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Figure legends

Figure 1. Genome-wide association study for wet -type AMD susceptibility loci.

The analyseis compared 100 stage 5b AMD cases with 200 population-based controls (stage three analysis). The x-axis represents genomic locations, and the y-axis shows $-\log_{10}$ (genotypic *P*-value). All of the SNPs on autosomal chromosomes with genotypic *P* values < 0.01 are plotted.

Figure 2. Determination of statistical significant SNPs.

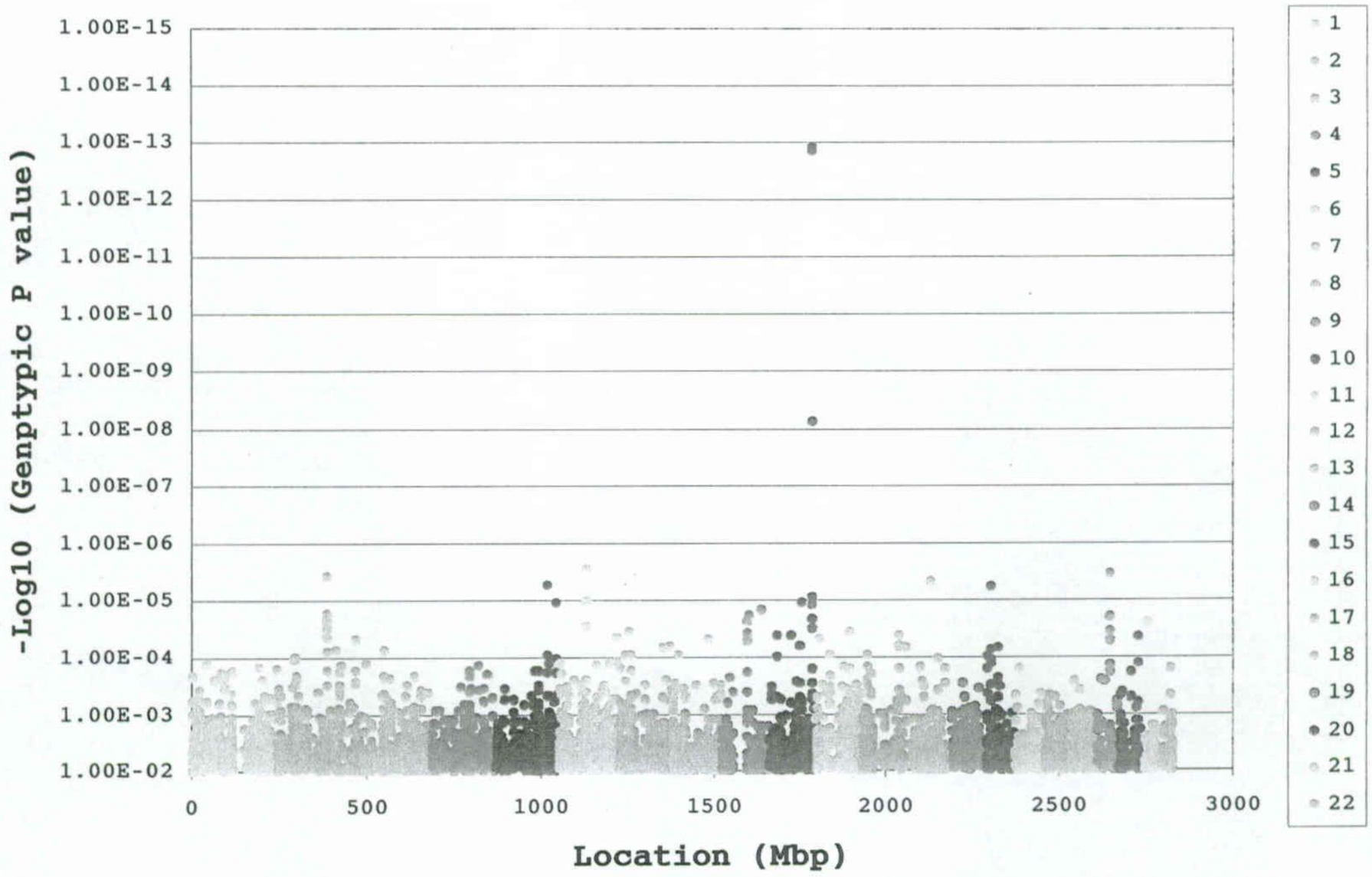
The Benjamini-Hochberg method to correct for multiple testing was used to identify SNPs significantly associated with AMD. A false discovery rate of 0.05 was used to determine statistical significance.

