Electronic Supplementary Material

TMEM106B protects *C9ORF72* expansion carriers against frontotemporal dementia

Marka van Blitterswijk, Bianca Mullen, Alexandra M. Nicholson, Kevin F. Bieniek, Michael G. Heckman, Matthew C. Baker, Mariely DeJesus-Hernandez, NiCole A. Finch, Patricia H. Brown, Melissa E. Murray, Ging-Yuek R. Hsiung, Heather Stewart, Anna M. Karydas, Elizabeth Finger, Andrew Kertesz, Eileen H. Bigio, Sandra Weintraub, Marsel Mesulam, Kimmo J. Hatanpaa, Charles L. White III, Michael J. Strong, Thomas G. Beach, Zbigniew K. Wszolek, Carol Lippa, Richard Caselli, Leonard Petrucelli, Keith A. Josephs, Joseph E. Parisi, David S. Knopman, Ronald C. Petersen, Ian R. Mackenzie, William W. Seeley, Lea T. Grinberg, Bruce L. Miller, Kevin B. Boylan, Neill R. Graff-Radford, Bradley F. Boeve, Dennis W. Dickson, and Rosa Rademakers

Corresponding author: Rosa Rademakers, PhD, Department of Neuroscience, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, USA. Email: Rademakers.Rosa@mayo.edu

Contents: Online Resource Table 1-2

Table 1: Associations of *TMEM106B* rs3173615 with disease when considering rs3173615 under a recessive model – analysis of extended cohort 1 (260 probands and 786 controls) and cohort 2 (586 patients and 1,302 controls)

			***TMEM106B* rs3173615 genotype information**			**Comparison with controls under a recessive model**	
Group	**N**	**MAF**	**CC**	**CG**	**GG**	**OR (95% CI)**	**P-value**
Cohort 1 – all available controls and *C9ORF72* repeat expansion carrier probands (FTD, FTD/MND, MND)							
Controls	786	40.5%	285 (36.3%)	366 (46.5%)	135 (17.2%)	1.00 (reference)	N/A
FTD, FTD/MND, and MND patients	260	38.8%	89 (34.2%)	140 (53.8%)	31 (11.9%)	0.66 (0.43 – 0.99)	0.044
FTD patients	69	35.5%	25 (36.2%)	39 (56.5%)	5 (7.2%)	0.38 (0.15 – 0.96)	0.020
FTD/MND patients	71	42.3%	17 (23.9%)	48 (67.6%)	6 (8.5%)	0.44 (0.16 – 0.97)	0.040
MND patients	120	38.8%	47 (39.2%)	53 (44.2%)	20 (16.7%)	0.97 (0.58 – 1.62)	0.91
Cohort 2 – all available controls and FTD or FTD/MND patients without *C9ORF72* repeat expansions or *GRN* mutations							
Controls	1302	41.4%	464 (35.6%)	598 (45.9%)	240 (18.4%)	1.00 (reference)	N/A
FTD and FTD/MND patients	586	39.3%	213 (36.3%)	285 (48.6%)	88 (15.0%)	0.78 (0.60 – 1.02)	0.068
FTD patients	531	39.8%	187 (35.2%)	265 (49.9%)	79 (14.9%)	0.77 (0.59 – 1.02)	0.065
Pathologically diagnosed	101	30.6%	45 (44.6%)	50 (49.5%)	6 (5.9%)	0.27 (0.12 – 0.63)	<0.001
Clinically diagnosed	430	42.0%	142 (33.0%)	215 (50.0%)	73 (17.0%)	0.92 (0.69 – 1.22)	0.55

FTD=frontotemporal dementia; MND=motor neuron disease; OR=odds ratio; CI=confidence interval; MAF=minor allele frequency. ORs, 95% CIs, and p-values result from logistic regression models where rs3173615 was considered under a recessive model (GG vs. CC or CG). For cohort 1, models were adjusted for gender. For cohort 2, models were adjusted for age (age at blood draw in controls, age at diagnosis in clinically diagnosed patients, and age at death in pathologically diagnosed patients) and gender.

Table 2: Associations of *TMEM106B* rs3173615 with disease when considering rs3173615 under other models

			Comparison with controls under an additive model		Comparison with controls under a dominant model		Comparison with controls under a co-dominant model: CG vs. CC		Comparison with controls under a co-dominant model: GG vs. CC	
Group	**N**	**MAF**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Cohort 1 – controls and *C9ORF72* repeat expansion carrier probands (FTD, FTD/MND, MND)										
Controls	376	43.2%	1.00 (reference)	N/A	1.00 (reference)	N/A	1.00 (reference)	N/A	1.00 (reference)	N/A
FTD, FTD/MND, and MND patients	260	38.8%	0.83 (0.66 – 1.05)	0.11	0.94 (0.67 – 1.31)	0.70	1.07 (0.75 – 1.52)	0.70	0.60 (0.36 – 0.99)	0.044
FTD patients	69	35.5%	0.72 (0.49 – 1.05)	0.087	0.86 (0.50 – 1.47)	0.57	1.06 (0.61 – 1.85)	0.83	0.35 (0.12 – 0.93)	0.036
FTD/MND patients	71	42.3%	0.96 (0.66 – 1.39)	0.83	1.55 (0.86 – 2.80)	0.13	1.94 (1.07 – 3.55)	0.030	0.60 (0.23 – 1.59)	0.30
MND patients	120	38.8%	0.83 (0.62 – 1.12)	0.22	0.75 (0.49 – 1.14)	0.18	0.76 (0.48 – 1.19)	0.23	0.73 (0.40 – 1.32)	0.30
Cohort 2 – controls and FTD or FTD/MND patients without *C9ORF72* repeat expansions or *GRN* mutations										
Controls	765	41.0%	1.00 (reference)	N/A	1.00 (reference)	N/A	1.00 (reference)	N/A	1.00 (reference)	N/A
FTD and FTD/MND patients	586	39.3%	0.93 (0.80 – 1.09)	0.38	1.01 (0.81 – 1.26)	0.94	1.09 (0.86 – 1.39)	0.47	0.81 (0.59 – 1.12)	0.20
FTD patients	531	39.8%	0.95 (0.81 – 1.11)	0.54	1.06 (0.84 – 1.34)	0.61	1.16 (0.91 – 1.48)	0.23	0.83 (0.59 – 1.15)	0.26
Pathologically diagnosed	101	30.6%	0.66 (0.48 – 0.90)	0.008	0.75 (0.49 – 1.16)	0.20	0.98 (0.63 – 1.53)	0.92	0.26 (0.10 – 0.62)	0.003
Clinically diagnosed	430	42.0%	1.05 (0.89 – 1.24)	0.59	1.17 (0.91 – 1.51)	0.21	1.23 (0.95 – 1.61)	0.21	1.03 (0.73 – 1.46)	0.88

FTD=frontotemporal dementia; MND=motor neuron disease; OR=odds ratio; CI=confidence interval; MAF=minor allele frequency. ORs, 95% CIs, and p-values result from logistic regression models where rs3173615 was considered under an additive model (effect of each additional G allele), a dominant model (CG or GG vs. CC), and a co-dominant model (CG vs. CC and GG vs. CC separately). For cohort 1, models were adjusted for gender. For cohort 2, models were adjusted for age (age at blood draw in controls, age at diagnosis in clinically diagnosed patients, and age at death in pathologically diagnosed patients) and gender.