Supplemental Information

SUPPLEMENTAL TABLE 4 List of Genes Involved in Iron Metabolism Further Analyzed Using WES Data Obtained on Both Patients

Gene	Full gene name	Protein
ABCB7	ATP-binding cassette, sub-family B	ABCB7
ALAS2	(MDR/TAP), member 7	ALACO
BMP6	Delta-aminolevulinate synthase 2	ALAS2 BMP6
	Bone morphogenetic protein 6	
CYBRD1	Cytochrome b reductase 1	CYBRD1
FTH1	Ferritin, heavy polypeptide 1	Ferritin H chain
FTL	Ferritin, light polypeptide	Ferritin L chain
FXN	Frataxin	Frataxin
GDF15	Growth differentiation factor 15	GDF15
GLRX5	Glutaredoxin 5	Glutaredoxin 5
GPI	Glucose-6-phosphate isomerase	Glucose-6-phosphate isomerase
HAMP	Hepcidin antimicrobial peptide	Hepcidin
HFE	Hemochromatosis	HFE
HFE2	Hemochromatosis type 2	Hemojuvelin
HM0X1	Heme oxygenase (decycling)1	Heme oxygenase-1
HM0X2	Heme oxygenase (decycling)2	Heme oxygenase-2
MON1A	MON1 homolog A	Vacuolar fusion protein MON1 homolog A
NEO1	Neogenin	Neogenin
SLC11A2	Solute carrier family 11, member 2	DMT1
SLC25A28	Solute carrier family 25, member 28	SLC25A28
SLC25A37	Solute carrier family 25, member 37	Mitoferrin-1
SLC39A1	Solute carrier family 39, member 1	ZIP1
SLC40A1	Solute carrier family 40, member 1	Ferroportin
SMAD4	SMAD family member 4	SMAD4
STEAP3	STEAP family member 3	STEAP3
TF	Transferrin	Transferrin
TFR2	Transferrin receptor 2	TfR2
TFRC	Transferrin receptor 1	TfR1
TWGS1	Twisted gastrulation homolog 1	TWGS1

Document laboratory findings of iron deficiency compatible with TMPRSS6 mutation (low hemoglobin, low MCV, very low transferrin saturation) Consider chronic blood loss, poor dietary intake, chronic inflammatory condition Assess response to oral iron therapy Hematological response obtained with Hematological response not obtained continuation of oral iron but with persistence of hypoferremia Attempt to discontinue oral iron therapy Document inability to sustain Document inappropriate hematological response despite evidence response to oral iron absorption test of iron stores Exclude cases not compatible with a congenital disorder (i.e. cases with a prior complete blood count that was normal) Consider molecular genetic testing for TMPRSS6 mutation

SUPPLEMENTAL FIGURE 1

Suggested diagnostic algorithm for the evaluation of IRIDA.