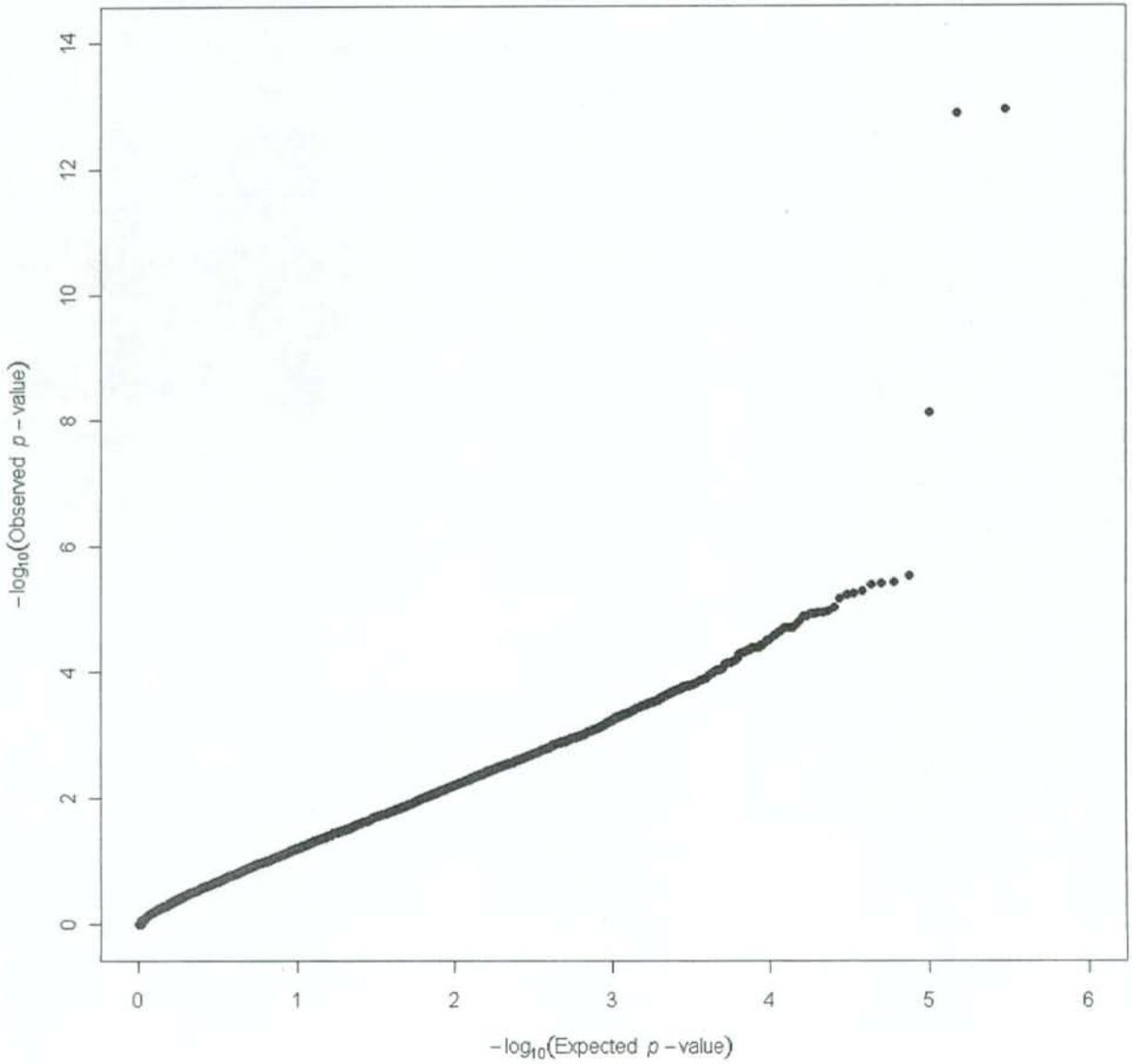
Figure 3. Haplotype block structure of the AMD-associated regions.

