

**Supplemental Table 1. Top 10 representative differentially expressed proteins.**

Gene ID	Gene Symbol	Protein Description	Log2 ratio	p value
<b>HRvsNormal</b>				
4501989	AFP	alpha-fetoprotein precursor	-1.05700	0.00673
156523970	AHSG	alpha-2-HS-glycoprotein preproprotein	-1.28433	0.00223
4502027	ALB	serum albumin preproprotein	-0.76733	0.01305
217272874	CCDC37	coiled-coil domain-containing protein 37	-1.37500	0.00588
261824039	HAUS4	HAUS augmin-like complex subunit 4 isoform 2	-1.07967	0.00525
112382257	INADL	inaD-like protein	-0.95600	0.00725
312433998	LTF	lactotransferrin isoform 2	-1.42800	0.00456
209862911	APOA1	apolipoprotein A-I preproprotein	-0.68800	0.00903
256818778	UNC80	protein unc-80 homolog isoform 2	-0.87400	0.00470
38505215	ZNF614	zinc finger protein 614	-0.85567	0.00758
<b>HRTXLvsHR</b>				
4757962	CDKN1B	cyclin-dependent kinase inhibitor 1B	0.19000	0.03786
4503123	CTGF	connective tissue growth factor precursor	-0.23400	0.02560
384081596	CTSL	cathepsin L1 isoform 2	-0.18367	0.04979
4504437	HMOX1	heme oxygenase 1	0.52633	0.00003
9558749	LOC101930123	eukaryotic elongation factor 2 kinase	-0.15733	0.03172
169646754	ANGPT2	angiopoietin-2 isoform c precursor	0.24233	0.00889
157311622	ACSM2B	acyl-coenzyme A synthetase ACSM2B,	-0.17467	0.03685
11967991	SOX17	transcription factor SOX-17	0.26300	0.01250
4505571	SQSTM1	sequestosome-1 isoform 1	0.22267	0.00019
167614488	TBC1D10B	TBC1 domain family member 10B	0.17600	0.01346
<b>Overlapping proteins of HRTXLvsNormal and HRTXLvsHR</b>				
169646754	ANGPT2	angiopoietin-2 isoform c precursor		
4757962	CDKN1B	cyclin-dependent kinase inhibitor 1B		
4503123	CTGF	connective tissue growth factor precursor		
384081596	CTSL	cathepsin L1 isoform 2		
4504437	HMOX1	heme oxygenase 1		
11967991	SOX17	transcription factor SOX-17		
4505571	SQSTM1	sequestosome-1 isoform 1		
167614488	TBC1D10B	TBC1 domain family member 10B		

**Supplemental Table 1.** Top 10 representative differentially expressed proteins between different groups and overlapping proteins of HRTXL vs. Normal and HRTXL vs. HR comparisons. Log2 ratio: a positive value indicates up-regulation; a negative value indicates down-regulation.  $p < 0.05$ .

**Supplemental Table 2.** Functions of differential proteins by GO analysis.

Function	GO ID	GO Term	HRvsNormal Down-regulated	HRTLvsHR Up-regulation	HRTLvsHR Down-regulation
Response to oxygen levels	GO:0051346	negative regulation of hydrolase activity	A2M; APOA1; ITIH2; SERPINF2; ZFYVE1; AMOT		
	GO:0036293	response to decreased oxygen levels		CDKN1B; HMOX1	ANGPT2; CTGF
	GO:0070482	response to oxygen levels		CDKN1B; HMOX1	ANGPT2; CTGF
	GO:0001666	response to hypoxia		CDKN1B; HMOX1	ANGPT2
Regulation of inflammatory response	GO:0050727	regulation of inflammatory response	A2M; AHSG; APOA1; SHPK		
	GO:0002526	acute inflammatory response	A2M; AHSG; SERPINF2		
	GO:0006954	inflammatory response	A2M; AHSG; APOA1; SERPINF2; SHPK		
Response to stimulus	GO:0032101	regulation of response to external stimulus	A2M; AHSG; APOA1; LTF; SERPINF2; SHPK		
	GO:0048583	regulation of response to stimulus		CDKN1B; HMOX1; SQSTM1; TBC1D10B; SOX17	ANGPT2; CTGF; CTSL
	GO:0009628	response to abiotic stimulus		CDKN1B; HMOX1	ANGPT2; CTGF
	GO:0070887	cellular response to chemical stimulus		CDKN1B; HMOX1; SQSTM1; ACSM2B	ANGPT2; CTGF; CTSL
	GO:0042221	response to chemical		CDKN1B; HMOX1; SQSTM1; ACSM2B	ANGPT2; CTGF; CTSL
	GO:0014070	response to organic cyclic compound		CDKN1B; HMOX1	ANGPT2; CTGF
	GO:0097305	response to alcohol		CDKN1B	CTGF
	GO:0046686	response to cadmium ion		CDKN1B; HMOX1	
	GO:0010033	response to organic substance		CDKN1B; HMOX1; SQSTM1	ANGPT2; CTGF; CTSL
Response to hormones	GO:0043627	response to estrogen		CDKN1B; HMOX1	CTGF
	GO:0048545	response to steroid hormone		CDKN1B; HMOX1	CTGF
	GO:0032355	response to estradiol		CDKN1B	CTGF
Regulation of enzyme	GO:0000079	regulation of cyclin-dependent		CDKN1B	

