Biallelic mutations in the *SARS2* gene presenting as congenital sideroblastic anemia

Elia Colin,[1] Geneviève Courtois,[1] Chantal Brouzes,[2] Juliette Pulman,[3] Marion Rabant,[4] Agnès Rötig,[3] Hélène Taffin,[5] Mathilde Lion-Lambert,[5] Sylvie Fabrega,[6] Lydie Da Costa,[7] Mariane De Montalembert,[8] Rémi Salomon,[5] Olivier Hermine[9] and Lucile Couronné[10]

[1]Laboratory of Cellular and Molecular Mechanisms of Hematological Disorders and Therapeutic Implications, INSERM U1163, Imagine Institute, University of Paris, Laboratory of Excellence GR-Ex; [2]Hematology Laboratory, Hôpital Necker-Enfants Malades, Assistance publique-Hôpitaux de Paris (AP-HP); [3]Laboratory for Genetics of Mitochondrial Disorders, INSERM U1163, Imagine Institute, University of Paris; [4]Department of Pathology, Hôpital Necker - Enfants Malades, Assistance Publique-Hôpitaux de Paris, University of Paris; [5]Department of Pediatric Nephrology, MARHEA, Hôpital Necker - Enfants Malades, Assistance Publique-Hôpitaux de Paris (AP-HP); [6]VVTG platform, SFR Necker; [7]Hematology Laboratory, Robert Debré Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP), University of Paris, Laboratory of Excellence GR-Ex; [8]Department of General Pediatrics and Pediatric Infectious Diseases, Reference Center for Sickle Cell Disease, Hôpital Necker - Enfants Malades, Assistance Publique-Hôpitaux de Paris (AP-HP), Université de Paris; [9]Hematology Department, Hôpital Necker - Enfants Malades, Assistance Publique - Hôpitaux de Paris (APHP), Laboratory of Cellular and Molecular Mechanisms of Hematological Disorders and Therapeutical Implications, INSERM U1163, Imagine Institute, University of Paris, Laboratory of Excellence GR-Ex and [10]Laboratory of Onco-Hematology, Hôpital Necker - Enfants Malades, Assistance Publique - Hôpitaux de Paris (APHP), Laboratory of Cellular and Molecular Mechanisms of Hematological Disorders and Therapeutical Implications, INSERM U1163, Imagine Institute, University of Paris, Laboratory of Excellence GR-Ex, Paris, France

Correspondence: ELIA COLIN - elia.colin@hotmail.fr

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Supplemental tables

Table S1

	Variables	**Proband**	**Normal reference range**
Blood biochemistry test	Urea (mmol/L)	34.4	1.6-6.5
	Creatinin (µmol/L)	171	26-42
	Uric acid (µmol/L)	790	120-320
	Sodium (mmol/L)	140	136-146
	Potassium (mmol/L)	5	3.1-4.7
	Calcium (mmol/L)	2.53	2.20-2.70
	Phosphate (mmol/L)	1.31	1.3-1.85
	Haptoglobin (g/L)	<0.08	0.47-1.25
	Total bilirubin (µmol/L)	10	0-17
	Lactate dehydrogenase (IU/L)	267	125-243
Blood Count	Hemoglobin (g/dL)	9	11.5-13.5
	Hematocrit (%)	25.7	34-40
	Mean Corposcular Volume (fL)	80	75-81
	White Blood Cells (G/L)	9.4	6.0-17.0
	Neutrophils (G/L)	5.8	1.5-8.5
	Platelets (G/L)	170	175-500
	Reticulocytes (G/L)	63	
	Schizocytes	<1%	
Iron status	Iron (µmol/L)	20	7.0-30
	Transferrin (g/L)	1.88	1.9-3.02
	Total Iron Binding Capacity (µmol/L)	47	45-80
	Transferrin saturation (%)	43	16-35
	Ferritin (µg/L)	1621	15-80

