Table 1:

Upregulation in HFE null primary RPE

	Fold change Experiment 1	Experiment 2	Mean
Transporters			
Slc12a1(sodium potassium chloride cotransporter 2/kidney specific absorptive isoform NKCC2)	3.2	3	3.1
Slc14a1(erythrocyte urea transporter/HUT11/RACH1)	11.12	14.46	12.8
Slc14a2(renal tubular urea transporter/HUT2/UT2)	2.8	2.65	2.7
Slc16a7(monocarboxylic acid transporter/MCT2)	3.47	4.8	4.1
Slc22a20(Organic anion transporter 6/OAT6)	3.99	2.1	3.1
Slc24a2(Retinal cone Na-Ca+K exchanger/NCKX2)	3.02	4.33	3.7
Slc30a8(zinc transporter/ZnT8)	3.1	2.44	2.8
Slc47a1(multidrug transporter/MATE1)	2.26	2.98	2.6
Slc4a4(sodium bicarbonate cotransporter/NBC)	2.4	3.28	2.8
Slc7a11(cystine/glutamate transporter/xCT)	**5.72**	**3.06**	**4.4**
Slc8a1(sodium calcium-exchange protein 1/NCX1)	2.37	3.08	2.7
Cell cycle related proteins			
Alcam(activated leukocyte cell adhesion molecule/CD166)- Cell migration and metastasis)	5.8	2.94	4.37
Amot(Angiomotin)- embryonic angiogenesis	3.54	3.96	3.75
Anln(Anillin) - cytokinesis	9.21	7.13	8.17
Anxa8(annexin A8)-Mammary gland involution	2.36	3.32	2.84
Apoa1(apolipoprotein A-I)- colon cancer progression marker	3.33	2.43	2.88
App(amyloid beta (A4) precursor protein)- prostate cancer progression	3.54	3.41	3.475
Arhgef6(Rac/Cdc42 guanine exchange factor)-stimulates Rho-dependent signals	2.18	2.54	2.36
Bcl11a(B-cell lymphoma 11A/zinc finger transcription factor)-proto-oncogene	2.54	2.18	2.36
Bcl2a1b(BCL2-related protein A1)- anti-apoptotic protein	2.95	3.21	3.08
Bmp4(bone morphogenetic protein 4)- Regulates expression of proto-oncogenes	2.47	5.79	4.13
Cav1(caveolae protein 1)- cell cycle progression	5.26	5.88	5.57
Cav2(caveolin 2)- cell cycle progression	2.71	3.33	3.02
Ccna2(cyclin A2)- G1/S and G2/M cell cycle progression	3.96	6.32	5.14
Ccnb1(cyclin B1)- G2M cell cycle progression	6.26	4.56	5.41
Ccnb2(cyclin B2)- cell cycle progression	4.94	2.04	3.49
Cdc25c(cell division cycle 25 homolog C)- G2/M cell cycle progression	2.91	4.44	3.675
Cdc2a(cell division cycle 2 homolog A)- G2/M cell cycle progression	4.1	2.69	3.395
Cdc2l5(cell division cycle 2-like 5)-cholinesterase-related cell division controller	2.18	2.48	2.33
Cdc37(cell division cycle 37 homolog)- cell cycle progression	2.01	4.33	3.17
Cdc45l(cell division cycle 45 homolog-like)-initiation of DNA replication	4.42	5.21	4.815
Cdca2(cell division cycle 2 homolog A)- cell cycle progression	4.88	6.75	5.815
Cdca5(cell division cycle associated 5)-Regulator of sister chromatid cohesion in mitosis	3.39	2.06	2.725

