Functional EPO-Hepcidin axis in Recombinant human EPO independent hemodialysis patient

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INTRODUCTION

A functional EPO-Hepcidin axis mandatory to maintain erythropoiesis.

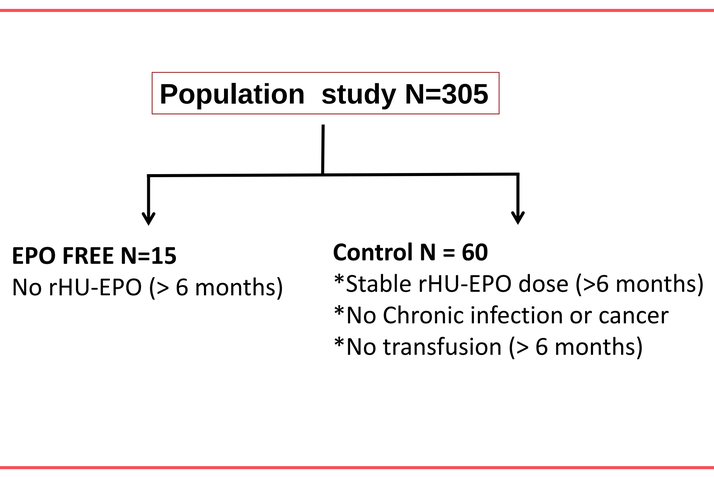
*** In CKD, anemia develops in response of multiple factors, but EPO deficiency and/or resistance remain the main cause. (1)**

Hepcidin, a key regulator of iron homeostasis, contributes to the iron-restricted anemia. (2)

*** Few hemodialysis patients remain independent of recombinant human EPO (=EPO free patients) (3)**

*** Persistence of EPO secretion have been suggested as the main mechanism (4)**

*** Mechanisms underlying this peculiar condition remain unclear**



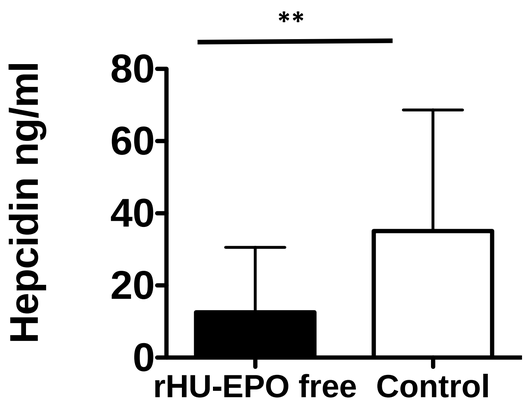
1/ Demographic characteristics

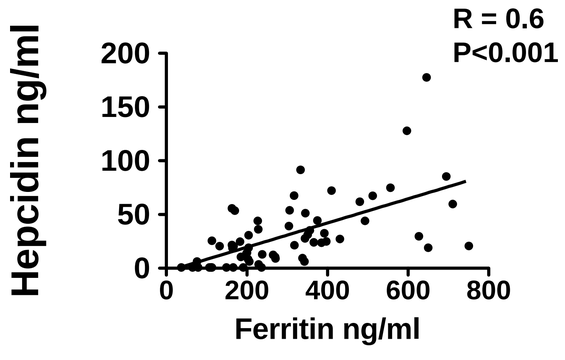
	EPO Free	Control	P-values
Gender : M/F	12/3	38/22	0.22
Age (mean-range)	66 (42-82)	68 (48-93)	0.17
Ethnie (N) - Caucassian - Magreb	 8 5	 34 14	 1.00 0.51
Nephropathy (N%) - Glomerular - Vascular - Tubulo-interstial - APKD	 7 (46%) 1 (6.6%) 3 (20%) 3 (20%)	 23 (38%) 21 (35%) 10 (17%) 2 (3%)	 0.57 0.05 0.71 0.26
Comorbidities - Diabetes - Hypertension - BMI	 7 (45%) 6 (40%) 27.1 +/-6.6	 22 (36%) 43 (61%) 25.4 +/- 6.81	 0.48 0.02 0.88
Liver disease	0	1/3	0.45
Dialysis duration (months, median)	91 (9-455)	41 (3-382)	<0.001
Renal Cysts	13/15 (86.6%)	20/60 (33%)	<0.001

