A time course of hepcidin response to iron challenge in patients with *HFE* and *TFR2* hemochromatosis

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Online Supplementary Table S1. Results of the oral iron test (details). (A) Time-course of serum iron levels (μg/dL). Median and interquartile range (in brackets) are shown for the five groups.

Time	0	4 h	8 h	12 h	24 h
Controls	113 (94 - 141)	146** (124 - 162)	98 (90 - 138)	89 (78 - 101)	108 (81 - 130)
C282Y/C282Y at diagnosis	163 (139 - 221)	217.5* (172 - 232)	189.5 (155 - 215)	171.5 (136 - 219)	183 (122 - 218)
C282Y/H63D at diagnosis	145 (89 - 156)	176.5* (139 - 207)	134.5 (120 - 149)	98 (90 - 118)	119 (115 - 173)
Iron-depleted patients	133 (127 - 161)	253** (236 - 281)	243** (217 - 269)	197* (175 - 213)	135 (116 - 143)
TFR2- patients	310 (270 - 350)	338 (298 - 378)	330.5 (283 - 378)	303 (256 - 350)	299.5 (219 - 380)

**P<0.05 and **P<0.01 as compared to basal at time 0.*

(B) Time-course of transferrin saturation levels (%). Median with interquartile range (in brackets) are shown for the five groups.

Time	0	4 h	8 h	12 h	24 h
Controls	34 (30 - 41)	43* (35 - 47)	29 (26 - 39)	25* (21 - 29)	32 (24 - 40)
C282Y/C282Y at diagnosis	70.5 (46 - 83)	79.5 (54 - 86)	74.5 * (51 - 81)	63.5 (52 - 78)	63.5 (54 - 83)
C282Y/H63D at diagnosis	45 (37 - 57)	59.5 * (45 - 60)	43 (40 - 45)	31 (27 - 37)	41.5 (36 - 54)
Iron-depleted patients	48 (40 - 51)	82** (79 - 83)	77** (68 - 80)	66 * (53 - 68)	48 (27 - 49)
TFR2- patients	95 (93 - 97)	98.5 (98 - 99)	93 (92 - 94)	91 (88 - 94)	83.5 (70 - 97)

**P<0.05 and **P<0.01 as compared to basal at time 0.*

(C) Time-course of serum hepcidin levels by ELISA (ng/mL). Median with interquartile range (in brackets) are shown for the five groups.

Time	0	4 h	8 h	12 h	24 h
Controls	59.6 (41.6 - 71.6)	92.2** (67.5 - 115.5)	100.6** (63.9 - 128.3)	103.6** (90.5 - 118.9)	49.8 (40.5 - 79.4)
C282Y/C282Y at diagnosis	41.9 (24 - 65.6)	44.2 (34.1 - 65.2)	54.7** (32.8 - 74.8)	58.7** (43 - 80.9)	48.3 (25.2 - 85.4)
C282Y/H63D at diagnosis	65.1 (50.8 - 71.1)	83.1* (77 - 103.5)	105.3 * (98.8 - 107)	107.1 (90.6 - 135.6)	69.7 (62.1 - 80.6)
Iron-depleted patients	9.6 (6.6 - 20)	11.4 (8.5 - 28.2)	13.9 (6.8 - 19)	29.1* (7.7 - 48.9)	10.9 (7 - 32.5)
TFR2- patients	1.8 (1 - 2.6)	4.6 (3.7 - 5.6)	6.1 (4.8 - 7.4)	5.2 (3.8 - 6.6)	9.2 (6.3 - 12)