Cdh2(N-Cadherin)- RPE cell detachment	2.49	3.9	3.195
Cdh3(P-Cadherin)- cell cycle progression	2.64	3.9	3.27
Cdkn2c(Cyclin-dependent kinase inhibitor 2C(p18))-inhibits cell growth depending on pRb	2.34	3.52	2.93
Cenpa(Centromere protein A)-chromosome segregation and spindle assembly during mitosis	3.08	3.68	3.38
Cenpc1(Centromere protein C1)-Kinetochore size and transition to anaphase	2.03	2.33	2.18
Cenpj(Centromere protein J)- centrosome integrity and normal spindle morphology	2.07	2.37	2.22
Cenpl(Centromere protein L)- kinetochore function and mitotic progression	5.76	2.28	4.02
Cenpp(Centromere protein P)- kinetochore function and mitotic progression	2.2	3.1	2.65
Cep110(Centromere protein 110)-centrosome duplication	2.73	2.34	2.535
Cep 55(Centromere protein 55)-cytokinesis	4.03	2.4	3.215
Chaf1a(chromatin assembly factor 1, subunit A (p150))-chromatin assembly	2.03	2.74	2.385
Ckap2l(cytoskeleton associated protein 2 like)	3.42	4.06	3.74
Crem(cAMP responsive element modulator)- regulator of cyclin A expression	2.24	3.78	3.01
Ect2(Epithelial cell transforming sequence 2 oncogene)-DNA synthesis and mitosis	10.04	7.43	8.735
Edn1(endothelin 1)-cell cycle progression	4.41	3.98	4.195
Edn3(endothelin 3)-G1/S cell cycle progression	5.16	3.56	4.36
Eln(Elastin)- cell cycle progression	4.34	4.8	4.57
Hdgfl1(hepatoma derived growth factor-like 1)- tumor progression	2.57	3	2.785
Incenp(Inner centromere protein)- chromosome alignment and seggregation	2.38	3.28	2.83
Kif1b(kinesin family member 1B)-motor protein that transports mitochondria	2.664	2.79	2.727
Kif22(kinesin family member 22)-chromosome movement during mitosis and meiosis	2.72	2.2	2.46
Kif3a(kinesin family member 3A)-motor protein for organelle transport during mitosis	3.7	2.35	3.025
Mapk4(mitogen-activated protein kinase 4)-promotes entry into cell cycle	3.61	2.08	2.845
Meis1(myeloid ecotropic viral integration site1)-cofactor for induction of myeloid leukemias	2.92	3.84	3.38
Met(met proto-oncogene)-Receptor for hepatocyte growth factor	2.54	4.12	3.33
Muc13(mucin 13, epithelial transmembrane)-tumor progression	3.06	2.3	2.68
Mybl1(myeloblastosis oncogene-like 1)-proliferation inducing transcriptional activator	3.44	4.68	4.06
NDC80(NDC80 homolog, kinetochore complex component)-required for chromosome segregation	5.86	5.12	5.49
Nes(nestin)-Trafficking of cellular factors to daughter cells during cell division	3.91	3.68	3.795
Net1(neuroepithelial cell transforming gene 1)-oncogene, a guanine nucleotide exchange factor	11.32	9.15	10.235
Nr4a2(Nuclear receptor subfamily 4, group A, member 2)	4.19	7.64	5.915
Nrn1(neuritin 1)-Post-mitotic differentiation	7.91	7.44	7.675
Pkn3(protein kinase N3)-contributes to invasiveness in cancer	3.62	3.07	3.345
Prkci(protein kinase C, lambda/iota)-involved in cell polarization	4.05	5.25	4.65
Rabep1(rabaptin)-RAB GTPase binding effector protein 1	2	8.68	5.34

RAD18(RAD18 homolog)-post replication repair function	4.75	4.48	4.615
RAN(RAN, member RAS oncogene family)-mitotic spindle regulation during meiosis	2.27	2.35	2.31
Rfc5(replication factor C (activator 1) 5)-DNA replication along with PCNA	2.21	2.88	2.545
Rhou(ras homolog gene family, member U)-stimulates quiescent cells to enter cell cycle	2.73	2.69	2.71
Sept3(septin 3)-cytokinesis	3	2.6	2.8
Sept6(septin 6)-cytokinesis	3.47	3.35	3.41
Serinc3(Serine incorporator 3)- cellular transformation	2.69	3.06	2.875
Skp2(S-phase kinase-associated protein 2 (p45))-regulation of G1/S transition	2.22	3.71	2.965
Tbx20(T-box 20)-transcriptional regulator	3.51	5.61	4.56
Thada(Thyroid adenoma associated)- gene inducing thyroid adenomas protein	4.18	2.78	3.48
Tiam2(T-cell lymphoma invasion and metastasis 2)- guanine nucleotide exchange factor	2.37	4.43	3.4
Tk1(thymidine kinase 1 (Tk1))- activity high in S-phase of cell cycle in proliferating cells	3.22	4.34	3.78
Topbp1(topoisomerase (DNA) II beta binding protein)-inhibits E2F1-dependent apoptosis during G1/S transition	5.05	2.17	3.61
Vcan(versican)-regulation of cell motility, growth and differentiation	2.55	3.06	2.805
Was(Wiskott-Aldrich syndrome homolog)-regulates the structure and dynamics of the actin cytoskeleton	6.82	27	16.91

