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An integrated map of structural variation in 2,504 human genomes

A list of authors and their affiliations appears at the end of the paper.

A large genome-wide association study of age-related macular degeneration highlights contributions of rare and common variants

Advanced age-related macular degeneration (AMD) is the leading cause of blindness in the elderly, with limited therapeutic options. Here we report on a study of >12 million variants, including 163,714 directly genotyped, mostly rare, protein-altering variants. Analyzing 16,144 patients and 17,832 controls, we identify 52 independently associated common and rare variants ($P < 5 \times 10^{-8}$) distributed across 34 loci. Although wet and dry AMD subtypes exhibit predominantly shared genetics, we identify the first genetic association signal specific to wet AMD, near *MMP9* (difference *P* value = 4.1×10^{-10}). Very rare coding variants (frequency <0.1%) in *CFH*, *CFI* and *TIMP3* suggest causal roles for these genes, as does a splice variant in *SLC16A8*. Our results support the hypothesis that rare coding variants can pinpoint causal genes within known genetic loci and illustrate that applying the approach systematically to detect new loci requires extremely large sample sizes.

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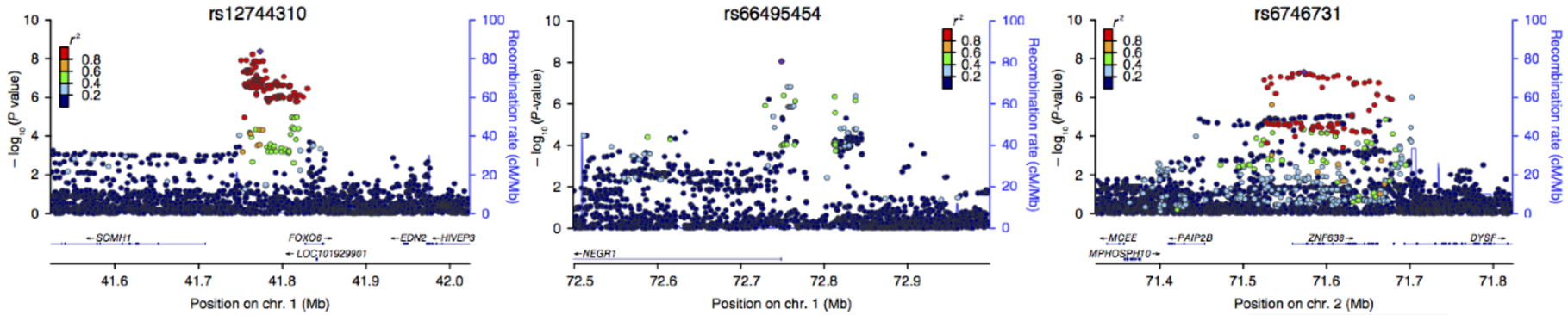

Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence

Table 1 Genomic loci and lead SNPs associated with intelligence in the meta-analysis based on $n = 78{,}308$

rsID	Annotation	Locus[a]	Ref	Alt	RefF	z	P value	Direction[b]	n	n_{GWS}
rs2490272	*FOXO3* intronic	6q21	T	C	0.63	7.44	9.96×10^{-14}	++++−+++	78,307	28
rs9320913	Intergenic	6q16.1	A	C	0.48	6.61	3.79×10^{-11}	++++−+++	78,307	13
rs10236197	*PDE1C* intronic	7p14.3	T	C	0.63	6.46	1.03×10^{-10}	+++++−++	78,286	35
rs2251499	Intergenic	13q33.2	T	C	0.26	6.31	2.74×10^{-10}	++++++++	78,307	22
rs36093924	*CYP2D7* ncRNA_intr	22q13.2	T	C	0.46	−6.31	2.87×10^{-10}	?−−?????	54,119	100
rs7646501	Intergenic	3p24.2	A	G	0.74	6.02	1.79×10^{-9}	?++−++++	65,866	5
rs4728302	*EXOC4* intronic	7q33	T	C	0.60	−5.97	2.42×10^{-9}	−−−+−−+−	78,307	45
rs10191758	*ARHGAP15* intronic	2q22.3	A	G	0.61	−5.93	3.06×10^{-9}	?−−?????	54,119	17
rs12744310	Intergenic	1p34.2	T	C	0.22	−5.88	4.20×10^{-9}	?−−−−−−−	65,866	28
rs66495454	*NEGR1* upstream	1p31.1	G	GTCCT	0.62	−5.75	9.08×10^{-9}	?−−?????	54,119	1
rs113315451	*CSE1L* intronic	20q13.13	A	ATTAT	0.43	5.71	1.15×10^{-8}	?++?????	54,119	1
rs12928404	*ATXN2L* intronic	16p11.2	T	C	0.59	5.71	1.15×10^{-8}	++++++++	78,307	19
rs41352752	*MEF2C* intronic	5q14.3	T	C	0.97	−5.68	1.35×10^{-8}	?−−?????	54,119	1
rs13010010	*LINC01104* ncRNA_intr	2q11.2	T	C	0.38	5.65	1.56×10^{-8}	++++++++	78,308	11
rs16954078	*SKAP1* intronic	17q21.32	A	T	0.21	−5.55	2.84×10^{-8}	?−−−−+−−	65,866	7
rs11138902	*APBA1* intronic	9q21.11	A	G	0.54	5.49	4.12×10^{-8}	+++++−++	78,307	1
rs6746731	*ZNF638* intronic	2p13.2	T	G	0.43	−5.46	4.88×10^{-8}	−−−−−+−−	78,307	1
rs6779302	Intergenic	3p24.3	T	G	0.37	−5.45	4.99×10^{-8}	?−−?????	54,119	1