**P<0.05 and **P<0.01 as compared to basal at time 0.*

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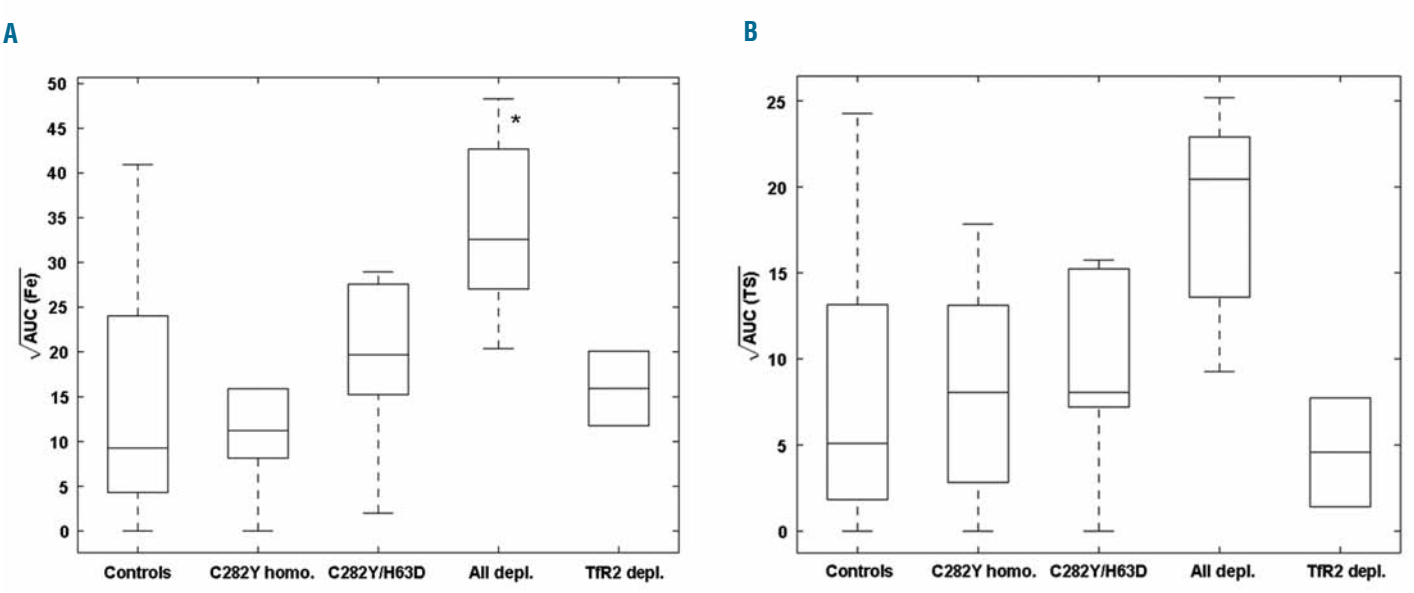
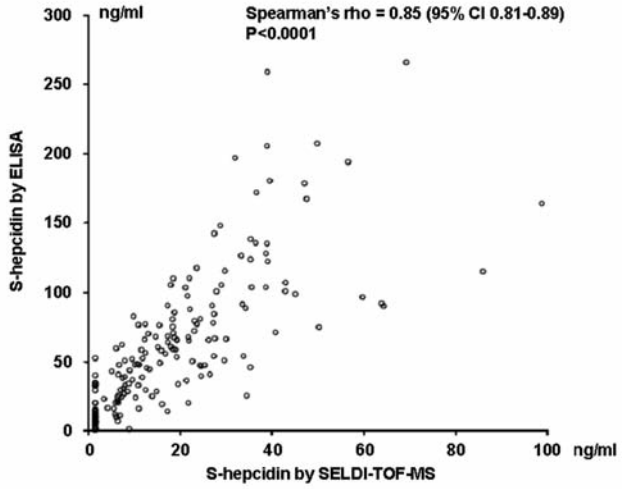
Online Supplementary Table S1. (D) Time-course of serum hepcidin levels measured by mass spectrometry (ng/mL). Median with interquartile range (in brackets) are shown for the five groups.

Time	0	4 h	8 h	12 h	24 h
Controls	10.3 (7 - 18)	22.1** (16 - 27.4)	27.6* (21.6 - 38.7)	34.4** (21.2 - 39)	11.7 (6.7 - 23.1)
C282Y/C282Y at diagnosis	12.2 (7.9 - 19.2)	21.8* (8.8 - 26.4)	20.7* (13.9 - 33.7)	18.8* (12.5 - 24.4)	16.8 (8 - 34.5)
C282Y/H63D at diagnosis	22.4 (13.1 - 35.4)	28 (23.7 - 34.3)	36 (18 - 45.1)	37.8* (27 - 63.8)	18.4 (7.3 - 18.7)
Iron-depleted patients	1.5 (1.5 - 1.5)	1.5 (1.5 - 8)	1.5 (1.5 - 7.7)	1.5* (1.5 - 17.3)	1.5 (1.5 - 1.5)
TFR2-patients	1.4 (1.4 - 1.4)	1.4 (1.4 - 1.4)	1.4 (1.4 - 1.4)	1.4 (1.4 - 1.4)	1.4 (1.4 - 1.4)

**P<0.05 and **P<0.01 as compared to basal at time 0.*



Online Supplementary Figure S1. Box plots of square root areas under the curves (AUC) of serum iron (A) and transferrin saturation (B) in the five groups studied. C282Y homozygous and C282Y/H63D compound heterozygotes patients after iron depletion are grouped together. *Significantly different from controls (*P*=0.0019). Other significant differences: all patients at diagnosis *versus* all iron-depleted patients (*P*=0.0015); C282Y homozygotes at diagnosis *versus* C282Y depleted patients (*P*=0.0014); C282Y/H63D at diagnosis *versus* all iron-depleted patients (*P*=0.014).



Online Supplementary Figure S2. Correlation between the two methods used to assay serum hepcidin. Total number of paired measures n=185.