Dyserythropoiesis evaluated by the RED score and hepcidin:ferritin ratio predicts response to erythropoietin in lower-risk myelodysplastic syndromes

Sophie Park,[1,2] Olivier Kosmider,[3] Frédéric Maloisel,[4] Bernard Drenou,[5] Nicolas Chapuis,[6] Thibaud Lefebvre,[7] Zoubida Karim,[6] Hervé Puy,[6] Anne Sophie Alary,[3] Sarah Ducamp,[7] Frédérique Verdier,[7] Cécile Bouilloux,[1,2] Alice Rousseau,[7] Marie-Christine Jacob,[8] Agathe Debliquis,[9] Agnes Charpentier,[10] Emmanuel Gyan,[11] Bruno Anglaret,[12] Cecile Leyronnas,[13] Selim Corm,[14] Borhane Slama,[15] Stephane Cheze,[16] Kamel Laribi,[17] Shanti Amé,[18] Christian Rose,[19] Florence Lachenal,[20] Andrea Toma,[21] Gian Matteo Pica,[22] Martin Carre,[1,2] Frédéric Garban,[1,2] Clara Mariette,[1,2] Jean-Yves Cahn,[1,2] Mathieu Meunier,[1,2] Olivier Herault,[23] Pierre Fenaux,[24] Orianne Wagner-Ballon,[25] Valerie Bardet,[26] Francois Dreyfus[27] and Michaela Fontenay[3]

[1]Department of Hematology, CHU Grenoble-Alpes, Grenoble; [2]Institute for Advanced Biosciences, INSERM U1209, CNRS UMR 5309, Grenoble; [3]Assistance Publique-Hôpitaux de Paris (AP-HP), Service d'Hématologie Biologique, Hôpitaux Universitaires Paris Centre, Institut Cochin, Université Paris Descartes; [4]SOL Hematology, Clinique Saint Anne, Strasbourg; [5]Department of Hematology, Hôpital Emile Muller, CH de Mulhouse; [6]INSERM UMR1149, CNRS 8252 - Centre de Recherche sur l'Inflammation (CRI) Equipe "Hème, Fer et Pathologies Inflammatoires", Labex GREX, Centre Français des Porphyries - Hôpital Louis Mourier HUPNVS, Paris; [7]Institut Cochin, INSERM U1016, CNRS UMR 8104, Paris Descartes University; [8]Institut de Biologie et Pathologie, Immunology, CHU Grenoble-Alpes, Grenoble; [9]Hematology Laboratory, Mulhouse Hospital; [10]Department of Hematology, Hôpital St Philibert, Lille; [11]Department of Hematology, CHU de Tours; [12]CH de Valence; [13]Institut Daniel Hollard, Grenoble; [14]Medipole de Savoie, Challes les Eaux; [15]Department of Hematology, CH d'Avignon; [16]Department of Hematology, CHU Caen; [17]Department of Hematology , CH Le Mans; [18]Department of Hematology, Hôpital Civil, CHU Strasbourg; [19]Department of Hematology, Hôpital Saint Vincent de Paul, Lille; [20]Department of Hematology CH Pierre Oudot, Bourgoin-Jallieu; [21]Department of Hematology, Hôpital Universitaire Henri Mondor, AP-HP, Université Paris 12, Créteil; [22]Department of Hematology, CH Métropole Savoie, Chambery; [23]Laboratoire d'Hématologie, CHU Tours; [24]Department of Hematology, Saint Louis Hospital, AP-HP, Université Paris Diderot; [25]Département d'Hématologie et Immunologie Biologiques, Hôpital Universitaire Henri Mondor, Creteil; [26]Service d'Hématologie Immunologie Transfusion, Hôpitaux Universitaires Paris Ile de France-Ouest, AP-HP and [27]Department of Hematology, Cochin Hospital, Paris V, France
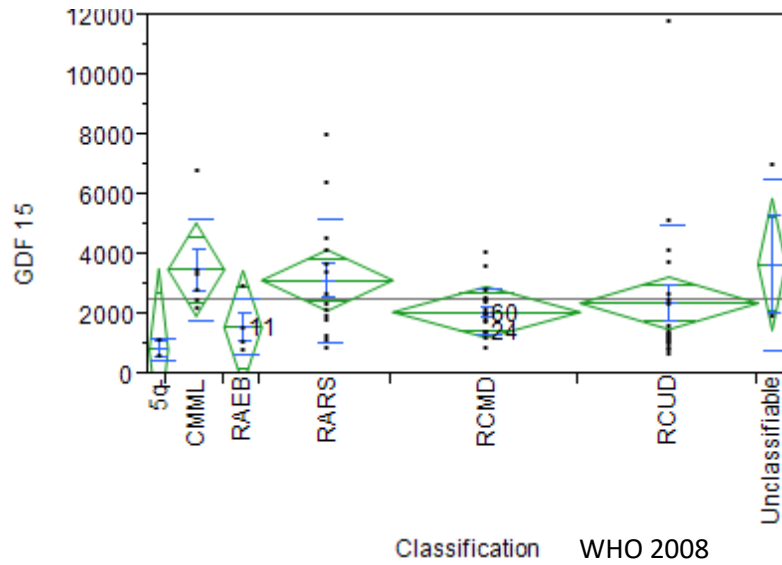
Supplemental figures