Table 2:

Downregulation in HFE null primary RPE

	Fold change Experiment 1	Experiment 2	Mean
Transporters			
Slc10a6(Sodium-dependent organic anion transporter/sodium-bile acid cotransporter family)	2.54	3.65	3.095
Slc11a2(Divalent metal transporter (DMT1))	2.56	2.52	2.54
Slc12a2(sodium potassium chloride cotransporter 2/secretory isoform NKCC1)	5.57	5.85	5.71
Slc12a4(Erythroid K-Cl cotransporter1/KCC1/single cell volume homeostasis)	2.23	2.38	2.305
Slc16a6(monocarboxylate transporter 7/MCT7)	1.99	2.7	2.345
Slc16a9(monocarboxylate transporter 9/MCT9)	5.94	3.19	4.565
Slc1a5(Sodium-dependent neutral amino acid transporter type 2/ATB0)	2.37	2.18	2.275
Slc22a12(Urate anion exchanger 1/URAT1)	2.9	2.33	2.615
Slc25a23(Mitochondrial ATP-Mg/Pi carrier protein 2/APC2)	3.68	3.83	3.755
Slc25a3(mitochondrial phosphate carrier protein/PTP)	2.58	2.19	2.385
Slc27a1(Fatty acid transport protein 1/FATP1)	2.89	2.39	2.64
Slc35c2(Ovarian cancer overexpressed gene 1/OVCOV1)	2.02	2.26	2.14
Slc38a7(sodium-dependent amino acid/proton antiporter)	2.02	3.43	2.725
Slc39a13(zinc transporter member 13/ZIP13)	2.15	2.52	2.335
Slc39a14(zinc transporter member 14/ZIP14)	6.12	2.62	4.37
Slc43a3(mouse embryonic epithelial gene 1/EEG1)	4.52	7.28	5.9
Slc4a2(anion exchanger/AE2)	2.84	3.84	3.34
Slc6a8(Creatine transporter 1/CRT)	3.23	2.74	2.985
Slc6a9(sodium- and chloride-dependent glycine transporter 1/GLYT1)	2.01	2.2	2.105
Tap1(transporter 1/ATP-binding cassette transporter/ABC transporter, MHC 1)	2.43	2.46	2.445
Fcgrt(Fc fragment of IgG transporter)	6.8	8.44	7.62
Cell cycle related proteins			
Alpl(alkaline phosphatase,liver/bone/kidney/tissue non-specific)-growth and development of bones and teeth	7.92	4.78	6.35
Alx4(aristaless-like homeobox 4)-Transcription factor involved in skull and limb development	4.12	3.44	3.78
Angptl4(angiopoietin-related protein)-inhibits proliferation,migration and tubule formation of endothelial cells	14.95	22.11	18.53
Anp32a(Acidic nuclear phosphoprotein pp32)-tumor suppressor involved in caspase-dependent and independent apoptosis	4.08	2.9	3.49
Apod(Apolipoprotein D)-tumor suppressor	3.32	2.82	3.07
Apoe(Apolipoprotein E)-lipoprotein metabolism	5.99	3.53	4.76
Aprt(adenine phosphoribosyl transferase)-decreases cell viability	3.04	2.98	3.01
B2m(beta-2 microglobulin)-major histocompatibility complex class I	4.11	3.66	3.885
Bcap31(B-cell receptor-associated protein 31)-CASP8-mediated apoptosis	2.36	2.4	2.38
Btg1(B-cell translocation gene 1)-negatively regulates cell proliferation;anti-proliferative	2.7	3.4	3.05
C1qtnf5(C1q and tumor necrosis factor related protein 5)-role in late-onset retinal degeneration	10.4	9.65	10.025