Squares shaded pink or red indicate significant linkage disequilibrium between SNP pairs (bright red indicates pairwise $D' = 1$), white squares indicate no evidence of significant linkage disequilibrium, and blue squares indicate pairwise $D' = 1$ without statistical significance. Locations of the regions on each chromosome are shown in scales above.

Genes within the views are shown by arrows. SNPs with a genotypic *P*- value < 10^{-6} in stage three analysis are indicated by open arrowheads. Haplotype block including these SNPs are surrounded with bold lines.

(A.) Haplotype block patterns on chromosome 10. rs10490924 and rs3750848 waere included in block two within the *LOC387715* gene region. rs2672587 is located between block two and three. rs10510110 is located on block one together with the *PLEKHA1* gene.


-Log10 (Genptypic P value)
1.00E-15
1.00E-14
1.00E-13
1.00E-12
1.00E-11
1.00E-10
1.00E-09
1.00E-08
1.00E-07
1.00E-06
1.00E-05
1.00E-04
1.00E-03
1.00E-02
0
500
1000
1500
2000
2500
3000
Location (Mbp)
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22


−log10(Observed p − value)
−log10(Expected p − value)
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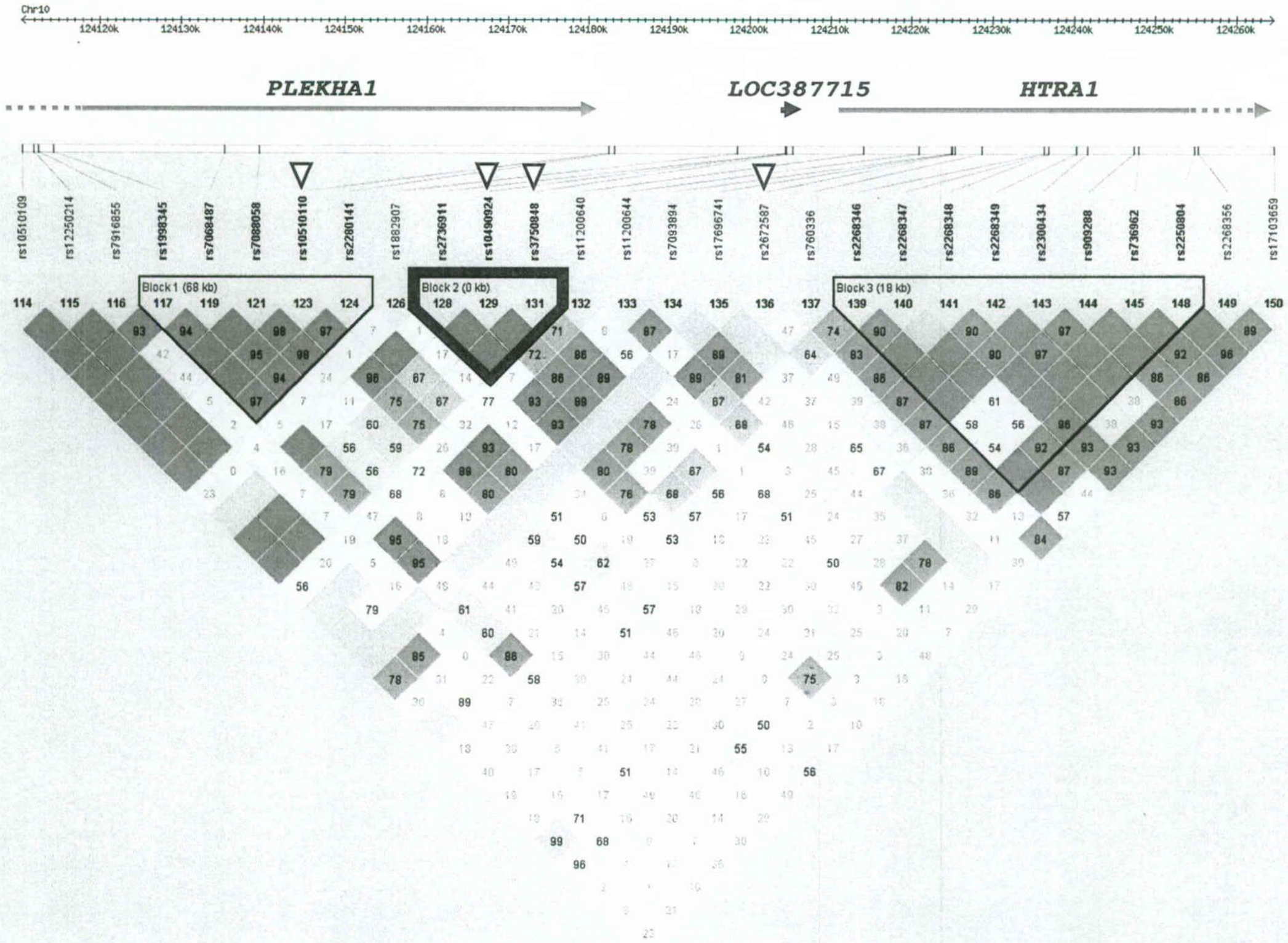
2
4
6
8
10
12
14
0
1
2
3
4
5
6