Sup Figure 1. Barcode representation of the genetic lesions associations. Each column represents an individual sample and each line represents a gene.

Karyotype: white: normal, black: abnormal; grey:NA
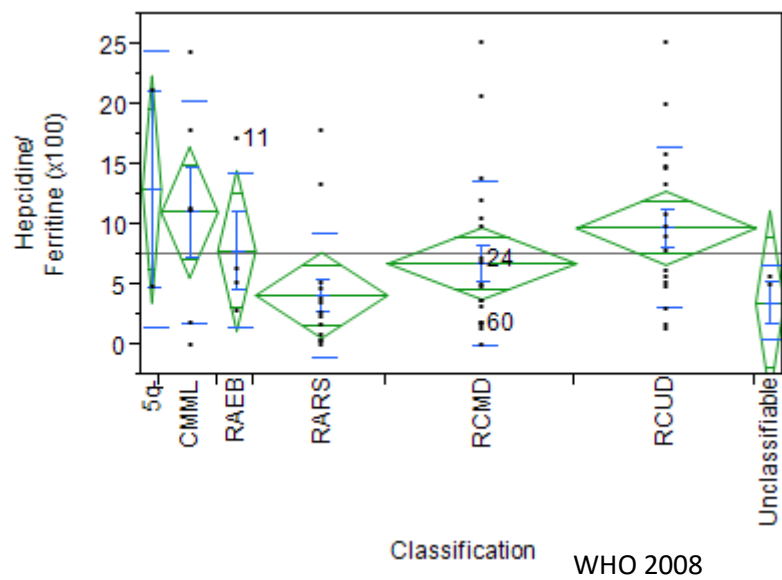
IWG 2006: white: no, black: yes

Sup Figure 2.