Supplemental Table 1: Laboratory data of the proband at diagnosis

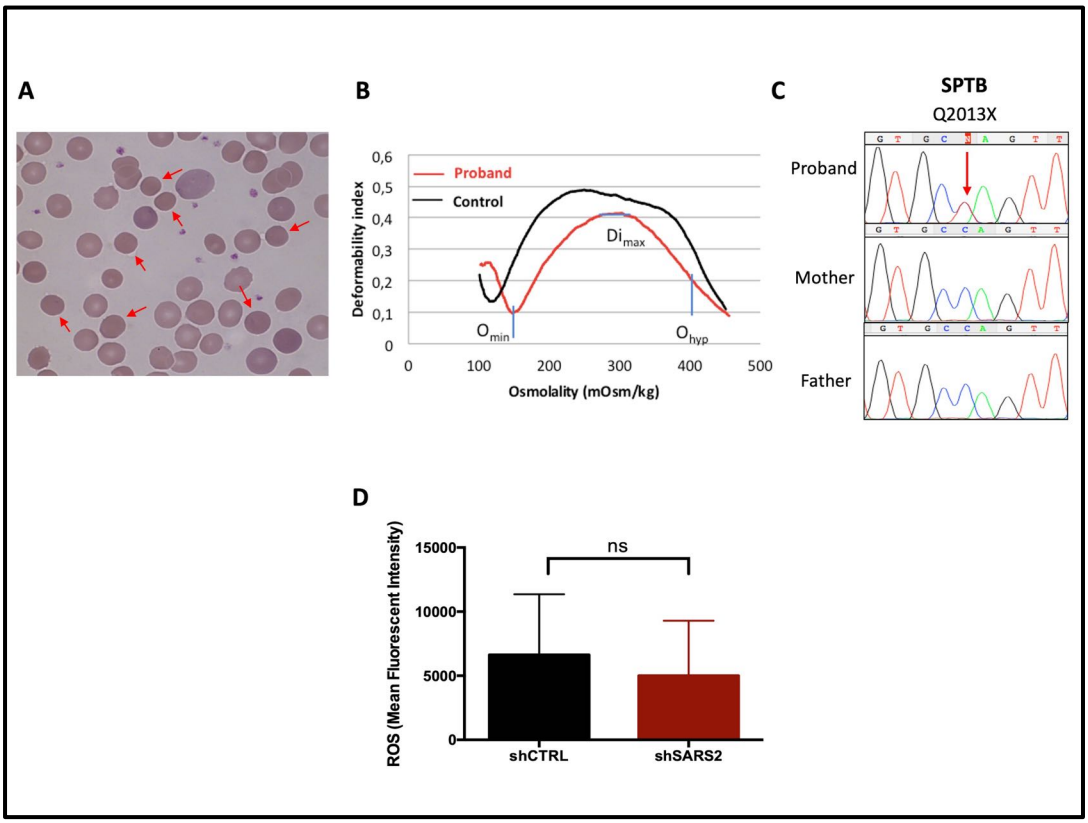
Table S2

Authors, year	**Gender**	**Family**	**Diagnosis**	**Age at diagnosis**	**Anemia**	**Hemoglobin at diagnosis (g/dL)**	**Other cytopenia**	**Age at death**	***SARS2* mutation**
This article	M	1	HUPRA syndrome	3 years old	Yes	9	No	5 years old	compound heterozygous c1031G>A (p.R344Q) c.1205G>A (p.R402H)
Belostotsky *et al*, 2011	M	2	HUPRA syndrome	4 months	Yes	9	Thrombocytopenia, leukopenia	14 months	homozygous c.1169A>G (p.D390G)
Belostotsky *et al*, 2011	F	2	HUPRA syndrome	7 months	Yes	4,8	Leukopenia	10 months	homozygous c.1169A>G (p.D390G)
Belostotsky *et al*, 2011	F	3	HUPRA syndrome	4 months	No	N/A	No	13 months	homozygous c.1169A>G (p.D390G)
Rivera *et al,* 2013	F	4	HUPRA syndrome	15 months	Yes	8,4	No	26 months	homozygous c.1205G>A (p.R402H)
Rivera *et al,* 2013	M	4	HUPRA syndrome	2 months	Yes	7,6	No	21 months	homozygous c.1205G>A (p.R402H)
Linnankivi *et al,* 2016	M	5	Progressive spastic paresis	10 years old	No	N/A	No	Alive	homozygous c.1347>A (splicing mutation)
Zhou *et al*, 2021	F	6	HUPRA syndrome	4 years old	Yes	8,7	No	5 years old	compound heterozygous c.667G>A (p.V223M) c.1205G>A (p.R402H)

Supplemental Table 2: Hematological and molecular findings in patients carrying pathogenic *SARS2* variants.[7-9] N/A: not available

Supplemental figures

Figure S1



Supplemental Figure 1

(**A**) Peripheral blood smear of the patient showing the presence of spherocytes. (**B**) Ektacytometry curves of the proband and a control. O_{min} represents the osmolarity at which 50% of the cells hemolyze. Di_{max} is the maximum elongation that the red blood cells can achieve under shear stress. O_{hyp} is the osmolarity at which the Dimax is 50% of its maximum value. In the proband, the right shift of the O_{min} indicates a reduced surface to volume ratio; the Di_{max} decrease reflects decreased red cell deformability due to a loss of surface area; and the left shift of the O_{hyp} corresponds to the dehydration of the cells (**C**) Sanger-sequencing validation of *SPTB* c.6037C>T (p.Q2013X) mutation detected by NGS. Red arrow indicates the position of the nucleotide's substitution. **(D)** At day 6 of the second phase of culture, reactive oxygen species (ROS) production was measured by flow cytometry in shCTRL and shSARS2-transduced cells using the CellROX deep red reagent. Results are represented as Mean Fluorescence Intensity of the stained cells. Error bars represent standard deviation (SD) from mean of three independent experiments. *P*-values are determined by two-tailed *t*-test. ns: not significant.