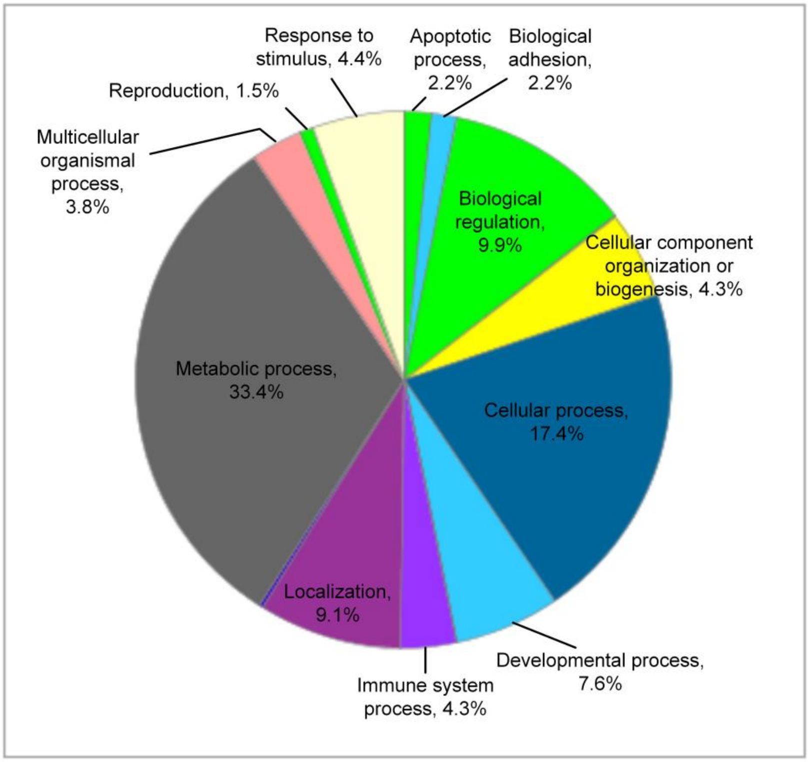
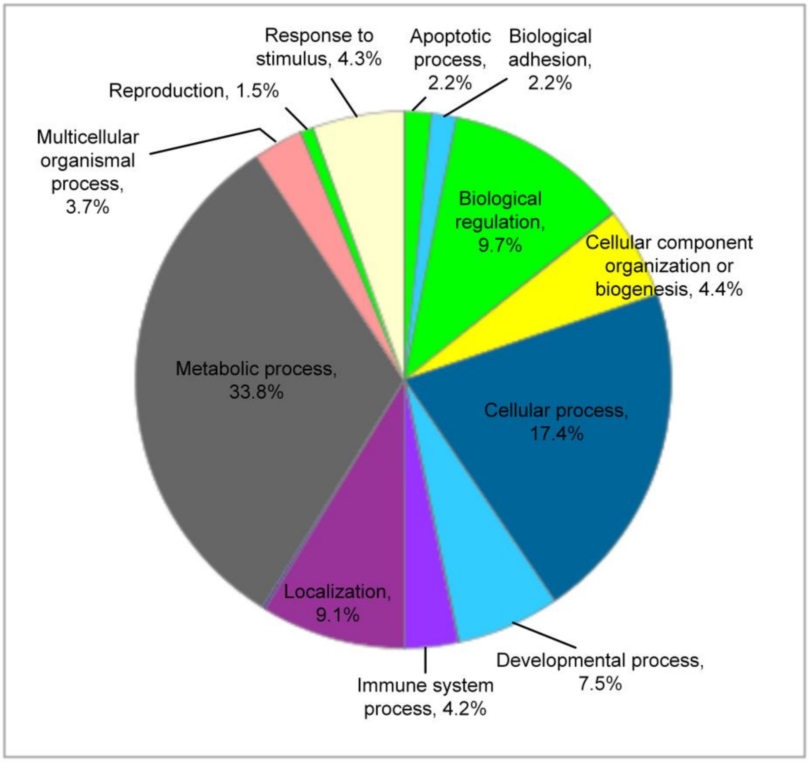
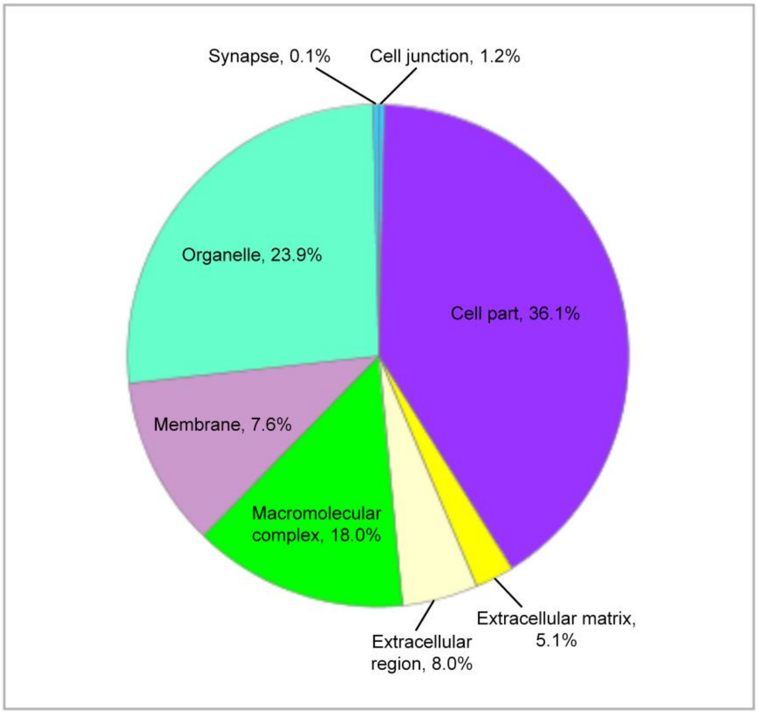

