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Mapping of Gene Expression Reveals CYP27A1 as a Susceptibility Gene for Sporadic ALS

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Published in:
 PLoS ONE

DOI:
[10.1371/journal.pone.0035333](https://doi.org/10.1371/journal.pone.0035333)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
 Publisher's PDF, also known as Version of record

Publication date:
 2012

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Diekstra, F. P., Saris, C. G. J., van Rheenen, W., Franke, L., Jansen, R. C., van Es, M. A., van Vught, P. W. J., Blauw, H. M., Groen, E. J. N., Horvath, S., Estrada, K., Rivadeneira, F., Hofman, A., Uitterlinden, A. G., Robberecht, W., Andersen, P. M., Melki, J., Meininger, V., Hardiman, O., ... Brown Jr., R. H. (2012). Mapping of Gene Expression Reveals CYP27A1 as a Susceptibility Gene for Sporadic ALS. *PLoS ONE*, 7(4), Article e35333. <https://doi.org/10.1371/journal.pone.0035333>

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Locus	Illumina probe identifier	SNP	Minor allele	LD with index SNP (rs4674345) r^2	GWAS discovery SNP association		GWAS replication SNP association		Joint GWAS SNP association		eQTL p value after permutations		Expression variance explained (R^2)
					OR	p	OR	p	OR	p	Discovery	Replication	Combined data
<i>CYP27A1</i> ,													
Chr. 2	ILMN_1704985	rs4674345	G	1	1.08	0.049	1.23	1.32×10^{-4}	1.12	1.84×10^{-4}	1.65×10^{-46}	1.19×10^{-47}	0.62
		rs2303565	G	0.66	1.09	0.020	1.22	2.25×10^{-4}	1.13	8.79×10^{-5}	2.35×10^{-42}	2.34×10^{-35}	0.57
		rs1554622	C	0.79	1.09	0.027	1.19	1.00×10^{-3}	1.11	3.98×10^{-4}	2.93×10^{-56}	1.27×10^{-51}	0.65
		rs7607369	A	0.58	1.09	0.017	1.19	1.06×10^{-3}	1.12	2.61×10^{-4}	6.27×10^{-35}	1.08×10^{-32}	0.55
		rs1863704	A	0.55	1.10	0.016	1.18	2.37×10^{-3}	1.12	2.26×10^{-4}	1.75×10^{-31}	3.98×10^{-28}	0.52
		rs3770214	A	0.54	1.10	0.016	1.17	3.95×10^{-3}	1.12	3.14×10^{-4}	1.05×10^{-31}	3.07×10^{-27}	0.52
		rs4674338	A	0.66	1.09	0.020	1.16	6.46×10^{-3}	1.11	7.51×10^{-4}	1.70×10^{-42}	1.26×10^{-42}	0.59
		rs921968	C	0.39	1.09	0.020	1.15	0.012	1.11	7.88×10^{-4}	1.06×10^{-26}	1.71×10^{-22}	0.48

The direction of effect for all SNP-transcript pairs was the same; for each SNP, the minor allele was associated with increased *CYP27A1* expression levels. LD estimates with SNP rs4674345 and SNP association results in the joint GWAS data were based on a total of 3,568 ALS patients and 10,163 controls. The gene expression explained variance (R^2) was estimated from expression data from both discovery and replication eQTL datasets combined. *CYP27A1*, cytochrome P450, family 27, subfamily A, polypeptide 1; Chr., chromosome; LD, linkage disequilibrium; GWAS, genome-wide association study; OR, odds ratio; eQTL, expression quantitative trait locus; ALS, amyotrophic lateral sclerosis.