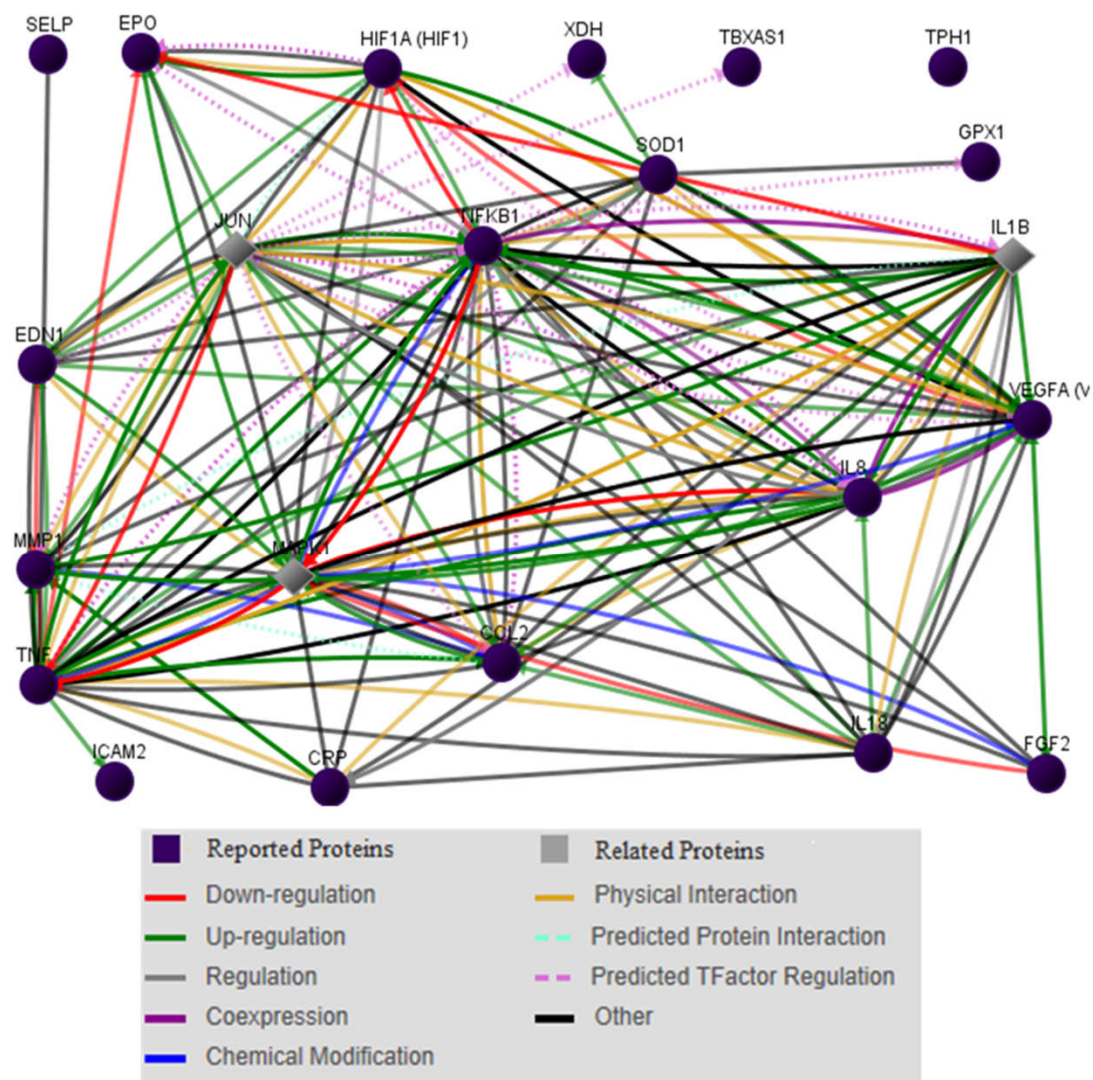
<b>activity</b>		protein serine/threonine kinase activity			
<b>Immune response</b>	GO:0006959	humoral immune response	A2M; BST1; LTF		
<b>Regulation of metabolic process</b>	GO:0030500	regulation of bone mineralization	AHSG; LTF		
	GO:0070167	regulation of biomineral tissue development	AHSG; LTF		
	GO:0032963	collagen metabolic process			CTGF; CTSL
	GO:0051247	positive regulation of protein metabolic process		CDKN1B; HMOX1; SQSTM1; SOX17	CTGF
	GO:0044259	multicellular organismal macromolecule metabolic process			CTGF; CTSL
	GO:0009746	response to hexose		CDKN1B	ANGPT2; CTGF
	GO:0009749	response to glucose		CDKN1B	ANGPT2; CTGF
	GO:0044236	multicellular organismal metabolic process			CTGF; CTSL
	GO:0034284	response to monosaccharide		CDKN1B	ANGPT2; CTGF
	GO:0009743	response to carbohydrate		CDKN1B	ANGPT2; CTGF
	GO:0010712	regulation of collagen metabolic process			CTGF
	GO:0010714	positive regulation of collagen metabolic process			CTGF
	GO:0044246	regulation of multicellular organismal metabolic process			CTGF
	GO:0044253	positive regulation of multicellular organismal metabolic process			CTGF
<b>Regulation of biosynthetic process</b>	GO:0032965	regulation of collagen biosynthetic process			CTGF
	GO:0032967	positive regulation of			CTGF

