Supporting Information

Jiao et al. 10.1073/pnas.0907564106

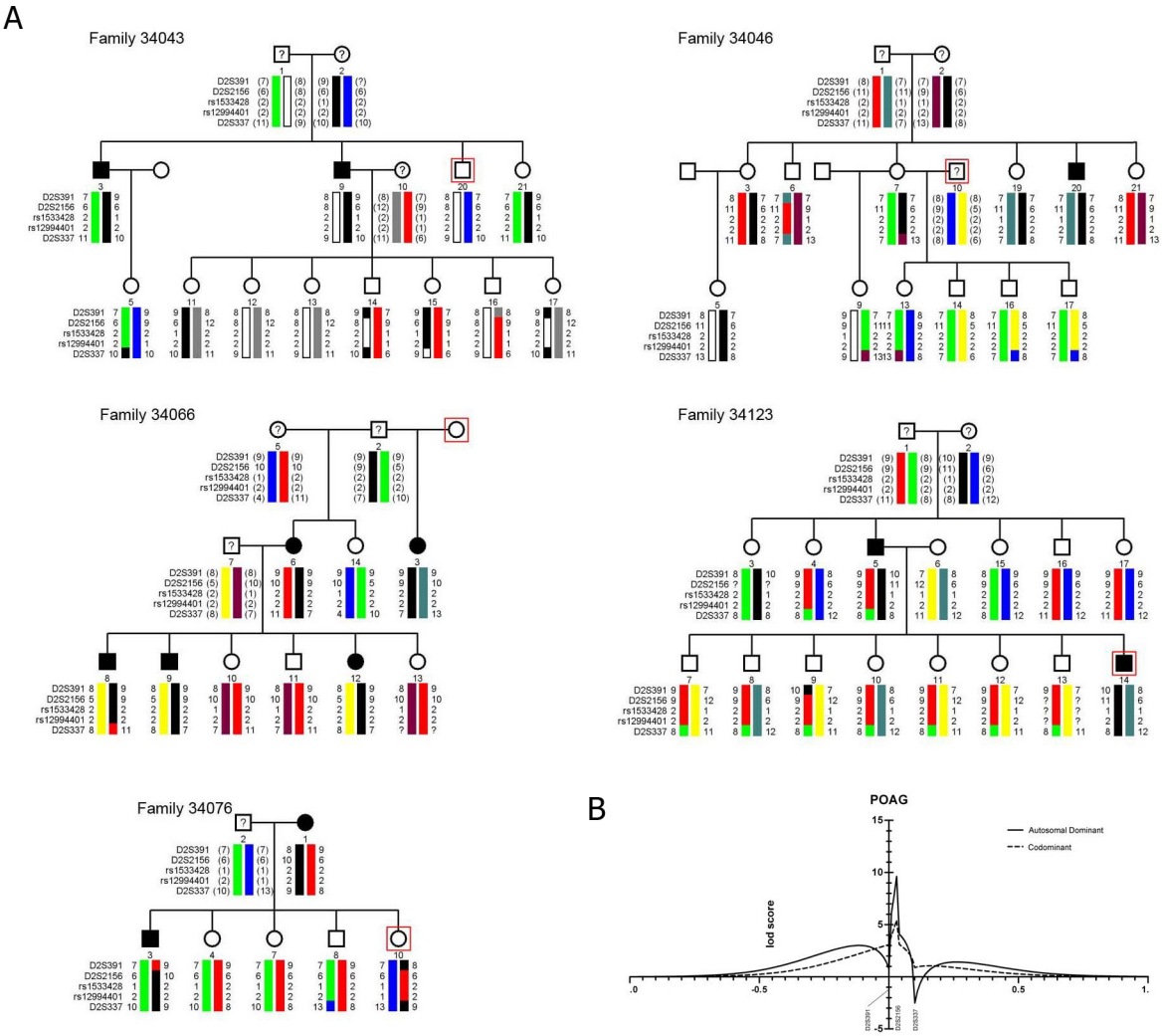

Fig. S1. (*A*)Pedigrees of the 5 families giving $P > 95\%$ for being linked to D2S2156 under the autosomal dominant and codominant models. Circles represent females, squares represent males, and filled individuals are affected with POAG. Haplotypes are shown for the 6 markers included in Table 1. (*B*) Multipoint linkage analysis of families with $P > 0.95$ of being linked with chromosome 2 markers in the region around D2S2156 (Table 1). Solid line: multipoint LOD score obtained from 5 linked families with the autosomal dominant model; dashed line: multipoint LOD score obtained from 5 linked families with the codominant model. Locations are shown on the *x* axis with D2S391 at the origin and D2S2156, rs1533428, and rs12994401 localized together (0 cM).

