAACTAAGTAAGTAGCCC
 Exon 1A

B

	HRE-5	HRE-4	HRE-3	HRE-2	HRE-1
Homo_sapiens	AGTTT GCGTGG CTCT---CCACC CACGT TCTGA---TGCTG CACGT ACCTA---ACCT CACGT CTCAG-----GGAGG GCGTG GTTTG				
Pan_troglodytes	AGTTTGTGTGGGTCT---CCACC CACGT TCTGA---TGCTG CACGT ACCTA---ACCT CACGT CTCAG-----GGAGG GCGTG GTTTG				
Pongo_pygmaeus	AGTTTGCAGGGTCT---CCACCCATGCTCTGA---TGCTG CACGT ACCTA---ACCT CACGT CTCAG-----GGAGG GCGTG GTTTG				
Macaca_mulatta	AGTTT GCGTGG CTCT---CCACCCACGCTCTGA---TGCTG CACGT ACCTA---ACCT CACGT CTCAG-----GGAGG GCGTG GTTTG				
Mus_musculus	GTTCTGCC-CATTTT---CCACCTTTACTTTGA---TGTGG CACGT AC-TG---ACCTCCCTTCTCAC-----GAAGGGTGC GGTTTG				
Rattus_norvegicus	ATTCTGCCTCACTTT---CCACCTCTGCTTTGA---TGTGG CACGT AC-TG---ACCTCCCGTCTCAC-----GAAGGGTGC GGTTTG				
Equus_caballus	GGTTTGCATGGCTTT---TCAATCATACTCTGA---TGCTG CACGT ACCTA---GGCT CACGT CTCAG-----GAAGGGTGTGGTTTG				
Canis_familiaris	GGTTTGCATGGCTTT---TTACTCACACTCTGA---TGCTG CACGT ACCTA---AGCCTACACCTTAG-----GAGGGTGTGGCTTG				
Bos_taurus	TCTCGGGTTTGTGTG---TTACCTATACTCTGA---CACTG CACGT ACCTA---ACTTTACGTTTCAG-----GAAGGGTGTGGTTTG				

Figure S1

Promoter sequence of DMT1-1A. (A) Presence of 5 HREs (Hypoxia Responsive Element) in the promoter of DMT1. HRE consensus sequences are indicated in bold. Arrows indicate the forward or reverse position of the HREs. Gray boxes represent primers used for CHIP. +1 = transcription start site. (B) Conservation of HREs (in red) among eutherian mammals.

A**B****C****Figure S2**

(A) *DMT1+IRE* and *Dcytb* mRNA levels in duodenum scrapings from vil-cre+/HIF-1 α ^{flox/flox}, vil-cre+/HIF-2 α ^{flox/flox} mice and WT littermates under normal or 2 months iron restricted diet as determined by RT-PCR. (B) *Hepcidin* mRNA levels in liver from vil-cre+/HIF-2 α ^{flox/flox} mice and WT littermates under normal or 2 months iron restricted diet as determined by RT-PCR. (C) Blood parameters of vil-cre+/HIF-2 α ^{flox/flox} mice and WT littermates after 2 months iron restricted diet.

Primers used in real-time PCR		
gene	Forward	Reverse
<i>HEPC1</i>	5'-CCTATCTCCATCAACAGATG-3'	5'-AACAGATACCACACTGGGAA-3'
<i>DMT1+IRE</i>	5'-TGTTTGATTGCATTGGGTCTG-3'	5'-CGCTCAGCAGGACTTTCGAG-3'
<i>DMT1-IRE</i>	5'-TCCTGGACTGTGGACGCTC-3'	5'-GGTGTTTCAGAAGATAGAGTTCAGG-3'
<i>DCYTB</i>	5'-ACGGTTCTCATGGGAGTGAC-3'	5'-GAAGGCCACGCGTATTTGTA-3'
<i>FN-1</i>	5'-CTACCATTAGAAGGATTGACCAGCTA-3'	5'-ACTGGAGAACCAAATGTCATAATCTG-3'
<i>Glut-1</i>	5'-GGGCATGTGCTTCCAGTATGT-3'	5'-ACGAGGAGCACCGTGAAGAT-3'
<i>18S</i>	5'-GTAACCCGTTGAACCCATT-3'	5'-CCATCCAATCGGTAGTAGCG-3'

Primers used for CHIP		
name	Forward	Reverse
DMT1 (HRE)	5'-CTCTGATGTCTGCTCGTGGA-3'	5'-TGAAACCATTAACCCCAAGC-3'
c-Myc (negative control)	5'-GGGCTGTGTTTAGAGGCTAGG-3'	5'-CACCCACTCTTGAGGCAGTT-3'

Primers used for DMT1-1A cloning and HRE mutagenesis		
name	Forward 5'-3'	Reverse 5'-3'
DMT1-1A	CTAGGCTTGCCCTCGAGTTCTGTCTTGTAGTCTCTG XhoI	GGTGCAGAACAAGCTTGACTTTCCCAATGCCA HindIII
HRE1-DMT1	GGCTTTGGAGGGCTCGAGTTGCCTCTTG XhoI	CAAGAGGCAACTCGAGCCCTCCAAAGCC XhoI
HRE2-DMT1	TAATTGGTTTACCTCTCGAGTCAGAGGAGCAGAG XhoI	CTCTGCTCCTCTGACTCGAGAGGTGAAACCAATTA XhoI
HRE3-DMT1	CATAATTGCCTCAGTGCTGCTCGAGCCTATATGGAAAAT XhoI	ATTTTCCATATAGGCTCGAGCAGCACTGAGGCAATTATG XhoI
HRE4-DMT1	CAGCATTCCACCCTCGAGCTGAGACTCCTCA XhoI	TGAGGAGTCTCAGCTCGAGGGTGGAAATGCTG XhoI
HRE5-DMT1	CAAGTCCGGAGTTTCTCGAGCTCTGATGTCTGC XhoI	GCAGACATCAGAGCTCGAGAACTCCGGACTTG XhoI

Table S1

Primers used for real-time PCR, Chromatin Immunoprecipitation (ChIP) and cloning