Response to stimulus, 4.4%
Apoptotic process, 2.2%
Biological adhesion, 2.2%
Reproduction, 1.5%
Multicellular organismal process, 3.8%
Biological regulation, 9.9%
Cellular component organization or biogenesis, 4.3%
Metabolic process, 33.4%
Cellular process, 17.4%
Localization, 9.1%
Developmental process, 7.6%
Immune system process, 4.3%

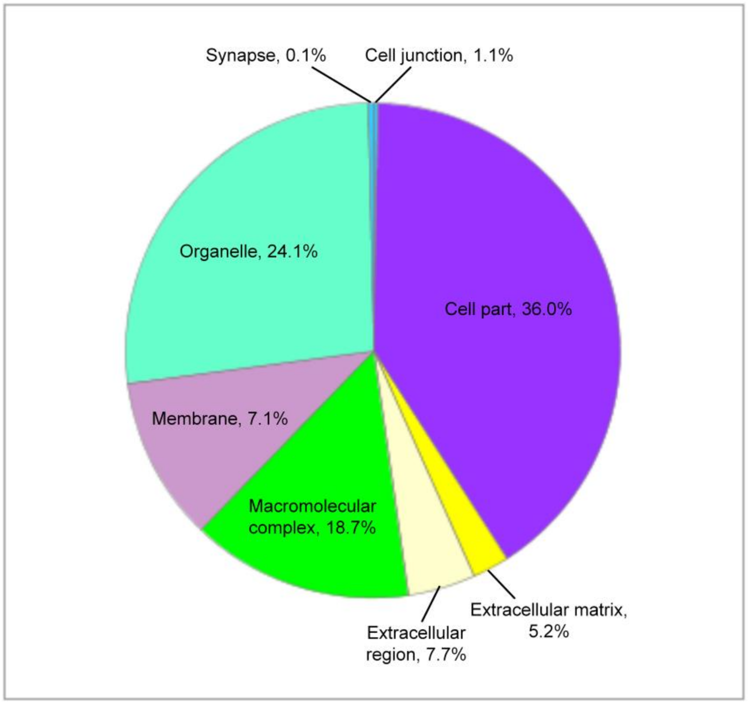
1A


Response to stimulus, 4.3%
Apoptotic process, 2.2%
Biological adhesion, 2.2%
Reproduction, 1.5%
Multicellular organismal process, 3.7%
Biological regulation, 9.7%
Cellular component organization or biogenesis, 4.4%
Metabolic process, 33.8%
Cellular process, 17.4%
Localization, 9.1%
Developmental process, 7.5%
Immune system process, 4.2%