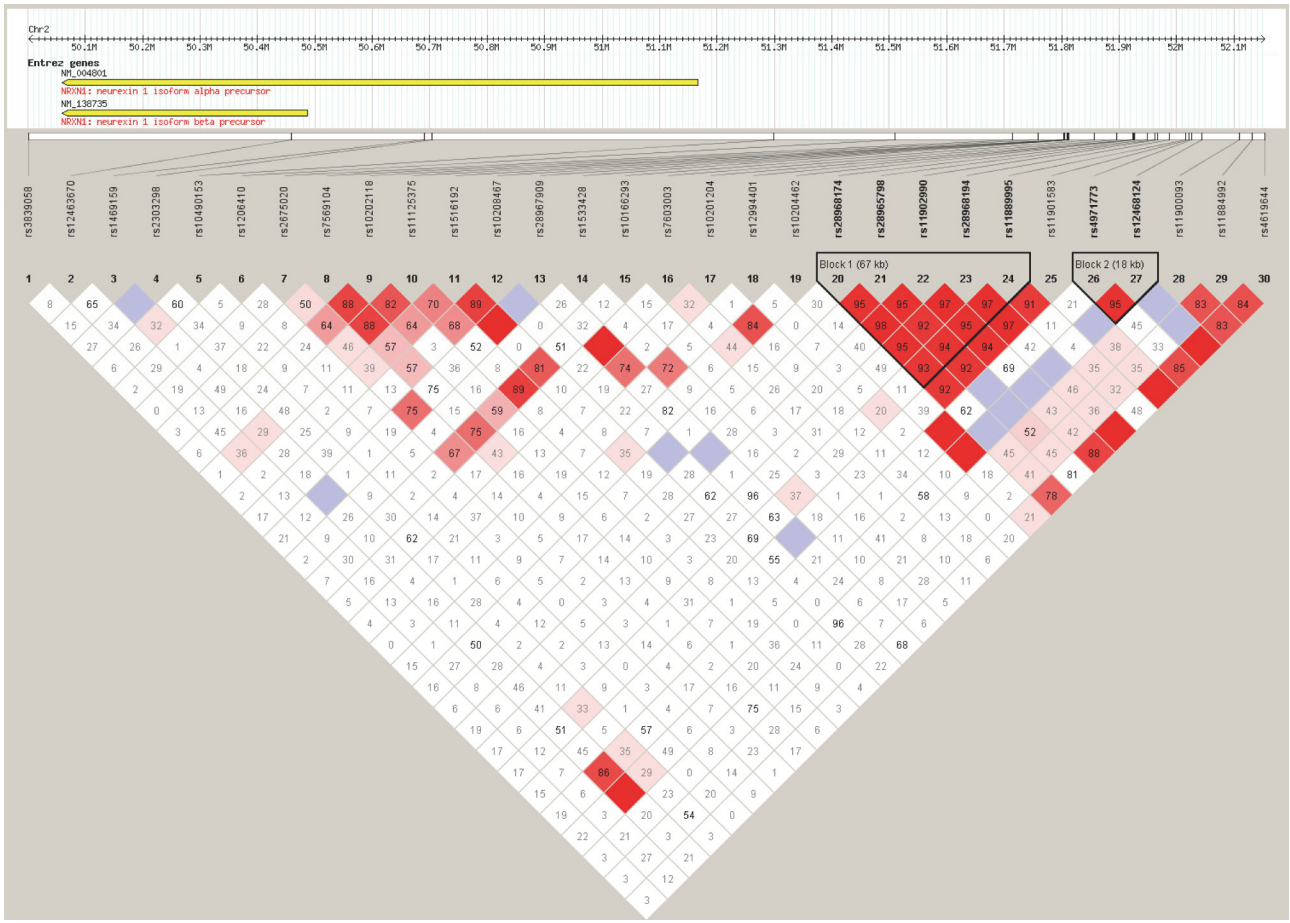

Fig. S2. The pairwise D′ Hapview plot for SNPs in Chromosome 2 using these BFSG samples. The pairwise D′ Hapview plot was generated for 30 SNPs in the region based on combined cases-control data for POAG.

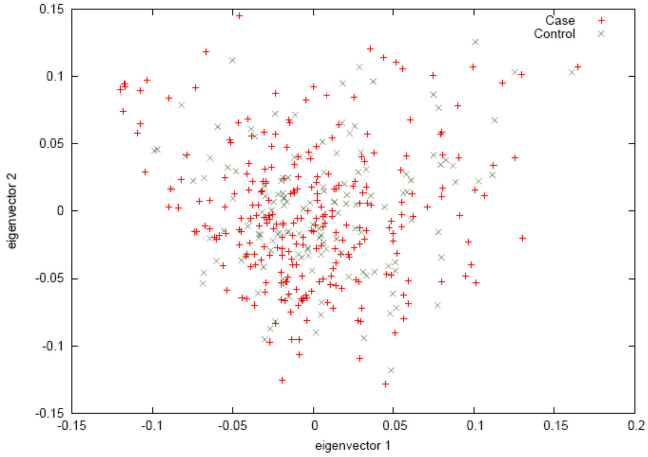

Fig. S3. Analysis of stratification in all (discovery plus replication) POAG cases and controls from BFSG. Stratification between cases and controls was assessed with 28 AIMS typed in 252 cases and 130 controls. Eigenvector 1 (*x* axis) and Eigenvector 2 (*y* axis) represent the two most important principal components. Red pluses represent cases and the gray xs represent controls.

