Molecular analysis of 42 patients with congenital dyserythropoietic anemia type II: new mutations in the *SEC23B* gene and a search for a genotype-phenotype relationship

Achille Iolascon,[1,2] Roberta Russo,[1,2] Maria Rosaria Esposito,[1,2] Roberta Asci,[1] Carmelo Piscopo,[1,2] Silverio Perrotta,[3] Madeleine Fénéant-Thibault,[4] Loïc Garçon,[5] and Jean Delaunay[6]

[1]CEINGE Biotecnologie Avanzate, Napoli, Italy; [2]Department of Biochemistry and Medical Biotechnologies, University Federico II of Naples, Italy; [3]Department of Pediatrics, Second University of Naples, Italy; [4]Service de Biochimie, Hôpital de Bicêtre, Le Kremlin-Bicêtre, France; [5]Service d'Hématologie Générale, Hôtel-Dieu, Paris, France, and [6]INSERM U 779, Faculté de Médecine Paris-Sud, Univ Paris-Sud, Le Kremlin-Bicêtre, France

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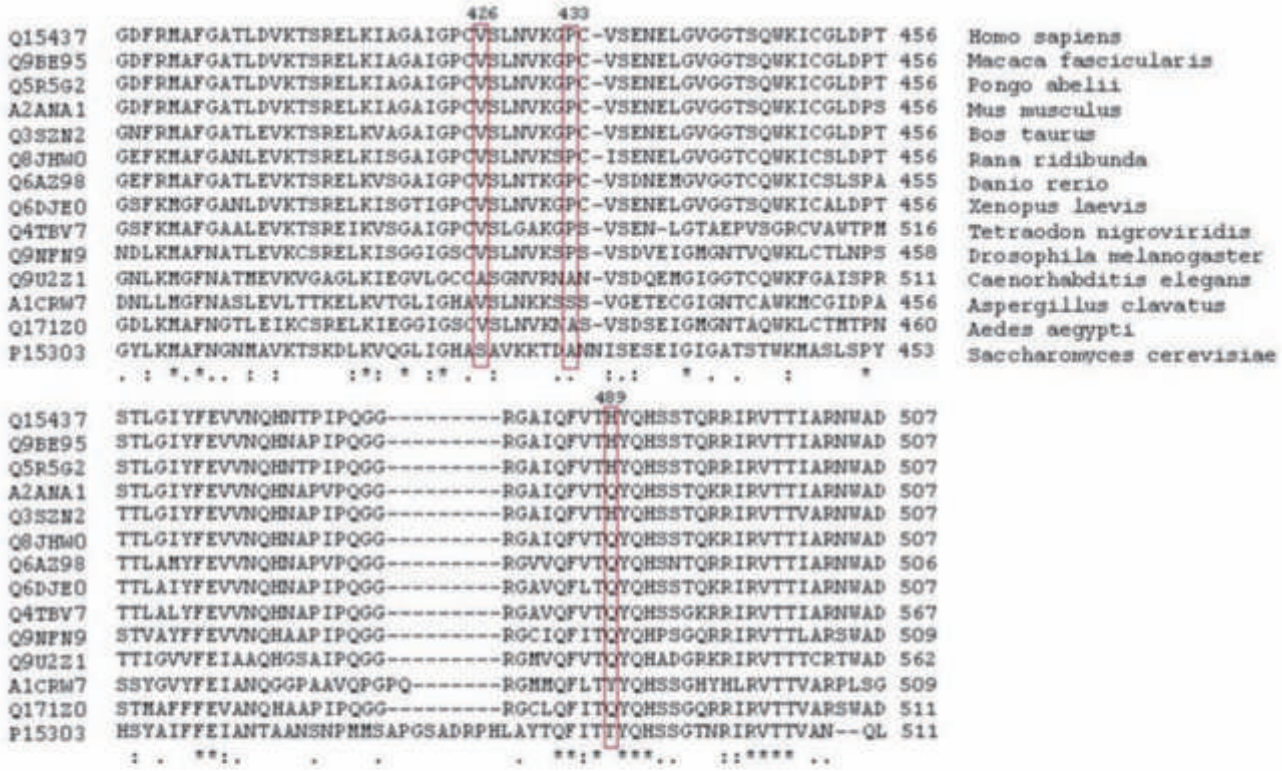
Online Supplementary Table S1. Topographical distribution of *SEC23B* mutations in CDA II patients.