1B

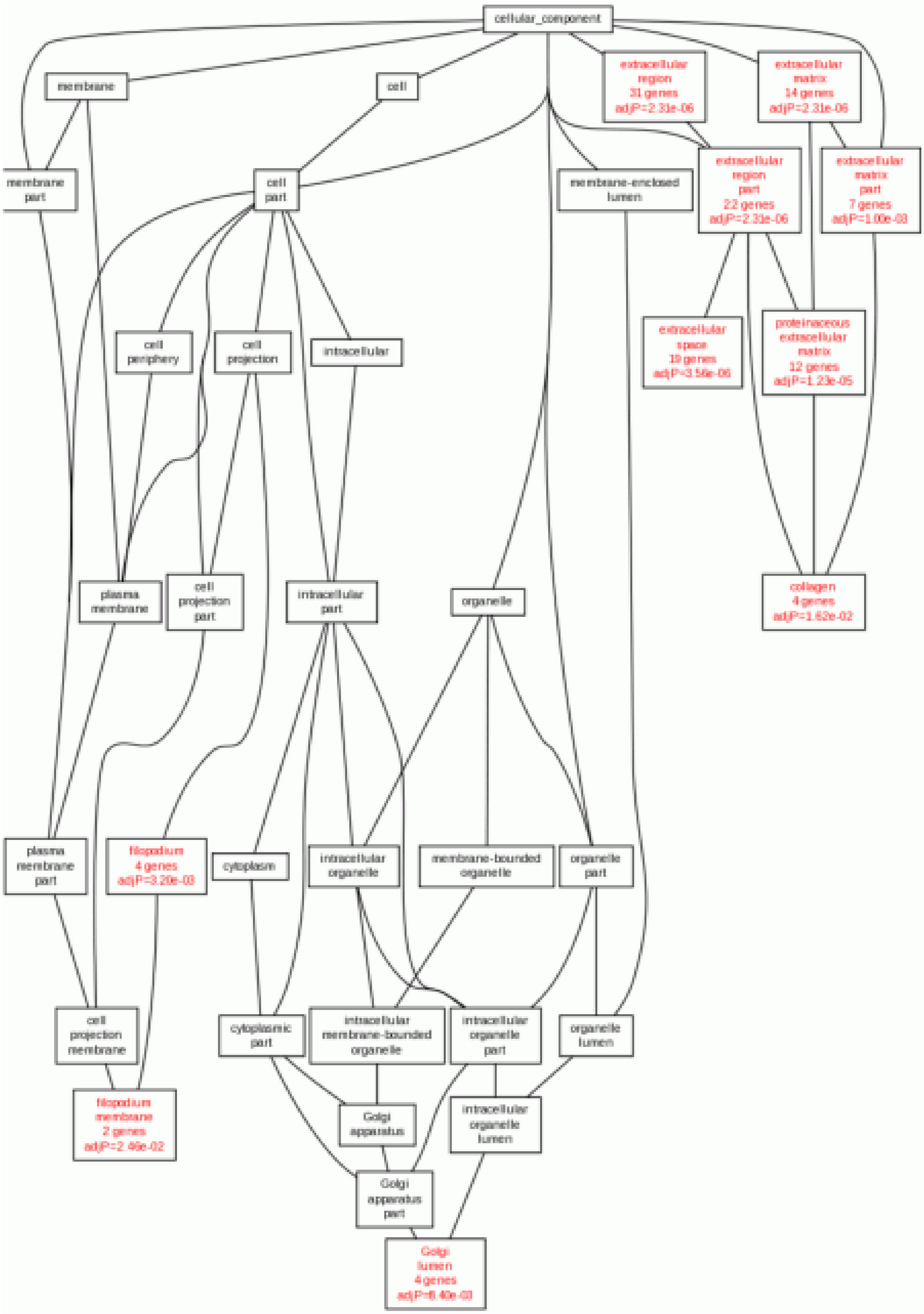


1C

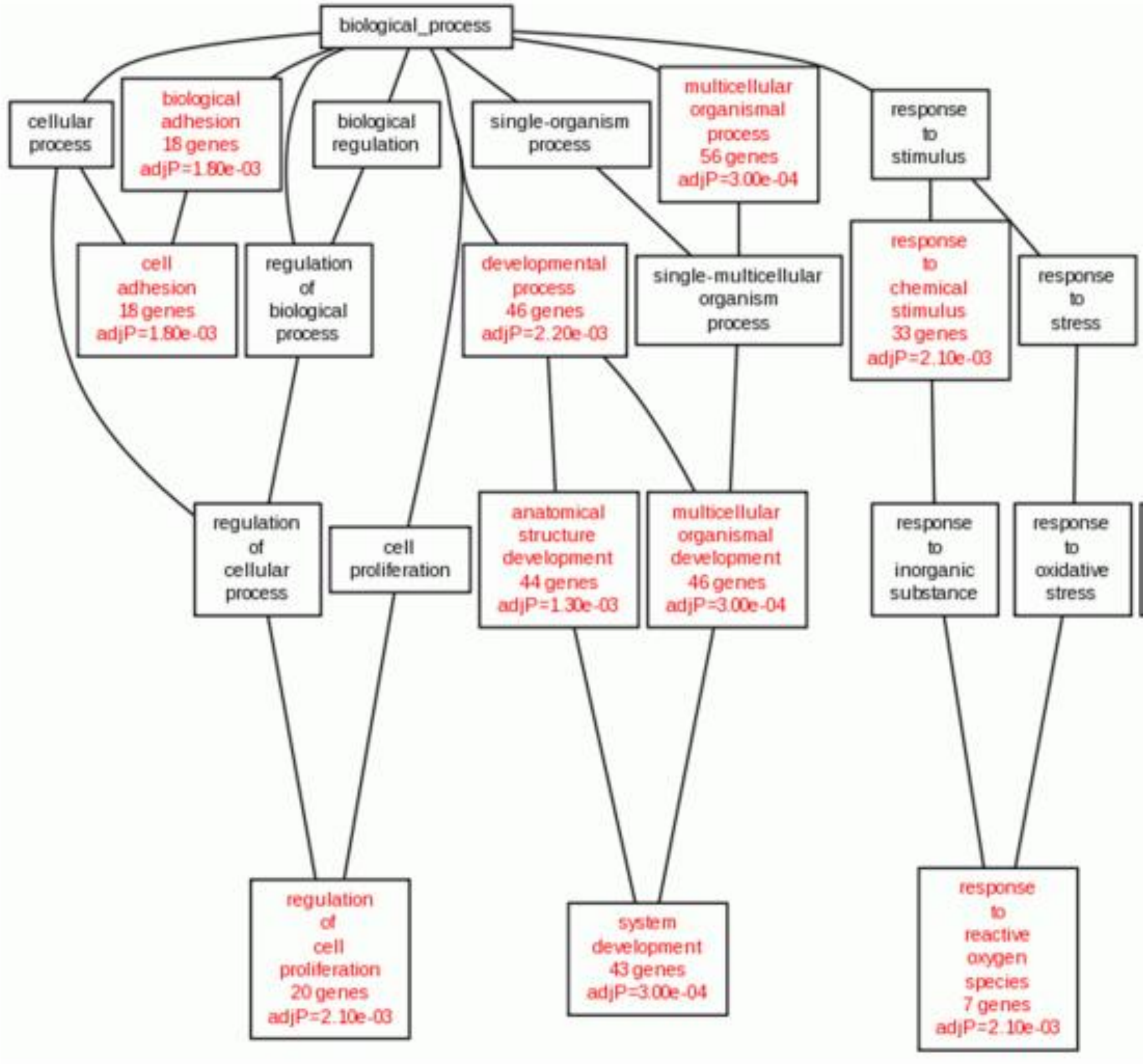


1D

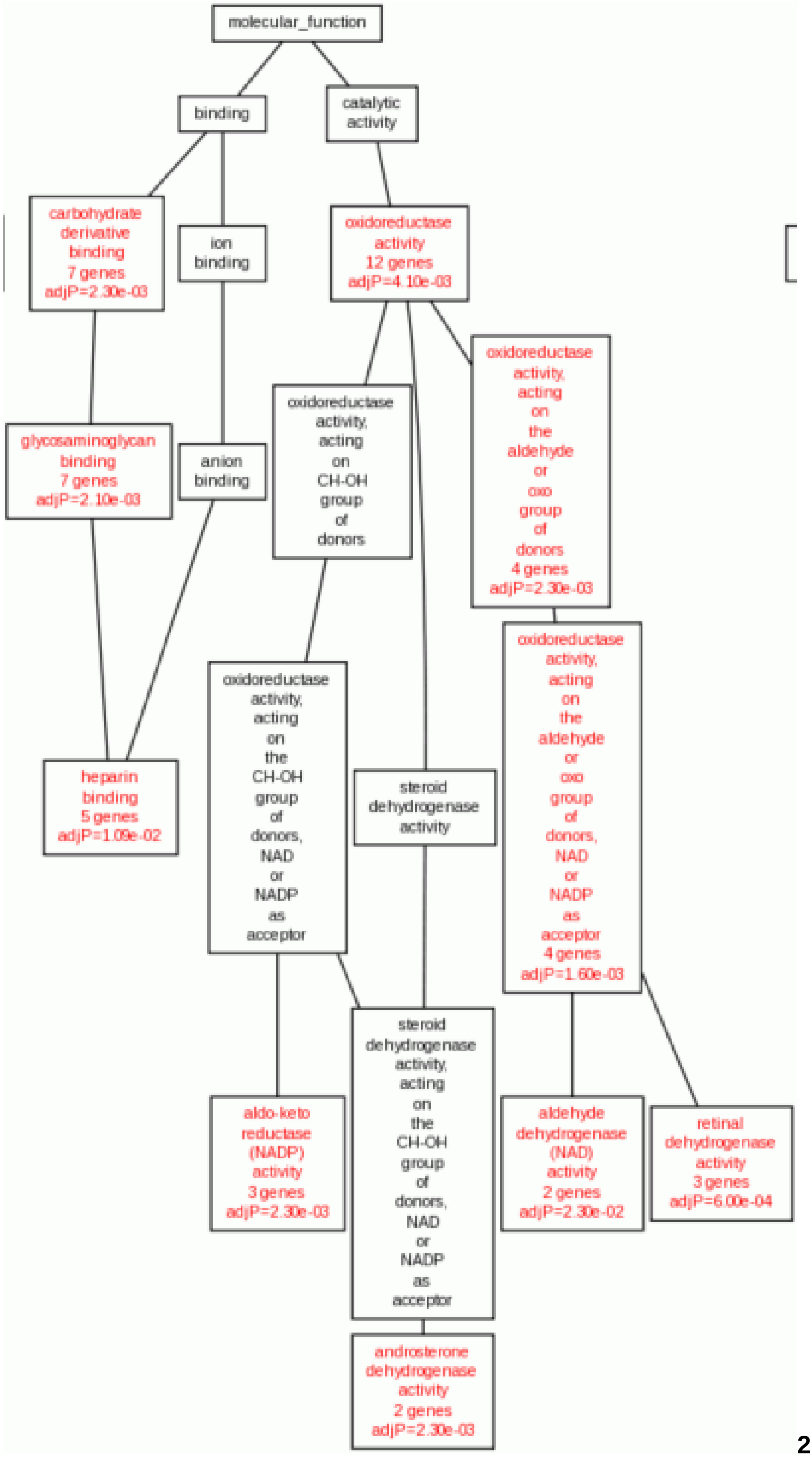
Supplemental Figure 1. Gene ontology analysis using PANTHER for all highly expressed genes (detection p value < 0.012) in non-glaucoma control or glaucoma cases, using Illumina BeadChip data. A) Biological process in controls; B) Biological process in cases; C) Cellular component in controls; D) Cellular component in cases.


cellular_component
membrane
cell
extracellular region 31 genes adjP=2.31e-06
extracellular matrix 14 genes adjP=2.31e-06
membrane part
cell part
membrane-enclosed lumen
extracellular region part 22 genes adjP=2.31e-06
extracellular matrix part 7 genes adjP=1.00e-03
extracellular space 19 genes adjP=3.56e-06
proteinaceous extracellular matrix 12 genes adjP=1.23e-05
cell periphery
cell projection
intracellular
plasma membrane
cell projection part
intracellular part
organelle
collagen 4 genes adjP=1.62e-02
plasma membrane part
filopodium 4 genes adjP=3.20e-03
cytoplasm