Table S1. Top 5 families for autosomal recessive dominant and codominant models

Marker	bp	cM	0	0.01	0.05	0.1	0.2	0.3	0.4	Z_{max}	θ_{max}
Codominant model											
D2S391*	46,265,004	73.8	−0.27	−0.22	−0.07	0.03	0.08	0.06	0.02	0.09	0.22
D2S2156	51,111,121	77.1	5.27	5.14	4.62	3.96	2.61	1.32	0.34	5.27	0
rs1533428	51,870,909		2.40	2.33	2.08	1.76	1.13	0.56	0.15	2.40	0
rs12994401	51,983,897		0.30	0.29	0.26	0.23	0.15	0.07	0.02	0.30	0
D2S337*	61,523,435	84.1	−0.21	−0.05	0.22	0.31	0.28	0.15	0.04	0.31	0.11
Autosomal dominant model											
D2S391*	46,265,004	73.8	−5.85	−4.69	−2.70	−1.54	−0.49	−0.11	−0.01	0.00	0.5
D2S2156	51,111,121	77.1	9.91	9.73	8.97	7.97	5.80	3.42	1.07	9.91	0
rs1533428	51,870,909		2.39	2.44	2.47	2.35	1.80	1.04	0.30	2.48	0.04
rs12994401	51,983,897		−0.31	−0.24	−0.06	0.04	0.09	0.07	0.02	0.10	0.25
D2S337*	61,523,435	84.1	−3.03	−2.53	−1.08	−0.28	0.24	0.25	0.09	0.25	0.3

*Used in initial genome wide scan (1).

1. Nemesure B, et al. (2003) A genome-wide scan for primary open-angle glaucoma (POAG): The Barbados Family Study of Open-Angle Glaucoma. *Hum Genet* 112(5–6):600–609.

Table S2. Genotype and association results of rs1533428 and rs12994401 from POAG cases and controls

Snps	rs1533428						rs12994401					
Group	Discovery group		Replication group		Combined group		Discovery group		Replication group		Combined group	
Phenotype	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control
	(n = 127)	(n = 64)	(n = 116)	(n = 65)	(n = 243)	(n = 129)	(n = 127)	(n = 64)	(n = 122)	(n = 64)	(n = 249)	(n = 128)
TT genotype (n)	55	7	52	8	107	15	46	1	42	1	88	2
CT genotype (n)	40	25	30	27	70	52	13	14	17	8	30	22
CC genotype (n)	32	32	34	30	66	62	68	49	63	55	131	104
Risk allele (T) frequency, %	59.06	30.47	57.76	33.08	58.44	31.78	41.34	12.50	41.39	7.81	41.37	10.16
Genotypic P values	1.46E−05		4.81E−05		1.20E−09		6.37E−07		1.09E−06		2.87E−12	
Trend P values	4.38E−06		1.18E−04		2.37E−09		9.83E−06		2.10E−07		1.11E−11	
Allelic P values	1.33E−07		6.58E−06		4.48E−12		1.07E−08		1.76E−11		1.46E−18	
Recessive P values	6.49E−06		8.25E−06		2.35E−10		1.53E−07		4.40E−07		3.21E−13	
Dominant P values	6.08E−04		0.023		5.37E−05		2.05E−03		3.95E−06		5.49E−08	
HWE P values	8.50E−05	5.32E−01	4.15E−07	6.19E−01	2.42E−10	4.24E−01	6.06E−19	1.00E + 00	3.46E−15	2.90E−01	1.90E−32	5.10E−01

Table S3. Association results SNPs in chromosome 2p based on all (combined discovery and replication groups) cases and controls

