Carboxy-terminal fragment of fibroblast growth factor 23 induces heart hypertrophy in sickle cell disease

Marie Courbebaisse,[1,2,3,4] Hind Mehel,[2] Camille Petit-Hoang,[2] Jean-Antoine Ribeil,[5] Laurent Sabbah,[6] Véronique Tuloup-Minguez,[2] David Bergerat,[2] Jean-Benoit Arlet,[7,8] Aurélie Stanislas,[5] Jean-Claude Souberbielle,[2,3] Hervé Le Clésiau,[9] Rodolphe Fischmeister,[10] Gérard Friedlander[1,2,4] and Dominique Prié[1,2,3]

[1]Université Paris Descartes, Sorbonne-Paris-Cité, Faculté de Médecine, Paris; [2]INSERM U1151-CNRS UMR8253, Paris; [3]Service de Physiologie Explorations Fonctionnelles Hôpital Necker-Enfants Malades Assistance Publique-Hôpitaux de Paris; [4]Service de Physiologie Explorations Fonctionnelles Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris; [5]Département de Biothérapie, Hôpital Necker-Enfants Malades Assistance Publique-Hôpitaux de Paris; [6]Unité Fonctionnelle de Cardiologie Adultes, Hôpital Necker-Enfants Malades Assistance Publique-Hôpitaux de Paris; [7]Service de Médecine Interne, Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris; [8]INSERM U1163, CNRS 8254, Institut IMAGINE, Paris; [9]Centre de Santé et d'Assurance Maladie Agence de Seine-Saint-Denis, Bobigny and [10]INSERM UMR-S 1180 Université Paris-Sud, Université Paris-Saclay, Châtenay-Malabry, France

Correspondence: dominique.prie@inserm.fr
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Table 1: Comparisons of the control group and SCD patients according to haemoglobin anomalies

	Sickle cell disease group n = 77	**Control group n = 172**	**P**	**SS group n=52**	**SB, SC, SD group n=25**	**P**
Age (years)	29.4 ± 9.3	32.2 ± 8.4	0.0249	28.8 ± 8.6	30.5 ± 10.6	0.5023
Gender (male)	37.7% (29)	40.0% (69)	0.78	36.5% (19)	40.0 % (10)	0.8054
BMI (kg/m^2)	22.3 ± 3.6	26.9 ± 4.2	<0.0001	21.4 ± 2.8	24.2 ± 4.3	0.0059
Systolic blood pressure (mmHg)	117.5 ± 11.7	124.5 ± 13.1	0.0011	117.2 ± 11.4	118.1 ± 12.6	0.5781
Diastolic blood pressure (mmHg)	68.4±8.6;	78.7±9.2	<0.0001	68 ± 9.8	69.1 ± 5.2	0.7822
Hemoglobin (g/dL)	9.2±2.0	13.5±1.7	<0.0001	8.4 ± 1.5	11.0 ± 1.8	<0.0001
Mean corpuscular volume (μm^3)	80.8±12.3	84.2±6.2	0.0261	83.7 ± 13.3	74.9 ± 6.9	0.0003
Serum ferritin (µg/L)	160 [8-3555]	60.0 [6.0-409.0]	<0.0001	166 [25-3555]	108 [8-798]	<0.0001
Serum creatinine (µmol/L)	56.2±14.9	81.2±17.7	<0.0001	51.7 ± 14.5	65.6 ± 11.0	<0.0001
eGFR ($ml/min/1.73m^2$)	125.5±20	95.8±17.9	<0.0001	NA	NA	
Measured GFR ($ml/min/1.73m^2$)	NA	NA		115.7 ± 34.7	100.2 ± 19.7	0.0146
Serum phosphate (mmol/L)	1.12±0.18	1.13±0.25	0.727	1.14 ± 0.19	1.07 ± 0.15	0.0818
Serum calcium (mmol/L)	2.30 ± 0.08	2.36±0.1	<0.0001	2.30 ± 0.08	2.30 ± .0.09	0.9087
25(OH)-vitamin D (ng/mL)	10 [3-39]	9 [3-33]	0.06	9 [3-39]	13 [4-33]	0.2050
Serum calcitriol (pg/mL)	49 [5.0-131.0]	55.0 [21.0-146.0]	0.0003	43 [5.0-131.0]	57 [24-76]	0.3686
cFGF23 (RU/ml) Nl < 150 RU/ml	419 [35-9944]	55.0 [15.8-1615.0]	<0.0001	563 [49-9944]	152 [35-5016]	0.0018

Results are expressed as mean ± SD; median [min-max]. BMI: body mass index; eGFR: estimated glomerular filtration rate. SS patients were homozygous for the S mutation. SC, SD, and SB patients had S hemoglobin mutation plus C or D hemoglobin or β-thalassemia trait respectively

Table 2 : **Characteristics of echocardiographic parameters in SCD patients.**

	All SCD patients (n = 77)	SS genotype (n= 52)	non-SS genotype (n = 25)	P (SS versus non-SS)
initial aorta diameter (mm)	29.6±3.4	30.1±3.5	28.6±2.8	0.0416
left atrial diameter (mm)	34.9±6.8	35.8±7.2	33±5.2	0.057
left ventricle end diastolic diameter (mm)	50.9±4.8	52.4±3.8	47.8±5.4	0.0001
left ventricle end systolic diameter (mm)	30.6±4.6	32.0±4.2	27.6±4.0	0.0001
left ventricular mass indexed to body surface area (g/m^2)	113.1±28.9	121.7±26.6	95.1±25.1	0.0001
left ventricle ejection fraction (%)	64.7±7.1	63.4±6.9	67.4±7	0.0251
fraction of shortening(%)	40.1±6.2	39.1±6.1	42.2±6.1	0.0382
systolic pulmonary arterial pressure (mmHg)	27.3±5.8	28.8±5.7	23.6±4.4	0.0006
E (m/s)	0.96±0.21	1±0.21	0.89±0.18	0.0349
A (m/s)	0.59±0.14	0.59±0.14	0.59±0.14	0.888
E' (m/s)	0.18±0.08	0.17±0.05	0.19±0.13	0.4261
E/A	1.71±0.59	1.79±0.77	1.59±0.44	0.1706
E/E'	5.84 ± 1.86	6.12±1.95	5.26±1.56	0.0562