Patient	Exon	Nucleotide change	Effect on protein	Mutation status
Nonsense mutations				
2; 13; 15	3	c. 235 C>T	R79X *	Comp het
8	6	c. 649 C>T	R217X *,†	Het
18	7	c. 790 C>T	R264X *	Comp het
35a, 35b	10	c. 1201 C>T	R401X *	Comp het
15; 31	14	**c. 1648 C>T**	**R550X**	Comp het
Frameshift mutations				
6	9	c. 1063 (delG)	D355IfsX8 *	Comp het
20	17	**c. 1962-64 (delT)**	**T654TfsX13**	Comp het
Missense mutations				
2; 11; 13; 16; 17; 22; 23; 27; 35a, 35b; 37	2	c. 40 C>T	R14W *,†	Comp het
40	2	c. 40 C>T	R14W	Het
19; 39	2	c. 53 G>A	R18H *	Comp het
5; 7; 12; 14; 24; 25; 30; 32; 33; 34; 36; 38	4	c. 325 G>A	E109K *,†	Hom
22; 28	4	c. 325 G>A	E109K	Comp het
10	8	c. 953 T>C	I318T *	Hom
16; 28	8	c. 953 T>C	I318T	Comp het
6	10	c.1157 A>G	Q386R *	Comp het
1a, 1b; 3	12	c.1385 A>G	Y462C *	Hom
20; 21; 26; 31	13	c. 1489 C>T	R497C *,†	Comp het
29	13	c. 1489 C>T	R497C	Hom
17	13	**c. 1508 G>A**	**R503Q**	Comp het
19; 31; 39	14	c. 1571 C>T	A524V *	Comp het
27	14	**c. 1589 G>A**	**R530Q**	Comp het
15	15	**c. 1685 A>G**	**Y562C**	Comp het
4	17	**c. 1968 T>G**	**F656L**	Het
9	18	c. 2101 C>T	R701C†	Het
21; 37	18	c. 2101 C>T	R701C	Comp het
18	19	**c. 2166 A>C**	**K723Q**	Comp het
Splicing mutations				
23	6	c. 689 +1 G>A *,†		Comp het

Hom, mutations in the homozygous state; comp het, mutations in the compound heterozygous state; del, deletions; ins, insertions. In bold, novel mutations, not contained in references 13 and 14†.*

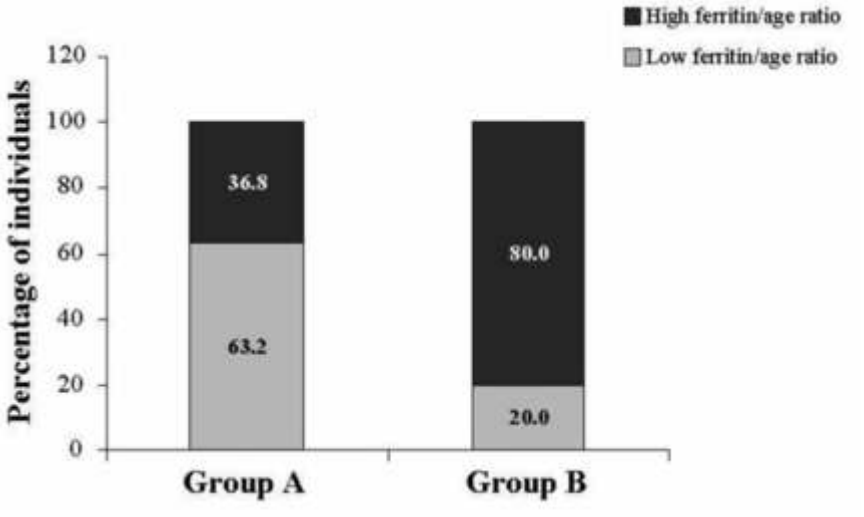
Online Supplementary Figure 1S. Multiple DNA sequence alignment of the SEC23B protein. Fourteen species were aligned using Database UniProtKB release 15.0 of Mar-25-2009; program NCBI BLASTP 2.2.17 [Aug-26-2007] on services.uniprot.org (http://services.uniprot.org/blast/). The species' name, protein number and portions of the sequence are shown for each mutation discovered. Mutated amino acids are highlighted showing the conservation among species. *residues identical in all sequences in the alignment. : conserved substitutions observed. .semi-conserved substitutions observed



Absolute allele and genotype frequencies

	rs4309927 G>A V426I					rs17807673 C>T P433L					rs2273526 C>G H489Q				
	Genotype n(%)			*Allele n(%)*		*Genotype n(%)*			*Allele n(%)*		*Genotype n(%)*			*Allele n(%)*	
	GG	GA	AA	G	A	CC	CT	TT	C	T	CC	CG	GG	C	G
Controls n=50	44 (88.0)	6 (12.0)	0 (0.0)	94 (94.0)	6 (6.0)	39 (78.0)	10 (20.0)	1 (2.0)	88 (88.0)	12 (12.0)	44 (88.0)	5 (10.0)	1 (2.0)	93 (93.0)	7 (7.0)
Cases n=40	33 (82.5)	6 (15.0)	1 (2.5)	72 (90.0)	8 (10.0)	36 (90.0)	4 (10.0)	0 (0.0)	76 (95.0)	4 (5.0)	30 (75.0)	9 (22.5)	1 (2.5)	69 (86.3)	11 (13.7)

Online Supplementary Figure 2S. Multiple DNA sequence alignment of three single nucleotide polymorphisms of SEC23B protein. Fourteen species were aligned using Database UniProtKB release 15.0 of Mar-25-2009; program NCBI BLASTP 2.2.17 [Aug-26-2007] on services.uniprot.org (http://services.uniprot.org/blast/). The species' name, protein number and portions of the sequence are shown for each single nucleotide polymorphism discovered. Mutated amino acids are highlighted with the red box, showing the conservation among species. * residues identical in all sequences in the alignment. : conserved substitutions observed. .semi-conserved substitutions observed. The table contains the allele and genotype frequencies in both control subjects and patients.



Online Supplementary Figure 3S. Correlation analysis of *ferritin level/dosage age* ratio. Patients with one nonsense + one missense mutation (group B, n=10) have a higher ferritin level/age ratio compared with patients with two missense mutations (group A, n=19) (OR=6.9, 95% CI: 1.1-41.8, *P*=0.03, χ^2 test).