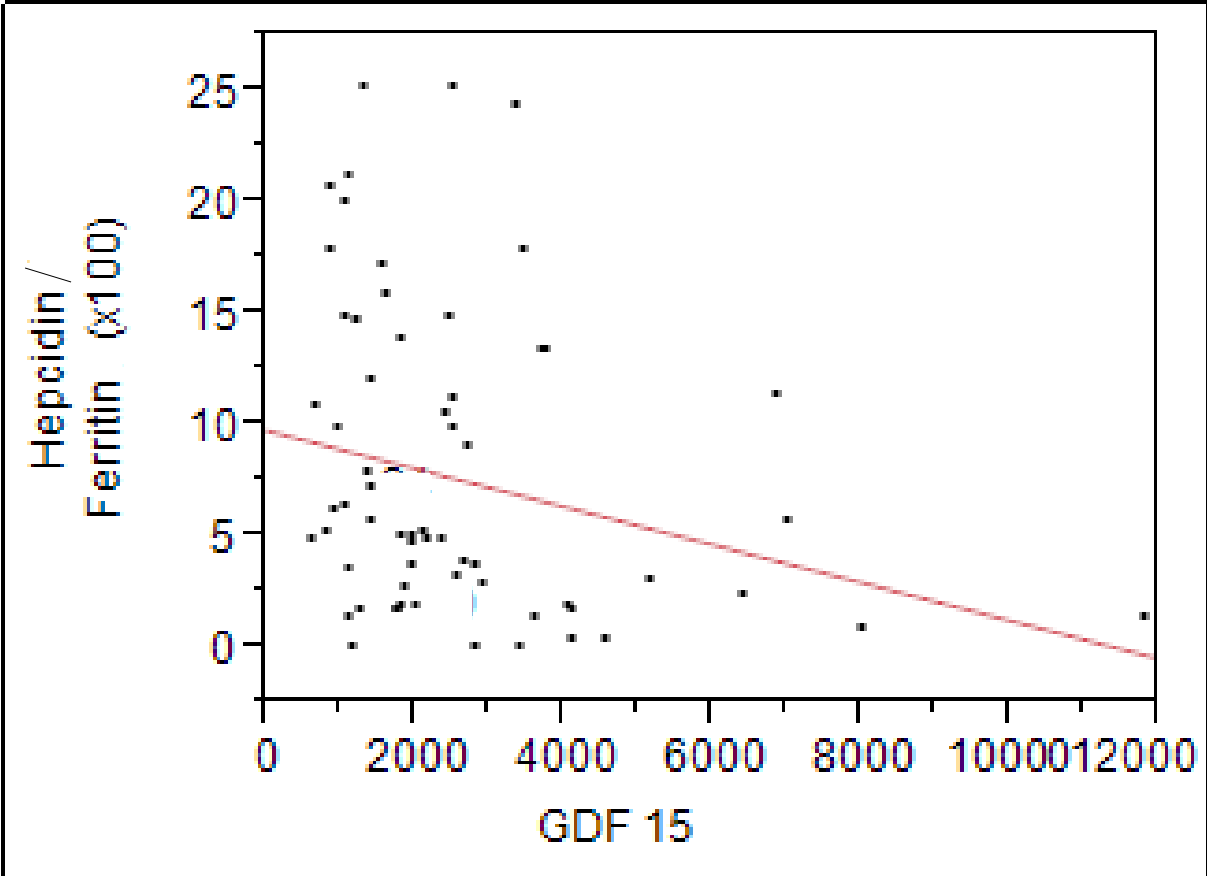GDF-15 according to WHO classification (2008)

P=0.02, Wilcoxon test

Ratio hepcidin/ferritin according to WHO classification (2008)