		N		Risk allele frequency, %		P	
SNPs	Risk allele	POAG	Control	POAG	Control	Allelic	Bonferroni correction
rs10202118	C	240	123	68.90	52.31	1.23E−05	3.69E−04
rs11125375	G	242	123	60.33	48.37	2.09E−03	6.27E−02
rs10208467	G	246	124	86.79	79.84	1.38E−02	4.14E−01
rs7603003	A	239	124	60.11	54.32	1.34E−01	4.02
rs2303298	A	249	127	6.02	2.36	2.60E−02	7.80E−01
rs12463670	T	246	124	20.12	14.11	4.51E−02	1.35
rs1469159	A	249	128	83.53	82.81	8.01E−01	2.40E + 01
rs10490153	T	243	130	75.51	73.85	6.16E−01	1.85E + 01
rs1206410	G	246	128	87.4	83.98	1.99E−01	5.97
rs2675020	G	246	128	53.05	49.61	3.72E−01	1.12E + 01
rs7569104	A	241	124	26.97	25.58	6.49E−01	1.95E + 01
rs1516192	T	241	124	45.02	38.71	1.03E−01	3.09
rs28967909	G	239	126	96.82	96.83	9.79E−01	2.94E + 01
rs10166293	G	248	126	76.41	75.79	8.51E−01	2.55E + 01
rs10201204	G	244	126	43.85	40.48	3.79E−01	1.14E + 01
rs10204462	G	246	124	26.63	21.77	1.50E−01	4.50
rs11889995	A	242	123	17.15	9.45	4.70E−03	1.41E−01
rs4619644	T	251	128	66.73	61.33	1.40E−01	4.20
rs11900093	G	239	128	8.59	7.03	4.63E−01	1.39E + 01
rs11884992	T	249	124	7.63	6.88	7.03E−01	2.11E + 01
rs28968194	A	240	123	93.23	91.41	3.59E−01	1.08E + 01
rs4971773	C	239	124	12.24	8.76	1.59E−01	4.77
rs28965798	C	246	124	94.51	93.15	4.58E−01	1.37E + 01
rs11902990	T	244	127	93.03	91.73	5.21E−01	1.56E + 01
rs12468124	G	248	128	11.49	8.2	1.61E−01	4.83
rs11901583	A	241	128	92.95	92.58	8.54E−01	2.56E + 01
rs28968174	T	244	124	93.24	91.94	5.18E−01	1.55E + 01
rs3839058	T	241	124	46.68	45.56	7.75E−01	2.33E + 01

Table S4. Male and female specific penetrances for the codominant model (derived assuming $\alpha = 0.181$)

Liability class	Gender	Penetrance		
Unaffected	Male	0.01	0.54	0.99
	Female	0.01	0.27	0.98
POAG	Male	0.01	0.54	0.99
	Female	0.01	0.27	0.98
GS-1	Male	0.01	0.4	0.74
	Female	0.01	0.2	0.74
GS-2	Male	0.01	0.27	0.49
	Female	0.01	0.14	0.49

Table S5. Diagnostic criteria for POAG; ++, most complete classification data; +, less complete but sufficient for classification

Diagnostic test	Criteria
Visual field	
++	At least two abnormal visual field tests by Humphrey automated perimetry, as defined by computer-based objective criteria, i.e., positive results of hemimeridional analyses of threshold tests (C24–2 or C30–2 full-threshold program) and/or the presence of one or more absolute defects in the central 30 degrees (as tested with the C64 suprathreshold program; 3-zone strategy), with ophthalmologic interpretation as definite or suspect glaucomatous field loss
+	Less than two abnormal visual field tests or an inability to perform reliable automated perimetry (because of severe visual impairment or infirmity), with ophthalmologic interpretation as definite glaucomatous field loss
Optic disc	
++	At least two signs of optic disc damage present in fundus photographs and/or the ophthalmologic evaluation, including either a horizontal or vertical cup-disc ratio $\geq$0.7, narrowest remaining neuroretinal rim $\leq$0.1 disc diameters, notching, asymmetry in cup–disc ratios between eyes $>$0.2, or disc hemorrhages
+	Less than two signs of optic disc damage as described above (or unavailable photographs), with an ophthalmologic assessment or clinical record documenting definite glaucomatous optic nerve damage
Ophthalmologic examination	
++	Clinical diagnosis of definite POAG after examination by the study ophthalmologist to exclude other possible causes for disc and field changes
+	Previous POAG history and treatment and/or visual field and disc damage, although a definite POAG diagnosis was not made at the time of the BFSG visit (e.g., because of inconclusive or incomplete data); the study ophthalmologist confirmed the diagnosis through record review or rE-examination

Those with POAG had a minimum of at least one plus (+) sign in each of the three categories.

Table S6. Age and IOP by GROUP

Group	Variable	N	Mean	Std Dev	Minimum	Maximum
Affected with positive family history	AGE	218	70.2	12.0	27.0	91.0
	IOP	218	26.2	9.2	9.7	80.3
Unaffected with positive family history	AGE	36	62.8	10.8	35.0	85.0
	IOP	37	17.0	3.7	11.3	27.3
Affected with negative family history	AGE	51	74.6	10.0	49.0	93.0
	IOP	51	29.0	11.2	14.7	81.0
Unaffected with negative family history	AGE	129	60.8	9.2	48.0	91.0
	IOP	129	20.0	3.5	13.7	34.7