

Supplementary Table 1: urinary and serum hepcidin values of IRIDA patients reported in the literature

Reference	Melis, M A, et al. Haematologica. 2008	Finberg, K E, et al. Nature Genet. 2008	Ramsay, A J, et al. Hum Mol Genet. 2009	Beutler, E, et al. Blood Cells Mol Dis. 2010
Urinary hepcidin (ng/mg creatinine)	2374-8649-1962-3468	1828 - 421- 4055 - 3329 - 113	5069-5350	830-1222-1627
Method	ELISA	ELISA	ELISA	ELISA
Normal values (ng/mg creatinine)	70-1762	71-1567	71-1567	
Reference	Melis, M A, et al. Haematologica. 2008	De Falco, L, et al. Hum Mutat. 2010	Guillem, F, et al. Hum Mutat. 2012.	
Serum hepcidin ($\mu\text{g/L}$ or nM)	133 - 450 - 304 - 198 $\mu\text{g/L}$	9.8 - 5.6 - 17 - 9 - 7.5 - 5.8 -13 nM	4288* - 62 - 81 $\mu\text{g/L}$	
Method	ELISA	TOF-MS	ELISA	
Normal values	18-237 $\mu\text{g/L}$	median = 4.7 nM in 57 normal individuals	29-254 $\mu\text{g/L}$ (males) 16-288 $\mu\text{g/L}$ (females)	

Each hepcidin value corresponds to one individual patient.

* after IV iron injection

Supplementary Table 2 : Tmprss6 mutations reported in the literature

N. of patients	Mutation 1 Nucleotide/amino acid change	Mutation 1 Domain	Mutation 2 Nucleotide/amino acid change	Mutation 2 Domain	Ethnicity	References
2	c.1906_1907insGC (p.K636fs)	Protease	c.1906_1907insGC (p.K636fs)	Protease	Turkish	Finberg et al. ³⁸
2	c.1813delG (p.A605fs)	Protease	IVS13+1G>A (c.1582+1G>A)	LDLRA 2	Northen European	Finberg et al. ³⁸
2	IVS16+1G>C (c.2140+1G>C)	Protease	Not identified	n.a.	Nigerian	Finberg et al. ³⁸
2	c.1324 G>A (p.G442R)	CUB 2	c.1561G>A (p.D521N)	LDLRA 2	Northen European	Finberg et al. ³⁸
2	c.2320 C>T (p.R774C)	Protease	Not identified	n.a.	African American	Finberg et al. ³⁸
1	IVS15-1G>C (c.1869-1G>C)	Protease	IVS15-1G>C (c.1869-1G>C)	Protease	Nigerian	Finberg et al. ³⁸
1	c.1065C>A (p.Y355*)	CUB 2	c.1383delA (p.E461fs)	LDLRA 1	African American	Finberg et al. ³⁸
1	c.1179 T>G (p.Y393*)	CUB 2	c.1795 C>T (R599*)	CUB2	English	Guillem et al. ⁴⁷
5	IVS6+1G->C (c.658+1G>C)	CUB 1	IVS6+1G->C (c.658+1G>C)	CUB 1	Italian	Melis et al. ³⁷
2	c.467 C>A, c.468 C>T (p.A118D)	SEA	c.2172_2173insCCCC (p.P686 fs)	Protease	Spanish	Ramsay et al. ⁶⁶
1	c.1561 G>A (p.D521N)	LDLRA 2	c.1564 G>A (p.E522K)	LDLRA 2	French	Silvestri et al. ⁶³
1	IVS17-1G>C (c.2278-1G>C)	Protease	IVS17-1G>C (c.2278-1G>C) g.29139_30192 del 1054 (prot. del 30 aa)	Protease	Indian	Edison et al. ⁸⁴
1	c.1025 C>T (p.S304L)	CUB1		LDLR-1/-2	Swiss	Tchou et al. ⁵³
1	c.1982 G>C (p.S623T)	Protease	c.1982 G>C (p.S623T)	Protease	Italian	Tchou et al. ⁵³
1	c.422 A>G (p.Y141C)	SEA	c.422 A>G (p.Y141C)	SEA	Indian	De Falco et al. ⁴⁶
1	c.749 T>C (p.I212T)	SEA	c.926 G>A (p.R271Q)	CUB1	Italian	De Falco et al. ⁴⁶
3	c.1025 C>T (p.S304L)	CUB 1	c.1025 C>T (p.S304L)	CUB1	Arabian	De Falco et al. ⁴⁶
1	c.611 delC (p.L166fs)	SEA	c.790 delG (p.Q229fs)	CUB1	Austrian	De Falco et al. ⁴⁶
2	c.855 delG (p.W247fs)	CUB 1	c.855 delG (p.W247fs)	CUB1	Greek	De Falco et al. ⁴⁶
3	c.1796 C>A (p.S561*)	Activation Site	c.1796 C>A (p.S561*)	Activation Site	Arabian	De Falco et al. ⁴⁶
1	c.1642 C>A (p.C510S)	LDLRA 2	c.1822_1823 inc CC (p.S570fs)	Activation Site	Algerian	De Falco et al. ⁴⁶
1	c.442A>G (p.Y141C)	SEA	c.442A>G (p.Y141C)	SEA	Lebanon	Altamura et al. ⁶⁵
2	c.2137C>T (p.L674F)	Protease	IVS13+1G>A (c.1582+1G>A)	LDLRA 2	Belgian	Beutler et al. ⁵¹
1	c.497delT (p. L166fs)	SEA	c.497delT (p. L166fs)	SEA	Dutch	Beutler et al. ⁵¹
1	c.2105 G>T (p.C702F)	Protease	c.2383G>A (p. V795I) (\$)	Protease	Dutch	Cuijpers et al. ⁸³
1	c.1807G>C (p.G603R)	Protease	IVS7+1G>T (c.863+1G>T)	CUB 1	Korean	Choi et al. ⁸⁵
2	c.1813 delG (p.A605fs)	Protease	c.1813 delG (p.A605fs)	Protease	Algerian	Guillem et al. ³⁹
2	c.704T>C; (p.L235P)	CUB 1	c.1253A>G; (p. Y418C)	CUB 2	French	Guillem et al. ³⁹
1	c.340 G>A (p.E114K)	SEA	c.2293 C>G (p.P765A)	Protease	French	Guillem et al. ³⁹
1	c.1025 C>T (p.S304L)	CUB1	IVS8-1433del9 (c.1001-11_1001-3delTCCTGGTCC)	CUB2	Italian	Guillem et al. ³⁹
1	c.1025 C>T (p.S304L)	CUB1	IVS8-1433del9 (c.1001-11_1001-3delTCCTGGTCC)	CUB2	Italian	Pellegrino et al. ⁶¹
1	IVS15-21 C>G (c.1869-21C>G)	Protease	Not identified	n.a.	Portuguese	Pellegrino et al. ⁶¹