intracellular organelle
membrane-bounded organelle
organelle part
cell projection membrane
cytoplasmic part
intracellular membrane-bounded organelle
intracellular organelle part
organelle lumen
filopodium membrane 2 genes adjP=2.46e-02
Golgi apparatus
intracellular organelle lumen
Golgi apparatus part
Golgi lumen 4 genes adjP=6.40e-03

2A


biological_process
cellular process
biological adhesion 18 genes adjP=1.80e-03
biological regulation
single-organism process
multicellular organismal process 56 genes adjP=3.00e-04
response to stimulus
cell adhesion 18 genes adjP=1.80e-03
regulation of biological process
developmental process 46 genes adjP=2.20e-03
single-multicellular organism process
response to chemical stimulus 33 genes adjP=2.10e-03
response to stress
regulation of cellular process
cell proliferation
anatomical structure development 44 genes adjP=1.30e-03
multicellular organismal development 46 genes adjP=3.00e-04
response to inorganic substance
response to oxidative stress
regulation of cell proliferation 20 genes adjP=2.10e-03
system development 43 genes adjP=3.00e-04
response to reactive oxygen species 7 genes adjP=2.10e-03

2B


molecular_function
binding
catalytic activity
carbohydrate derivative binding 7 genes adjP=2.30e-03
ion binding
oxidoreductase activity 12 genes adjP=4.10e-03
oxidoreductase activity, acting on the aldehyde or oxo group of donors 4 genes adjP=2.30e-03
glycosaminoglycan binding 7 genes adjP=2.10e-03
anion binding
oxidoreductase activity, acting on CH-OH group of donors
oxidoreductase activity, acting on the aldehyde or oxo group of donors, NAD or NADP as acceptor 4 genes adjP=1.60e-03
oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor
heparin binding 5 genes adjP=1.09e-02
steroid dehydrogenase activity
steroid dehydrogenase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor
aldo-keto reductase (NADP) activity 3 genes adjP=2.30e-03
aldehyde dehydrogenase (NAD) activity 2 genes adjP=2.30e-02
retinal dehydrogenase activity 3 genes adjP=6.00e-04
androsterone dehydrogenase activity 2 genes adjP=2.30e-03