2/ EPO free patients restore their erythropoiesis

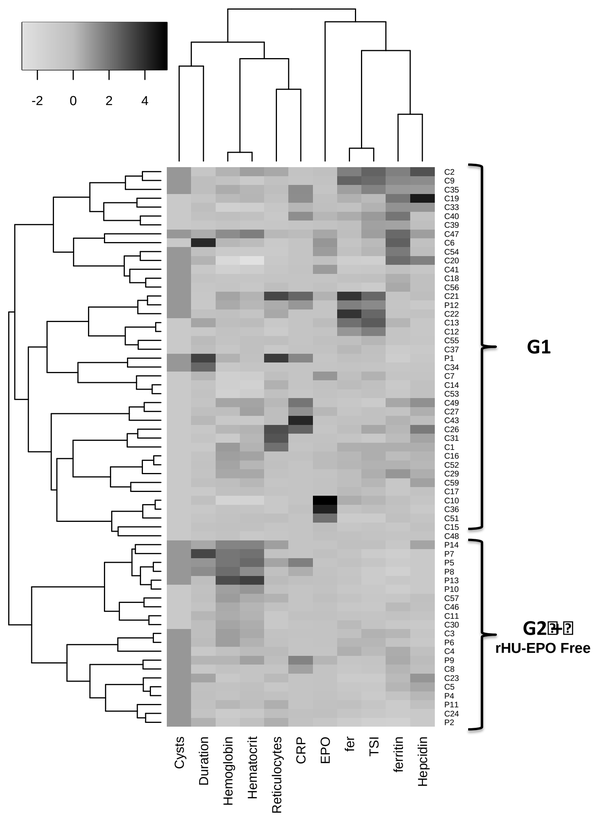
	EPO free	Control	P-values
Hemoglobin (g/dl)	12.1+/-0.99	11.1 +/-0.73	0.001
Hematocrite (%)	35.5+/-3.3	33.9+/-2.3	0.002
Reticulocytes (mm3)	62188 +/-42002	44856 +/-37228	0.002
Iron (µmol/l)	9.6 +/- 2.8	10.3 +/-3.2	0.400
Ferritin (µg/l)	183+/- 102	312 +/-166	0.001
TSI (%)	19 +/- 7	24.6 +/-6.4	0.022
Total Iron Dose (mg)	664 +/- 547	712+/-660	0.743
CRP (ng/ml)	4.85 +/- 3.43	4.1 +/- 6.11	0.584
PTH (pg/ml)	424 +/- 481	401 +/ 437	0.910
25-OH VitD (ng/ml)	31 +/- 7	29 +/- 7.9	0.591
EPO (Mu/ml)	13.5 +/-10	29.1+/-26.4	0.021

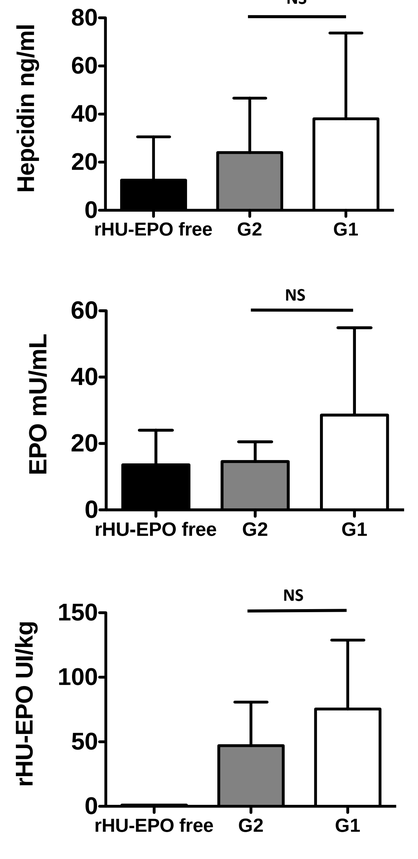
3/ Hepcidin is decreased in EPO free patients





4/ EPO free patients have a specific phenotype





CONCLUSIONS

*** We described a novel mechanism that contributes to the absence of rHU-EPO administration**

*** EPO free patients seem to have a functional EPO-Hepcidin axis.**

*** Lower Hepcidin allows better delivery of iron to erythroid progenitor .**

*** A specific combination of clinical and biological parameters help to detect rHu-EPO free patients (Longer dialysis duration, renal cyst, lower ferritin and hepcidin, Endogeous EPO secretion).**

*** Ferritin as a surrogate marker of Hepcidin status ?**

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