

**Extended Table 1.** Table of differentially expressed genes with logarithmic fold change  $\log(\text{G6PD}^{\text{KD}}/\text{control})$  less or equal to -1 among the 3216 differentially expressed genes in HUVECs. Genes are ordered by expression.

ENSEMBL	SYMBOL	GENENAME	G6PD <sup>KD</sup> vs ctrl: logFC	G6PD <sup>KD</sup> vs ctrl : FDR
ENSG00000160211	G6PD	glucose-6-phosphate dehydrogenase	-3.085117842535	0
ENSG00000049540	ELN	elastin	-2.506967765570	1.37716 e <sup>-59</sup>
ENSG00000187513	GJA4	gap junction protein alpha 4	-2.017167581098	0
ENSG00000140092	FBLN5	fibulin 5	-1.358019180929	1.33291 e <sup>-55</sup>
ENSG00000122641	INHBA	inhibin subunit beta A	-1.348684049315	2.05706 e <sup>-50</sup>
ENSG00000265107	GJA5	gap junction protein alpha 5	-1.307709107698	2.70104 e <sup>-87</sup>
ENSG00000136928	GABBR2	gamma-aminobutyric acid type B receptor subunit 2	-1.301767478588	2.82392 e <sup>-05</sup>
ENSG00000069482	GAL	galanin and GMAP prepropeptide	-1.298538650590	0.008167222
ENSG00000073737	DHRS9	dehydrogenase/reductase 9	-1.285747193423	4.44652 e <sup>-14</sup>
ENSG0000010671	BTK	Bruton tyrosine kinase	-1.244838434208	1.95983 e <sup>-08</sup>
ENSG00000161638	ITGA5	integrin subunit alpha 5	-1.242524748572	3.62902 e <sup>-76</sup>
ENSG00000111886	GABRR2	gamma-aminobutyric acid type A receptor rho2 subunit	-1.170703355055	0.034432473
ENSG00000132541	RIDA	reactive intermediate imine deaminase A homolog	-1.170038514697	4.01384 e <sup>-10</sup>
ENSG00000144674	GOLGA4	golgin A4	-1.168280446256	6.40297 e <sup>-94</sup>
ENSG00000173597	SULT1B1	sulfotransferase family 1B member 1	-1.167036673751	3.6327 e <sup>-109</sup>
ENSG00000125148	MT2A	metallothionein 2A	-1.106758601378	8.91307 e <sup>-39</sup>
ENSG00000134363	FST	follistatin	-1.105295654442	8.9845 e <sup>-30</sup>
ENSG00000116183	PAPPA2	pappalysin 2	-1.104796144010	0.000287774
ENSG00000113721	PDGFRB	platelet derived growth factor receptor beta	-1.100336318322	0.076995282
ENSG00000187689	AMTN	amelotin	-1.049357561835	2.10888 e <sup>-08</sup>
ENSG00000125740	FOSB	FosB proto-oncogene, AP-1 transcription factor subunit	-1.044894984992	5.12874 e <sup>-15</sup>
ENSG00000107165	TYRP1	tyrosinase related protein 1	-1.043852718115	6.31117 e <sup>-05</sup>
ENSG00000138378	STAT4	signal transducer and activator of transcription 4	-1.035287352096	5.35083 e <sup>-06</sup>
ENSG00000241945	PWP2	PWP2, small subunit processome component	-1.029257752058	0.010676468
ENSG00000050767	COL23A1	collagen type XXIII alpha 1 chain	-1.020922660842	0.000289029
ENSG00000197565	COL4A6	collagen type IV alpha 6 chain	-1.018591609403	2.50429 e <sup>-05</sup>

**Extended Table 2.** Reactome pathway enrichment analyses of the 3216 Differentially Expressed Genes (DEGs) identified comparing G6PD<sup>KD</sup> vs control. Pathways with adjusted p-value lower than 0.01 have been considered as enriched. Pathways are ordered by mean Fold Change (G6PD<sup>KD</sup> / control) reported in logarithmic scale in the table. Additionally, the fold change mean of the pathway genes has been calculated considering up and down-regulated genes separately.

ID	Pathway	DEGs in Pathway	Adjusted p-value	mean Fold Change of all genes (log)	mean Fold Change of upregulated genes (log)	mean Fold Change of downregulated genes (log)
R-HSA-216083	Integrin cell surface interactions	38	0.00507919	0.4771	0.6321	-0.5297
R-HSA-202733	Cell surface interactions at the vascular wall	54	0.00507919	0.3488	0.4647	-0.3315
R-HSA-1474244	Extracellular matrix organization	125	4.9669E-05	0.3422	0.4881	-0.4582
R-HSA-6785807	Interleukin-4 and Interleukin-13 signaling	46	0.00507919	0.3298	0.5565	-0.2951
R-HSA-1474228	Degradation of the extracellular matrix	56	0.00507919	0.29822	0.4316	-0.3450
R-HSA-1280215	Cytokine Signaling in Immune system	279	1.482E-06	0.2544	0.4976	-0.2411
R-HSA-449147	Signaling by Interleukins	185	0.00048029	0.2127	0.4796	-0.2347
R-HSA-6798695	Neutrophil degranulation	190	0.00048029	0.2023	0.3521	-0.22293
R-HSA-977225	Amyloid fiber formation	53	0.00507919	-0.0451	0.3252	-0.3529
R-HSA-69620	Cell Cycle Checkpoints	160	0.00507919	-0.1975	0.3004	-0.2750
R-HSA-68886	M Phase	207	0.00145827	-0.2174	0.2610	-0.2794