2C

Supplemental Figure 2. Pathway analysis of differentially expressed genes in glaucomatous SC endothelial cells using WebGestalt (web-based gene set analysis toolkit) in terms of cellular component (A), biological process (B), and molecular function (C). Red color indicates the significant enrichment while black color represents the lack of significance.

Supplemental Table 1. List of differentially expressed genes between glaucoma and non-glaucoma control SC endothelial cells with fold change (FC) of 2 and p value < 0.05.

ProbeID	TargetID	DEFINITION	FC	P Value
6900209	*ADAM19*	ADAM metallopeptidase domain 19 (meltrin beta)	5.06	0.022
5340129	*AKR1C2*	aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2; bile acid binding protein; 3-alpha hydroxysteroid dehydrogenase, type III) , transcript variant 1	-3.23	0.018
7210632	*AKR1C3*	aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	-2.50	0.001
3120598	*AKR1C4*	aldo-keto reductase family 1, member C4 (chlordecone reductase; 3-alpha hydroxysteroid dehydrogenase, type I; dihydrodiol dehydrogenase 4)	-2.78	0.047
1070477	*ALDH1A1*	aldehyde dehydrogenase 1 family, member A1	-2.63	0.019
3120196	*ALDH3A2*	aldehyde dehydrogenase 3 family, member A2, transcript variant 1	-2.17	0.004
1500358	*ANKRD29*	ankyrin repeat domain 29	-2.04	0.012
4590377	*ANKRD35*	ankyrin repeat domain 35	-2.50	0.04
7150634	*APOD*	apolipoprotein D	-7.69	0.017
770603	*BDNF*	brain-derived neurotrophic factor, transcript variant 4	2.24	0.041
730358	*C14ORF132*	chromosome 14 open reading frame 132	-2.22	0.02
1570341	*C3ORF72*	chromosome 3 open reading frame 72	-2.70	0.047
150474	*CA12*	carbonic anhydrase XII, transcript variant 1	-3.85	0.014
5290026	*CCDC85A*	coiled-coil domain containing 85A	2.55	0.023
4280301	*CCL26*	chemokine (C-C motif) ligand 26	2.36	0.028

6620121	*CCL8*	chemokine (C-C motif) ligand 8	-2.13	0.047
3460520	*CCND2*	cyclin D2	-8.33	0.001
2260424	*CDH10*	cadherin 10, type 2 (T2-cadherin)	-3.03	0.015
1770593	*CH25H*	cholesterol 25-hydroxylase	-2.33	0.022
7320041	*CHST15*	carbohydrate (N-acetylgalactosamine 4-sulfate 6-O) sulfotransferase 15	2.30	0.006
1850156	*CLDN23*	claudin 23	-3.70	0.034
520682	*CPA4*	carboxypeptidase A4	6.22	0.027
1090497	*CREG1*	cellular repressor of E1A-stimulated genes 1	-2.13	0.033
5340246	*CRIP2*	cysteine-rich protein 2	2.04	0.003
6110079	*CRYAB*	crystallin, alpha B	-2.38	0.016
7100731	*CYGB*	cytoglobin	-2.94	0.037
60132	*DCBLD2*	discoidin, CUB and LCCL domain containing 2	2.58	0.025
7650296	*DCN*	decorin, transcript variant C	-2.44	0.047
7040670	*DHRS3*	dehydrogenase/reductase (SDR family) member 3	2.94	0.018
5420528	*DNAJB4*	DnaJ (Hsp40) homolog, subfamily B, member 4	2.50	0.006
2100228	*DPT*	dermatopontin	-2.04	0.021
1190142	*EMILIN2*	elastin microfibril interfacer 2	-2.63	0.022
7150563	*ENC1*	ectodermal-neural cortex (with BTB-like domain)	2.32	0.03
2100612	*EZR*	ezrin, transcript variant 1	2.33	0.011
3290458	*FEZ1*	fasciculation and elongation protein zeta 1 (zygin I), transcript variant 1	-2.27	0.023
290593	*FGF2*	fibroblast growth factor 2 (basic)	2.10	0.042
1710484	*FMOD*	fibromodulin	-2.38	0.01
6560458	*GALNTL1*	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase-like 1	-2.33	0.02
5860402	*GLDN*	gliomedin	5.00	0.001
5570427	*GLS*	glutaminase	2.52	0.03
5690270	*GPRC5A*	G protein-coupled receptor, family C, group 5, member A	2.41	0.015
7150598	*GSTM3*	glutathione S-transferase M3 (brain)	-2.70	0.022
2970019	*HIST1H4H*	histone cluster 1, H4h	2.01	0.014
3460097	*HOXB2*	homeobox B2	2.80	0.007

