Supplementary Table S1: Mitochondrial gene-sets

Citrate cycle (TCA cycle): ACLY, ACO1, ACO2, CS, DLAT, DLD, DLST, FH, IDH1, IDH2, IDH3A, IDH3B, IDH3G, MDH1, MDH2, OGDH, OGDHL, PC, PCK2, PDHA1, PDHA2, PDHB, PDHX, SDHA, SDHB, SDHC, SDHD, SUCLA2, SUCLG1, SUCLG2

Fatty acid biosynthesis: ACACA, ACACB, FASN, MCAT, OXSM

Fatty acid elongation: ACAA2, ECHS1, HADH, HADHA, HADHB, MECR

Fatty acid metabolism: ACAA1, ACAA2, ACADL, ACADM, ACADS, ACADSB, ACADVL, ACAT1, ACOX3, ACSL1, ACSL4, ACSL5, ALDH1B1, ALDH2, ALDH3A2, ALDH7A1, ALDH9A1, CPT1A, CPT1B, CPT1C, CPT2, ECHS1, ECI1, ECI2, EHHADH, GCDH, HADH, HADHA, HADHB

Synthesis and degradation of ketone bodies: ACAT1, BDH1, HMGCL, HMGCS2, OXCT1

Ubiquinone and other terpenoid-quinone biosynthesis: COQ2, COQ3, COQ5, COQ6, COQ7

Oxidative phosphorylation: ATP5A1, ATP5B, ATP5C1, ATP5D, ATP5F1, ATP5G1, ATP5G2, ATP5G3, ATP5I, ATP5J, ATP5J2, ATP5L, ATP5O, ATP6, COX1, COX10, COX11, COX15, COX17, COX2, COX3, COX4I1, COX4I2, COX5A, COX5B, COX6A1, COX6A2, COX6B1, COX6B2, COX6C, COX7A1, COX7A2, COX7A2L, COX7B, COX7C, COX8A, CYC1, CYTB, ND1, ND2, ND3, ND4, ND4L, ND5, ND6, NDUFA1, NDUFA10, NDUFA12, NDUFA13, NDUFA2, NDUFA3, NDUFA4, NDUFA5, NDUFA6, NDUFA7, NDUFA8, NDUFA9, NDUFAB1, NDUFB10, NDUFB11, NDUFB2, NDUFB3, NDUFB5, NDUFB6, NDUFB7, NDUFB8, NDUFB9, NDUFC1, NDUFC2, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS5, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NDUFV3, PPA2, SDHA, SDHB, SDHC, SDHD, TCIRG1, UQCR10, UQCR11, UQCRB, UQCRC1, UQCRC2, UQCRFS1, UQCRH, UQCRQ

Pyrimidine metabolism: AK3, CTPS2, DHODH, DUT, NME1, NME1-NME2, NME2, NME3, NME4, NME6, NT5C, NT5C3, NT5M, NUDT2, PNPT1, TK2, TXNRD1, TXNRD2

Alanine, aspartate and glutamate metabolism: ABAT, ADSL, AGXT, AGXT2, ALDH4A1, ALDH5A1, CPS1, GLS, GLS2, GLUD1, GOT2, GPT2

Glycine, serine and threonine metabolism: AGXT, AGXT2, ALAS1, ALAS2, ALDH7A1, AMT, CHDH, DLD, DMGDH, GATM, GCAT, GLDC, GLYCTK, MAOA, MAOB, SARDH, SHMT1, SHMT2

Valine, leucine and isoleucine degradation: ABAT, ACAA1, ACAA2, ACAD8, ACADM, ACADS, ACADSB, ACAT1, ALDH1B1, ALDH2, ALDH3A2, ALDH6A1, ALDH7A1, ALDH9A1, AUH, BCAT1, BCAT2, BCKDHA, BCKDHB, DBT, DLD, ECHS1, EHHADH, HADH, HADHA, HADHB, HIBADH, HIBCH, HMGCL, HMGCS2, HSD17B10, IVD, MCCC1, MCCC2, MCEE, MUT, OXCT1, PCCA, PCCB

Valine, leucine and isoleucine biosynthesis: BCAT1, BCAT2, IARS2, LARS2, PDHA1, PDHA2, PDHB, VARS2

Lysine degradation: AADAT, AASS, ACAT1, ALDH1B1, ALDH2, ALDH3A2, ALDH7A1, ALDH9A1, BBOX1, DLST, ECHS1, EHHADH, GCDH, HADH, HADHA, OGDH, OGDHL

Arginine and proline metabolism: AGMAT, ALDH18A1, ALDH1B1, ALDH2, ALDH3A2, ALDH4A1, ALDH7A1, ALDH9A1, ARG2, CKMT2, CPS1, GATM, GLS, GLS2, GLUD1, GOT2, LAP3, MAOA, MAOB, NAGS, OAT, OTC, PRODH, PRODH2, PYCR1

Tryptophan metabolism: AADAT, ACAT1, ALDH1B1, ALDH2, ALDH3A2, ALDH7A1, ALDH9A1, CCBL2, ECHS1, EHHADH, GCDH, HADH, HADHA, KYNU, MAOA, MAOB, OGDH, OGDHL, WARS2

beta-Alanine metabolism: ABAT, ACADM, ALDH1B1, ALDH2, ALDH3A2, ALDH7A1, ALDH9A1, ECHS1, EHHADH, HADHA, HIBCH, MLYCD

Pyruvate metabolism: ACACA, ACACB, ACAT1, ACSS1, ACYP2, ALDH1B1, ALDH2, ALDH3A2, ALDH7A1, ALDH9A1, DLAT, DLD, HAGH, LDHA, LDHAL6B, LDHB, LDHD, MDH1, MDH2, ME1, ME2, ME3, PC, PCK2, PDHA1, PDHA2, PDHB, PDHX