Chr10
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124130k
124140k
124150k
124160k
124170k
124180k
124190k
124200k
124210k
124220k
124230k
124240k
124250k
124260k
PLEKHA1
LOC387715
HTRA1
rs10510109
rs12250214
rs7916855
rs1998345
rs7068487
rs7088058
rs10510110
rs2280141
rs1882907
rs2736911
rs10490924
rs3750848
rs11200640
rs11200644
rs7093894
rs17696741
rs2672587
rs760336
rs2268346
rs2268347
rs2268348
rs2268349
rs2300434
rs909288
rs736962
rs2250804
rs2268356
rs17103659
Block 1 (68 kb)
Block 2 (0 kb)
Block 3 (18 kb)

Table 1. Characteristics of AMD cases and control subjects in this study

Characteristic (AMD)					
Sex -no. (%)					
Male	73 (73.00)				
Female	27 (27.00)				
Mean age at recruitment- yr (SE)					
Total	74.56 (0.88)				
Male	73.64 (0.99)				
Female	77.04 (1.83)				
Age distribution - no. (%)					
	50s	60s	70s	80s	90s
Total	7 (7.00)	24 (24.00)	34 (34.00)	34 (34.00)	1 (1.00)
Male	6 (8.22)	17 (23.29)	29 (39.72)	20 (27.40)	1 (1.37)
Female	1 (3.70)	7 (25.93)	5 (18.52)	14 (51.85)	0 (0.00)

Characteristic (Control)						
Sex - no. (%)						
Male	91 (45.5)					
Female	109 (54.5)					
Mean age at recruitment - yr (SE)						
Total	71.00 (0.75)					
Male	71.00 (1.09)					
Female	71.00 (1.03)					
Age distribution - no. (%)						
	30s	40s	50s	60s	70s	80s
Total	3 (1.5))	4 (2.00))	18 (9.00)	43 (21.50)	96 (48.00)	36 (18.00)
Male	0 (0.00)	2 (2.20)	9 (9.89)	19 (20.88)	45 (49.45)	16 (17.58)
Female	3 (2.75)	2 (1.83)	9 (8.26)	24 (22.02)	51 (46.79)	20 (18.35)