360291	*HS.19193*	PREDICTED: hypothetical LOC400043	-2.00	0.012
5720768	*HS.407903*	cDNA DKFZp586B0220 (from clone DKFZp586B0220)	-2.17	0.034
50543	*HS.497591*	cDNA FLJ41846 fis, clone NT2RI3003162	2.08	0.015
6180259	*HSPB8*	heat shock 22kDa protein 8	-2.63	0.038
670386	*ID1*	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein, transcript variant 2	2.21	0.026
4040576	*IL6*	interleukin 6 (interferon, beta 2)	2.73	0.037
2100196	*ISG15*	ISG15 ubiquitin-like modifier	2.83	0.041
2970347	*ITPRIP*	inositol 1,4,5-triphosphate receptor interacting protein	2.18	0.002
4810424	*KCNK15*	potassium channel, subfamily K, member 15	-2.00	0.047
7550064	*KCTD5*	potassium channel tetramerisation domain containing 5	2.00	0.038
3850692	*KLF2*	Kruppel-like factor 2 (lung)	3.47	0.012
6060630	*KRT19*	Homo sapiens keratin 19	7.20	0.013
4390100	*LAMC2*	laminin, gamma 2, transcript variant 1	2.22	0.014
6280541	*LAMC3*	laminin, gamma 3	-2.27	0.012
2710064	*LOC387763*	PREDICTED: hypothetical LOC387763	-2.70	0.017
5050538	*LOC654096*	PREDICTED: similar to Ovarian cancer-related protein 10-2 (OVC10-2)	-2.04	0.005
730709	*LOC730525*	PREDICTED: hypothetical protein LOC730525	-3.57	0.019
3710048	*LOC731895*	PREDICTED: similar to transmembrane protein 28	2.98	0.003
3940017	*LOX*	lysyl oxidase	2.60	0.002
770156	*LRRN4CL*	LRRN4 C-terminal like	-2.44	0.032
1430487	*MGP*	matrix Gla protein	-4.55	0.048
5080131	*MGST1*	microsomal glutathione S-transferase 1, transcript variant 1a	-2.13	0.021
4670131	*MYO10*	myosin X	2.01	0.018
1110632	*NKX3-1*	NK3 homeobox 1	2.21	0.028
940731	*NR0B1*	nuclear receptor subfamily 0, group B, member 1	-2.22	0.047

7050066	*ODZ3*	odz, odd Oz/ten-m homolog 3 (Drosophila)	2.98	0.007
2680072	*OLFM1*	olfactomedin 1, transcript variant 1	-2.44	0.017
5420452	*OSR2*	PREDICTED: odd-skipped related 2 (Drosophila)	-4.76	0
4540682	*PALM*	paralemmin, transcript variant 1	-4.35	0.029
1740343	*PCSK5*	proprotein convertase subtilisin/kexin type 5	-2.04	0.039
6270768	*PLAC9*	placenta-specific 9	-2.94	0.032
7040477	*PLOD2*	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2, transcript variant 2	3.59	0.011
6480040	*PODN*	podocan	-2.94	0.029
4490739	*PPAP2A*	phosphatidic acid phosphatase type 2A, transcript variant 2	-2.08	0.011
4390754	*PPL*	periplakin	-3.03	0.048
6420008	*PROS1*	protein S (alpha)	-2.86	0.029
3440095	*PSG3*	pregnancy specific beta-1-glycoprotein 3	4.26	0.007
6350471	*PSG5*	pregnancy specific beta-1-glycoprotein 5	6.02	0.001
1690095	*PSG6*	pregnancy specific beta-1-glycoprotein 6, transcript variant 1	3.12	0.005
4120243	*PSG9*	pregnancy specific beta-1-glycoprotein 9	3.41	0.006
110382	*RAC2*	ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2)	3.85	0.003
6560592	*RAET1G*	retinoic acid early transcript 1G	-2.00	0.028
2100241	*RAPH1*	Ras association (RalGDS/AF-6) and pleckstrin homology domains 1, transcript variant 1	2.07	0.034
2340681	*RARRES1*	retinoic acid receptor responder (tazarotene induced) 1, transcript variant 1	3.24	0.027
1710142	*RGS4*	regulator of G-protein signalling 4	4.45	0.026
1230470	*RHOU*	ras homolog gene family, member U	-2.13	0.016
4730066	*SCN2A*	sodium channel, voltage-gated, type II, alpha subunit, transcript variant 2	-2.04	0.046