**Extended Table 3.** The table provides the nucleotide sequences for shRNA, MO, sgRNA and primers for genotyping, sequencing and qPCR used in this study.

Oligonucleotides		
shRNA targeting sequence: G6PD	5'-CAACAGATACAAGAACGTGAA-3'	TRCN0000025817 (McBrayer, Yarrington et al. 2012)
shRNA targeting sequence: PGD:	5'-GTGGATGATTTTCATCGAGAAA-3'	TRCN0000028584
Morpholino: MO-elna (Gene Tools)	5'-GATCAGTGTTGCGTTGCTCCT TCT-3	(Moriyama, Ito et al. 2016)
Morpholino: MO-elnb (Gene Tools)	5'-CCGGGCCATCCTGCTCTGTAATAAC-3'	(Moriyama, Ito et al. 2016)
Morpholino: MO-gata1 (Gene Tools)	5'-CTGCAAGTGTAGTATTGAAGATGTC-3'	ZDB-MRPHLNO-050208-10
g6pd sgRNA 1	5'-GGTCCCGAAAGGCTCCACTCGT-3' 5'-GAGTGGAGCCTTTTCGGGACCGA-3'	N/A
g6pd sgRNA 2	5'-GGAGGATATTTTGACGATTTGT-3' 5'-AAATCGTCAAATATCCTCCGA-3'	N/A
pgd sgRNA1	5'-GGACATGCAGCTGATCTGTGGT-3' 5'-CACAGATCAGCTGCATGTCCGA-3'	N/A
pgd sgRNA2	5'-GGAGAAGAATCTTCTGTTTGTGT-3' 5'-ACAAACAGAAGATTCTTCTCCGA-3'	N/A
elna sgRNA	5'-GGAAGATTCTACCCAATGGCGT-3' 5'-GCCATTGGGTAGAATCTTCCGA-3'	N/A
pgd specific oligo <i>pgd</i> <sup>uto71</sup>	5'ATTTAGGTGACACTATAG <b>GGACATGCAGCT GATCTGTGG</b> TTTTAGAGCTAGAAATAGCAAG-3'	N/A
g6pd specific oligo <i>g6pd</i> <sup>uto70</sup>	5'ATTTAGGTGACACTATAG <b>GGTCCCGAAAGG CTCCACTC</b> GTTTTAGAGCTAGAAATAGCAAG-3'	
Constant oligo	5'AAAGCACCGACTCGGTGCCACTTTTTCAAGTTGATAACGGACTAGCCTTATTTAACTTGCTATTTCTAGCTCTAAAAC-3'	(Gagnon, Valen et al. 2014)