Table 2. Summary of ten SNPs analyzed in this study

SNP	Nearest gene	Location		*P* value OR (95%CI)
rs10490924	*LOC387715*	10q26	Allele	9.70×10^{-15} 4.00 (2.79-5.74)
			Genotype	2.41×10^{-13}
			Heterozygote	6.11×10^{-6} 3.61 (2.02-6.46)
			Homozygote	1.19×10^{-13} 8.29 (4.62-14.89)
rs3750848	*LOC387715*	10q26	Allele	1.65×10^{-14} 3.97 (2.77-5.69)
			Genotype	3.39×10^{-13}

			Heterozygote	1.38×10^{-13}
				3.57 (1.99-6.39)
			Homozygote	6.48×10^{-6}
				8.24 (4.59-14.80)
rs2672587	*HTRA1*	10q26	Allele	1.67×10^{-10}
				3.14 (2.20-4.48)
			Genotype	8.02×10^{-9}
			Heterozygote	1.08×10^{-5}
				3.73 (2.01-6.92)
			Homozygote	2.91×10^{-8}
				4.63 (2.68-7.98)
rs2874794	*SH3BGRL2*	6q14	Allele	5.56×10^{-6}
				2.23 (1.58-3.17)
			Genotype	6.46×10^{-6}

			Heterozygote	3.05×10^{-6}
				2.21 (1.22-3.99)
			Homozygote	0.0087
				3.93 (2.22-6.96)
rs12462443	*ZNF507*	19q13	Allele	0.00016
				1.96 (1.39-2.76)
			Genotype	1.53×10^{-5}
			Heterozygote	3.70×10^{-6}
				3.94 (2.12-7.30)
			Homozygote	0.15
				1.60 (0.87-2.95)
rs2714212	*LRP1B*	2q22	Allele	0.0084
				1.87 (1.17-2.99)
			Genotype	4.04×10^{-6}

			Heterozygote	1.68×10^{-4}
				0.32 (0.088-1.16)
			Homozygote	0.089
				2.88 (1.65-5.05)
rs9599819	*DACH1*	13q21	Allele	0.61
				1.11 (0.75-1.65)
			Genotype	5.08×10^{-6}
			Heterozygote	5.77×10^{-4}
				1.73 (1.06-2.81)
			Homozygote	0.034
rs3763022	*SH2TC2*	5q33	Allele	2.18×10^{-6}
				6.44 (2.53-16.36)
			Genotype	1.78×10^{-5}
			Heterozygote	0.17

			Homozygote	5.59×10^{-6}
				6.62 (2.54-17.22)
rs12595534	TRPM1	15q13	Allele	4.26×10^{-5}
				2.13 (1.48-3.08)
			Genotype	1.10×10^{-5}
			Heterozygote	0.011
				8.91 (2.69-29.52)
			Homozygote	5.98×10^{-6}
				1.94 (1.19-3.16)
rs10510110	*PLEKHA1*	10q26	Allele	4.93×10^{-6}
				2.35 (1.62-3.43)
			Genotype	2.07×10^{-5}
			Heterozygote	9.50×10^{-6}
				2.92 (1.25-6.81)

	Homozygote	0.014
		3.09 (1.88-5.09)

Genome positions refer to the human March 2008 (build 36.3) assembly. *P* values were calculated for three models (allele, genotype, heterozygote and homozygote) using Fisher's exact test. OR, odds ratio; CI, confidence interval. ORs and CIs were calculated using Woolf's method.

感覚器障害研究事業

緑内障の危険因子の解明による診断法の開発、緑内障マウスを用いた
視神経保護薬の開発と予防・治療法への応用
(H18 - 感覚器 - 一般 - 002)

平成18-20年度　総合研究報告書

主任研究者　　岩田　岳

平成21年3月