C2(complement 2)-inhibits cancer progression by suppressing protein translation initiation	8.76	8.16	8.46
C3(complement 3)-tumor suppressor	4.22	4.56	4.39
Cadm3(cell adhesion molecule 3)-cell to cell adhesion	6.88	3.05	4.965
Ccndbp1(cyclin D-type binding-protein 1)-negative regulator of gene expression	2.76	3.3	3.03
Ccng1(Cyclin G1)- inhibitor of cell proliferation by p53 mediated G2/M phase arrest	2.17	2.43	2.3
Cdh11(cadherin 11)- cell to cell adhesion	2.84	2.88	2.86
Cdkn1a(cyclin-dependent kinase inhibitor 1A (p21/WAF1))- DNA synthesis inhibitor	4.83	2.6	3.715
Cdkn2b(cyclin-dependent kinase inhibitor 2B (p15)- induces cell cycle arrest	5.83	5.83	5.83
Cebpb(CCAAT/enhancer binding protein (C/EBP), beta)-inhibits cell proliferation	3.28	2.93	3.105
Cfb(complement factor B)- regulates immune response	19.14	19.18	19.16
Cfh(complement factor H)- downregulation increases susceptibility to AMD	6.75	2.51	4.63
Ch25h(Cholesterol 25-hydroxylase)-invloved in lipid metabolism and to repress cholesterol biosynthesis	7.44	10.77	9.105
Chl1(cell adhesion molecule with homology to L1CAM)-cell to cell adhesion	3.13	5.76	4.445
Clec11a(C-type lectin domain family 11, member a)-Suppresses SCF-stimulated erythrocyte proliferation	6.89	8.94	7.915
Cpxm1(carboxypeptidase X 1 (M14 family))-cell to cell interaction	6.86	9.26	8.06
Cst3(cystatin C)-mutation results in amyloid angiopathy	9.05	8.9	8.975
Cstb(cystatin B)-intracellular thiol protease inhibitor	3.62	3.94	3.78
Dbc1(deleted in bladder cancer 1)-Inhibits cell proliferation by negative regulation of the G1/S transition	4.41	3.99	4.2
Egfr(Epidermal growth factor receptor)-mutation results in many forms of cancer	4.1	7.66	5.88
Fastk(Fas-activated serine/threonine kinase)-important role in apoptosis	2.78	3.2	2.99
Fn1(Fibronectin 1)- maintenance of cell shape	3.06	2.51	2.785
Gadd45g(growth arrest and DNA-damage-inducible 45 gamma)-cell cycle arrest	8.09	5.79	6.94
Gpc1(glypican proteoglycan 1)- controls cell cycle	7.33	7.42	7.375
HBP1(HMG-box transcription factor 1)-regulation of the cell cycle and of the Wnt pathway	3.007	3.91	3.4585
Hic1(hypermethylated in cancer 1)-tumor suppressor	3.1	4.94	4.02
Lox(lysyl oxidase)-tumor suppressor	3.37	2.52	2.945
Mtap(methylthioadenosine phosphorylase)-downregulated in many forms of cancer	2.3	3.68	2.99
Mtch1(mitochondrial carrier homolog 1)-plays a role in apoptosis	4.34	3.86	4.1
Nedd8(Neural precursor cell expressed developmentally down-regulated)-promotes proteosomal degradation of cyclins	2.78	4.27	3.525
Ogn(osteoglycin (osteoinductive factor))-induces bone formation	25.6	22.3	23.95
Parp3(poly (ADP-ribose) polymerase family, member 3)-negatively regulates G1/S cell cycle progression	3.59	4.51	4.05
Pfdn5(prefoldin 5)-repress the transcriptional activity of the proto-oncogene c-Myc	4.54	3.4	3.97
Pik3r1(phosphatidylinositol 3-kinase regulatory subunit1 (p85 alpha)-mutation enhances insulin resistance	5.65	7.4	6.525
Pink1(PTEN-induced putative kinase protein 1)-protects cells from	6.44	5.4	5.92

stress induced mitochondrial dysfunction			
Ppap2b(Phosphatidate phosphohydrolase type 2b)-involved in cell adhesion	2.94	3.17	3.055
Prelp(Proline-arginine-rich end leucine-rich repeat protein)-anchor basement membranes to the underlying connective tissue	23.95	25.35	24.65
Rarres1(RAR-responsive protein TIG1)- downregulated in cancer	4.77	4.39	4.58
Rarres2(RAR-responsive protein TIG2)- potent growth inhibitor	86.13	73	79.565
St5(suppression of tumorigenicity 5)-tumor suppressor	2.81	3.24	3.025
Tnmd(tenomodulin)- acts as an angiogenesis inhibitor	6.21	5.33	5.77
Wasf2(WAS protein family, member 2)-regulates cell shape and motility	2.5	2.19	2.345
Wisp2(WNT1 inducible signaling pathway protein 2)-modulates bone turnover and is downregulated in tumors	4.9	5.25	5.075