P=0.11

Sup Figure 3. Correlation between hepcidin/ferritin levels and GDF-15 in myelodysplastic syndrome patients treated with epoetin zeta. R2= 0.043 and p=0.04. There is an inverse correlation between GDF-15 and hepcidin/ferritin levels.
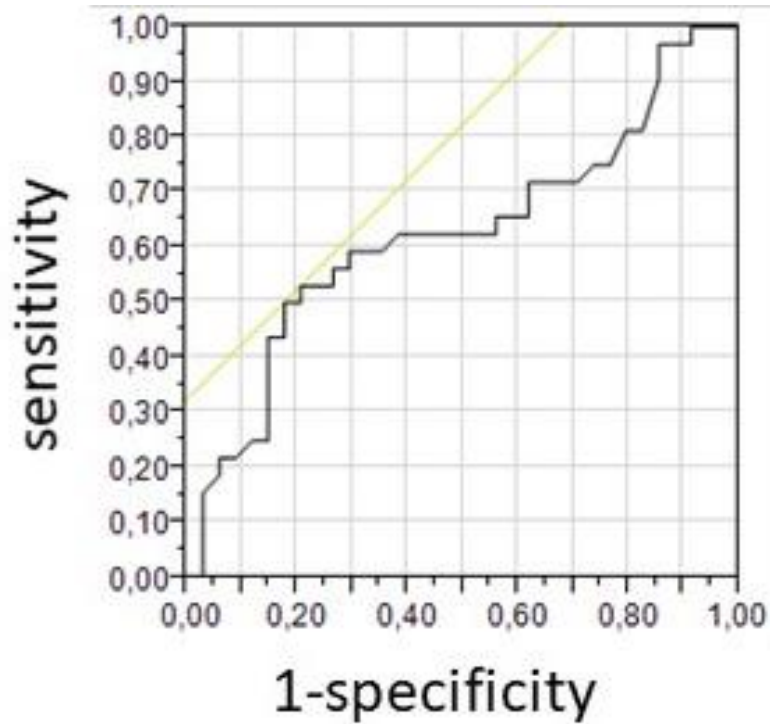

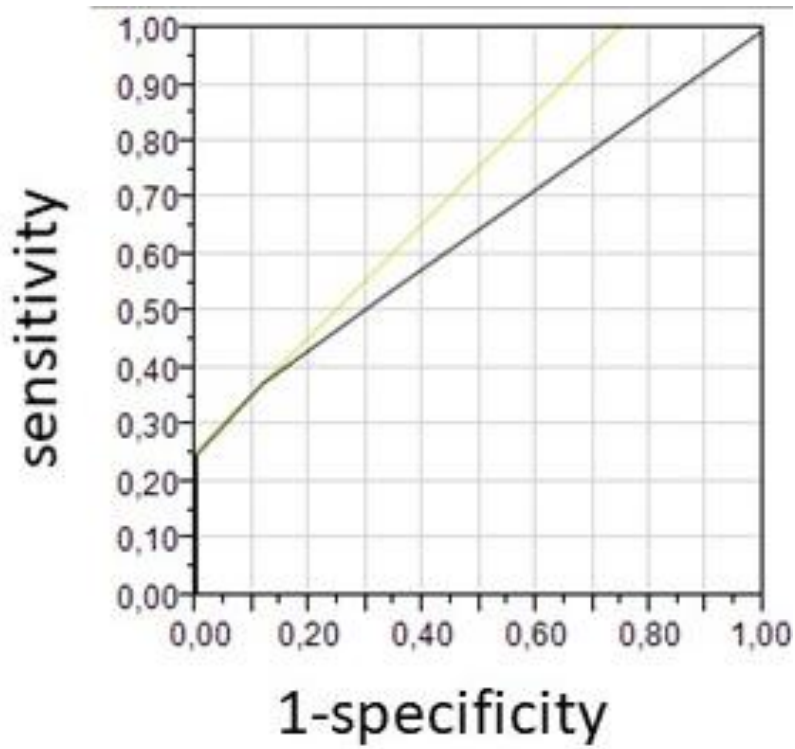Hepcidine/ferritinX100=9.74248-0.0008534*GDF15

P=0.04

R2 adjusted=0.043

Supplemental figures 4. ROC curves.

Sup Figure 4A. ROC curve for hepcidin/ferritin ratio. Area under the curve : 0.627. The best value of hepcidin/ferritin ratio for Sensitivity 53% and Specificity 79% is 9.

Sup Figure 4B. ROC curve for the Red score. Area under the curve : 0.645. The best value of the Red score for Sensitivity 37.5% and Specificity 89% is 4.

Sup Figure 4C. ROC curve for GDF-15. Area under the curve : 0.56. The best value of GDF-15 for Sensitivity 65.6% and Specificity 59% is 2000 pg/ml.