RT-qPCR	Forward primer (5'-3')	Reverse primer (5'-3')	References
Human <i>G6PD</i>	GCAAACAGAGTGAGCCCTTC	GAGTTGCGGGCAAAGAAGT	(Liu, Li et al. 2015)
Human <i>PGD</i>	CGGATCATCCTCCTGGTG	ATGATGTCACCAGTATCCAACAA	(Bhanot, Weisberg et al. 2017)
Human <i>KLF2</i>	GCACCGCCACTCACACCTG	CCGCAGCCGTCCCAGTTG	(Wang, Xiong et al. 2016)
Human <i>ELASTIN</i> (1)	GGCCATTCTGGTGGAGTTC C	AACTGGCTTAAGAGGTTTGCCT CCA	(Deslee, Woods et al. 2009)
Human <i>ELASTIN</i> (2)	AAAGCAGCAGCAAAGTTCGG	ACCTGGGACAACCTGGAATCC	(Gruemmer, Klein-Hitpass et al. 2005)
Human <i>LAMA4</i>	GGATGTCAGCGGAGAAATGG	CGACAGGGTGTGAAAGAATCC	
Human <i>COL4A1</i>	CCTGGTCTTGAAAGGTGATA AG	CCCGCTAT CCCTTGA TCTC	(Wang, Xiong et al. 2016)
Human <i>FN1</i>	CCATAAAGGGCAACCAAGAG	ACCTCGGTGTTGTAAGGTGG	(Luco, Pan et al. 2010)
Human <i>B-ACTIN</i>	GATGGAGTTGAAGGTAGTTT CGT	GCGGGAAATCGTGCGTAGCATT	
Mouse <i>B-actin</i>	GTA CTCTGTTGGATCGGTGG	AAACGCAGCTCAGTAACAGTCC	
Mouse <i>Pgd</i>	CACCTGCTGCCAAAGATCAG	TCAAACCTGGAACCTTCTGGGGA	
Mouse <i>Elastin</i>	TGGTATTGGTGGCATCGG	CCTTGGCTTTGACTCCTGTG	(Ambalavanan, Li et al. 2007)
Mouse <i>Cdh5</i>	GACAAGGATGTGGTGCCAGT	CTGCCATACTTGACCGTGA	
Mouse <i>Col4a1</i>	CTGGCACAAAAGGGACGAG	ACGTGGCCGAGAATTTCCACC	
Mouse <i>Vegfr2</i>	TAGCTGTCGCTCTGTGGTTCT	TGTCCCCTGCAAGTAATCTGAA	
Zebrafish <i>g6pd</i>	TTTAGCTCTCAGTGCCGGAG	CTGCCACAAAAGACGTCCAA	
Zebrafish <i>pgd</i>	GAGTTCGGCTGGTCTCTGAA	ATCTCGTGTCTGTACCCGTC	
Zebrafish <i>mcherry</i>	GAACGGCCACGAGTTGAGAG	CTTGGAGCCGTACATGAACTGA GG	
Zebrafish <i>elna</i>	AGGATATGGAGGAGCTGCTG	AGAATCTTCCAGCACCACCA	
Zebrafish <i>elnb</i>	GGAAGGTACCTCTGCTCTTG	TCCTGTTCCAACCTCCTCCAG	
Zebrafish <i>B-actin</i>	GTATCCACGAGACCACCTTC A	GAGGAGGGCAAAGTGGTAAAC	(Mugoni, Postel et al. 2013)
Zebrafish <i>pdgfrb</i>	CGTTCCCAGGAGCCTTTTCT	TTGGGATCAGGGATGGGGAT	(Ando, Wang et al. 2019)
Zebrafish <i>acta2</i>	AACACCCCCTCTGTTGACA	GCATAGAGAGACAGCACTGC	
Zebrafish <i>tie1</i>	CCTGTAGAACATTGGCAGCC	AATGTTTGGTCCGAACTGCC	
Zebrafish <i>cdh5</i>	GGACACTGGACAGAGAGCAA	ACACGTAGCTCCATTGGTT	

Genotyping Oligonucleotides	Forward Primer (5'-3')	Reverse Primer (5'-3')
<i>Mouse Pgd-F1-F2</i>	GGGACACGACAGTAAGTGTT	CAAGAGAGACAGGGGCTGAG
<i>Mouse Pgd-F3-F4</i>	TGTTCCCTCAGGCCAAACTCT	GTTCCCACTTTTGCAGCGAT
<i>Mouse Tie2:Cre</i>	CGCATAACCAGTGAAACAGCATT GC	CCCTGTGCTCAGACAGAAATGA GA
<i>Mouse Cdh5:CreERT2</i>	ACACCTGCTACCATATCA TCCTAC	CATCGACCGGTAATGCAG

<i>Zebrafish</i> <i>G6pd</i> <sup>sa24272</sup>	TGTTTGC GCAGAGGCTGGAA	GAGAGGAGAGAAACCATGGGAT
<i>Zebrafish</i> <i>pgd</i> <sup>sa24360</sup>	CAGAGCATTGCTGCCAAAGT	CGGCACATTAGAAAGCAAAGAG
<i>Zebrafish pgd</i> <sup>uto71</sup> <i>HMA</i>	TGCGACTGGGTTGGAGATG	ACAAAGCACGTCCTTCATCAG
<i>Zebrafish pgd</i> <sup>uto71</sup> <i>sequencing</i>	TGTTTCTTCAGGCCACACTT	GAGCAGAGATAGCCGTCCAT
<i>Zebrafis</i> <i>g6pd</i> <sup>uto72</sup> <i>sequencin</i> <i>g</i>	CCGGTCACTCTCTCAGATGT	CCCAGCGTTCGTTCTTTACATAA
<i>Zebrafis g6pd</i> <sup>uto70</sup> <i>HMA</i>	GAGAAGGGGAGGCCAAACTG	CCCAGCGTTCGTTCTTTACATAA
<i>Zebrafis g6pd</i> <sup>uto72</sup> <i>T7E1</i>	TTTGCTCTTTGGCCGAAGTG	GCGTTTCACATTCTGACTCCA
<i>Zebrafis pgd</i> <sup>uto73</sup> <i>T7E1</i>	TGTTTCTTCAGGCCACACTT	GAGCAGAGATAGCCGTCCAT
<i>Zebrafish elna</i>	CGAGGGCGGAGGTAGATTTT	ACTTTGCTGACTGTTTCATGGA

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