Results are expressed as mean±SD and as median [min-max]. A: late velocity of mitral inflow; E: early velocity of mitral inflow; E': early diastolic velocity of the mitral annulus; SCD: sickle cell disease

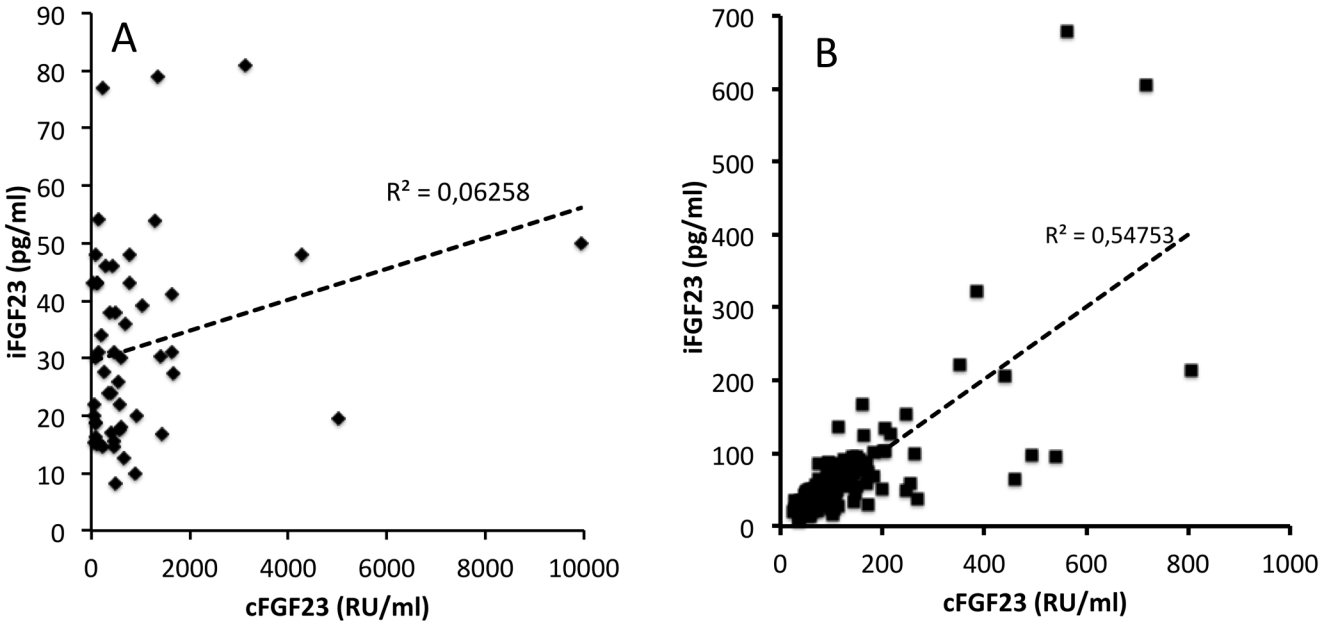

Figure S1: Lack of correlation between cFGF23 and iFGF23 in patients with SCD (A) by comparison with control subjects (B). The coefficient of correlation (R^2) is mentioned for each group.

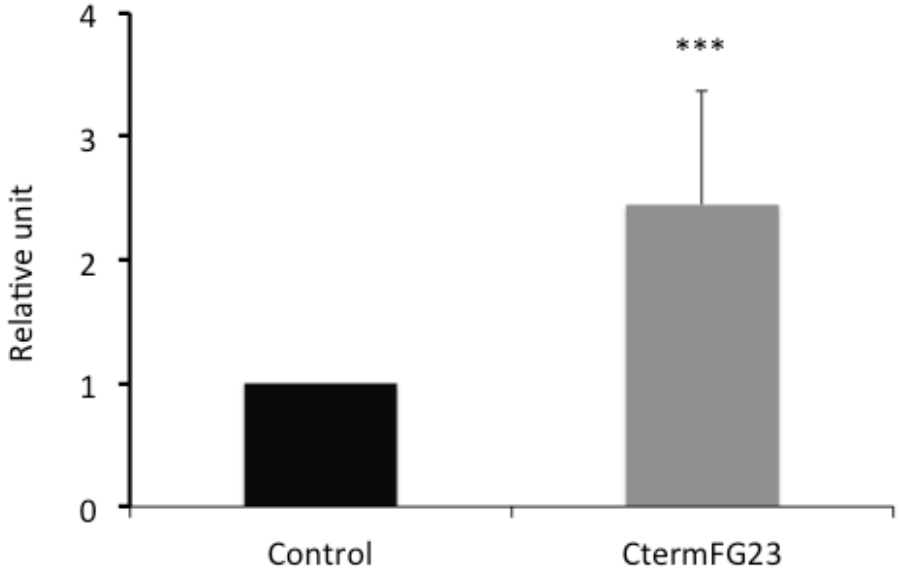

Figure S2: mRNA expression of β myosin Heavy chain β (MHC) in in adult rat ventricular myocytes. RT-PCR normalized to YWHAZ.. ***p=0.0008, Student's t test.