Glyoxylate and dicarboxylate metabolism: ACAT1, ACO1, ACO2, CS, GLYCTK, HAO2, MCEE, MDH1, MDH2, MUT, PCCA, PCCB

Propanoate metabolism: ABAT, ACACA, ACACB, ACADM, ACAT1, ACSS1, ACSS3, ALDH1B1, ALDH2, ALDH3A2, ALDH6A1, ALDH7A1, ALDH9A1, ECHS1, EHHADH, HADHA, HIBCH, LDHA, LDHAL6B, LDHB, MCEE, MLYCD, MUT, PCCA, PCCB, SUCLA2, SUCLG1, SUCLG2

Butanoate metabolism: ABAT, ACADS, ACAT1, ACSM1, ACSM2A, ACSM3, ACSM4, ACSM5, ALDH5A1, BDH1, ECHS1, EHHADH, HADH, HADHA, HMGCL, HMGCS2, L2HGDH, OXCT1, PDHA1, PDHA2, PDHB

One carbon pool by folate: ALDH1L1, ALDH1L2, AMT, ATIC, MTFMT, MTHFD1, MTHFD1L, MTHFD2, MTHFD2L, SHMT1, SHMT2

Porphyrin and chlorophyll metabolism: ALAS1, ALAS2, COX10, COX15, CPOX, EARS2, FECH, FTH1, FTMT, HCCS, MMAB, PPOX

Supplementary Table S2: PARIS-derived gene P-values for the lipid metabolism mitochondrial gene-set for primary open-angle glaucoma (POAG, 3430 cases) and normal tension glaucoma (NTG, 717 cases) versus controls (3108) in the combined GLAUGEN – NEIGHBOR dataset.

Lipid metabolism mitochondrial gene	**LD block count**	**Gene *P*-value**		**Other pathway?**
		POAG	**NTG**	
ACOX3	21	1.00	1.00	
ACACB	16	0.55	0.24	Carbohydrate metabolism
ALDH9A1	15	0.54	0.23	Carbohydrate metabolism
ACSL1	15	0.11	**0.020**	
MCAT	13	1.00	1.00	
ALDH7A1	13	0.34	1.00	Carbohydrate metabolism
BDH1	12	**< 0.0001**	**< 0.0001**	Carbohydrate metabolism
ALDH1B1	12	**0.046**	0.20	Carbohydrate metabolism
CPT1B	10	0.19	1.00	
HMGCS2	9	1.00	1.00	Carbohydrate metabolism
EHHADH	8	**0.044**	**0.0009**	Carbohydrate metabolism
ECI2	8	0.24	1.00	
ACADS	7	1.00	1.00	Carbohydrate metabolism
ACACA	6	0.27	0.06	Carbohydrate metabolism
CPT2	5	0.09	1.00	
ECHS1	5	**0.004**	**0.002**	Carbohydrate metabolism
CPT1A	5	0.13	1.00	
ACAA2	5	**0.024**	**0.0008**	
CPT1P	5	**0.037**	1.00	

Nb: Only genes with at least 5 LD blocks are presented.

Supplementary Table S3: PARIS-derived gene P-values for the carbohydrate metabolism mitochondrial gene-set for primary open-angle glaucoma (POAG, 3430 cases) and normal tension glaucoma (NTG, 717 cases) versus controls (3108) in the combined GLAUGEN – NEIGHBOR dataset .

Carbohydrate metabolism mitochondrial gene	**LD block count**	**Gene *P*-value**		**Other pathway?**
		POAG	**NTG**	
ME3	43	**0.0003**	0.30	
ABAT	31	**0.047**	0.31	
SUCLG2	26	0.77	1.00	
PCCA	25	1.00	0.45	
ACSS3	17	1.00	0.09	
ACACB	16	0.55	0.23	Lipid metabolism
MLYCD	16	0.27	0.25	
ALDH9A1	15	0.55	0.24	Lipid metabolism
ACYP2	14	**0.001**	0.43	
ACO1	14	1.00	1.00	
ACSM5	13	1.00	1.00	
ALDH7A1	13	0.36	1.00	Lipid metabolism
ALDH5A1	13	0.13	**0.024**	
IDH3A	12	0.27	1.00	
BDH1	12	**< 0.0001**	**< 0.0001**	Lipid metabolism
ALDH1B1	12	**0.046**	0.20	Lipid metabolism
ACSM2A	11	0.12	1.00	
ACSS1	11	1.00	0.00	
PCHC	10	1.00	1.00	
HMGCS2	9	1.00	1.00	Lipid metabolism
HUMNDME	9	0.28	0.26	
SDHC	8	1.00	1.00	
PCK2	8	1.00	1.00	
HIBCH	8	1.00	**0.025**	
IDH1	8	0.14	0.12	
EHHADH	8	0.05	0.00	Lipid metabolism
HAOX2	7	1.00	1.00	
ACADS	7	1.00	1.00	Lipid metabolism
GLOD2	7	1.00	1.00	
IDH3B	7	1.00	1.00	
SDHA	7	**0.013**	**0.012**	
LDHAL6B	6	1.00	**0.001**	
IDH2	6	0.12	1.00	
LDHD	6	1.00	**0.004**	
ACACA	6	0.27	0.06	Lipid metabolism
PDHA2	6	1.00	1.00	
OGDHL	5	0.11	1.00	
ECHS1	5	**0.004**	**0.003**	Lipid metabolism
PCB	5	0.02	1.00	
LDHB	5	1.00	**0.003**	
L2HGDH	5	1.00	1.00	
DLTS	5	**0.037**	1.00	
ACSM1	5	1.00	1.00	
HAGH	5	1.00	1.00	

NB: Only genes with at least 5 LD blocks are presented.