4890021	*SEPT3*	septin 3, transcript variant B	-2.38	0.025
770408	*SERPINE1*	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	4.33	0.043
5490692	*SEZ6L2*	seizure related 6 homolog (mouse)-like 2, transcript variant 2	2.98	0.019
4390450	*SGK*	serum/glucocorticoid regulated kinase	2.79	0.018
2030324	*SGK1*	serum/glucocorticoid regulated kinase 1 , transcript variant 1	2.82	0.012
6420731	*SLC20A1*	solute carrier family 20 (phosphate transporter), member 1	2.62	0.008
2630437	*SMOC2*	SPARC related modular calcium binding 2	-2.27	0.037
6760669	*SPRY1*	sprouty homolog 1, antagonist of FGF signaling (Drosophila), transcript variant 1	-3.85	0.013
2650730	*STC1*	stanniocalcin 1	-2.70	0.049
3140603	*SVIL*	supervillin, transcript variant 1	-2.38	0.047
4180296	*TBX18*	T-box 18	-2.38	0.029
1570646	*TFAP2A*	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha), transcript variant 3	2.02	0.014
7650358	*TGFBI*	transforming growth factor, beta-induced, 68kDa	2.02	0.023
3190379	*TGFBR3*	transforming growth factor, beta receptor III	-3.03	0.044
240523	*TMEM166*	transmembrane protein 166	2.42	0.027
2140242	*TNFAIP6*	tumor necrosis factor, alpha-induced protein 6 (TNFAIP6), mRNA.	-2.86	0.023
2360672	*TNFRSF19*	tumor necrosis factor receptor superfamily, member 19, transcript variant 2	-4.00	0.017
6660131	*TSPAN13*	tetraspanin 13	2.22	0.042
2320133	*TXNRD1*	thioredoxin reductase 1, transcript variant 4	2.07	0.004
2640369	*VIL2*	villin 2 (ezrin)	2.24	0.018
4390646	*ZHX2*	zinc fingers and homeoboxes 2	-2.17	0.04
6590026	*ZNF521*	zinc finger protein 521	-2.17	0.009

Supplemental table 2. List of POAG-associated genes with expression changes between glaucoma and non-glaucoma control SC endothelial cells. The first five genes were selected to further examine their expression using droplet digital PCR.

Probe ID	Gene Symbol	Gene Description	Fold Change	p value
4060358	***ABCA1***	ATP-binding cassette, sub-family A, member 1	-1.35	0.103
5550379	***CAV1***	caveolin 1, caveolae protein, 22kDa	1.79	0.035
620360	***CAV2***	caveolin 2	1.39	0.037
2120053	***CYP1B1***	cytochrome P450, family 1, subfamily B, polypeptide 1	-1.45	0.030
1070435	***GAS7***	growth arrest-specific 7, transcript variant c	-1.28	0.222
2690187	*AFAP1*	actin filament-associated protein 1	1.56	0.135
5690092	*ATOH7*	atonal homolog 7 (Drosophila)	1.03	0.484
4200678	*CDKN2B-AS1*	CDKN2B antisense RNA (non-protein coding)	1.00	0.976
6060440	*FNDC3B*	fibronectin type III domain containing 3B	1.18	0.273
3440491	*GALC*	galactosylceramidase	-1.09	0.589
6840156	*GMDS*	GDP-mannose 4,6-dehydratase	-1.12	0.541
1940037	*MYOC*	myocilin	1.14	0.243
2650497	*LRP12*	low density lipoprotein-related protein 12	1.11	0.023
5260215	*OPTN*	optineurin	-1.15	0.489
1260315	*PMM2*	phosphomannomutase 2	1.43	0.03
1450408	*SIX1*	SIX homeobox 1	1.03	0.362
4260047	*SIX6*	SIX homeobox 6	-1.04	0.162
2230730	*SRBD1*	S1 RNA binding domain 1	-1.09	0.296
780598	*TBK1*	TANK-binding kinase 1	-1.22	0.132
1470209	*TMCO1*	transmembrane and coiled-coil domains 1	-1.03	0.734
6650100	*WDR36*	WD repeat domain 36	1.00	0.990
3170280	*ZFPM2*	zinc finger protein, multitype 2	1.11	0.082