		collagen biosynthetic process			
	GO:0032964	collagen biosynthetic process			CTGF
	GO:0010557	positive regulation of macromolecule biosynthetic process		HMOX1; SQSTM1; SOX17	CTGF
<b>Cellular component movement</b>	GO:0051271	negative regulation of cellular component movement		CDKN1B; HMOX1	ANGPT2
	GO:0006928	cellular component movement		CDKN1B; HMOX1; SOX17	ANGPT2; CTGF
	GO:0051270	regulation of cellular component movement		CDKN1B; HMOX1;	ANGPT2
<b>Cell growth</b>	GO:0045765	regulation of angiogenesis		HMOX1	ANGPT2
	GO:0071850	mitotic cell cycle arrest		CDKN1B	
	GO:0001558	regulation of cell growth		CDKN1B; SOX17	CTGF
<b>Cell proliferation</b>	GO:0042127	regulation of cell proliferation		CDKN1B; HMOX1; SOX17	CTGF
	GO:0050673	epithelial cell proliferation		CDKN1B; HMOX1	
<b>Cell migration</b>	GO:0030336	negative regulation of cell migration		HMOX1	ANGPT2
	GO:0043537	negative regulation of blood vessel endothelial cell migration			ANGPT2
	GO:2000146	negative regulation of cell motility		HMOX1	ANGPT2
	GO:0040013	negative regulation of locomotion		HMOX1	ANGPT2
	GO:0010596	negative regulation of endothelial cell migration			ANGPT2
	GO:0016477	cell migration		HMOX1; SOX17	ANGPT2; CTGF
	GO:0048870	cell motility		HMOX1; SOX17	ANGPT2; CTGF
	GO:0043535	regulation of blood vessel endothelial cell migration			ANGPT2
<b>Cell death</b>	GO:0010942	positive regulation of		CDKN1B; SQSTM1	CTGF

		cell death			
<b>Tissue and cell development</b>	GO:0002576	platelet degranulation	A2M; ALB; APOA1; SERPINF2		
	GO:0070278	extracellular matrix constituent secretion			CTGF
	GO:0001525	angiogenesis		HMOX1; SOX17	ANGPT2; CTGF
	GO:0001944	vasculature development		HMOX1; SOX17	ANGPT2; CTGF
	GO:2000026	regulation of multicellular organismal development		CDKN1B; HMOX1; SOX17	ANGPT2; CTGF
	GO:0051094	positive regulation of developmental process		HMOX1; SOX17	ANGPT2; CTGF
	GO:0048514	blood vessel morphogenesis		HMOX1; SOX17	ANGPT2; CTGF
	GO:0048646	anatomical structure formation involved in morphogenesis		HMOX1; SOX17	ANGPT2; CTGF
	GO:0050793	regulation of developmental process		CDKN1B; HMOX1; SOX17	ANGPT2; CTGF
	GO:0001568	blood vessel development		HMOX1; SOX17	ANGPT2; CTGF
	GO:1901342	regulation of vasculature development		HMOX1;	ANGPT2
	GO:0051239	regulation of multicellular organismal process		CDKN1B; HMOX1; SOX17	ANGPT2; CTGF
	GO:0051495	positive regulation of cytoskeleton organization		CDKN1B	CTGF

**Supplemental Table 2.** Functions of differential proteins by GO analysis. GO ID: ID of Gene Ontology term used in Gene Ontology Project. GO Term: the name of Gene Ontology term.

## Supplemental Figure 1



**Supplemental Figure 1.** The network of reported proteins associated with HR generated in the GeneMANIA analysis. Protein names corresponded to gene symbols: SELP: P-selection; EPO: erythropoietin; HIF1: hypoxia inducible factor-1; XDH: xanthine dehydrogenase/oxidase; TBSAX1: thromboxane synthase; TPH1: tryptophan hydroxylase 1; SOD1: superoxide dismutase 1; GPX1: glutathione peroxidase 1; JUN: v-jun avian sarcoma virus 17 oncogene homolog; NFκB: nuclear factor κB; IL1B: interleukin 1, beta; END1: endothelin; VEGFA: vascular endothelial growth factor A; MMP1: matrix metalloproteinase-1; MARK1: microtubule affinity-regulating kinase 1; IL8: interleukin 8; CCL2: monocyte chemoattractant protein-1; TNF: tumor necrosis proteins; ICAM2: intercellular adhesion molecules; CRP: C-reaction protein; IL18: interleukin 18; FGF2: fibroblast growth factors-2.