

Table e-1. The genotyping results of known *C9orf72* genetic modifiers (*TMEM106B* rs1990622, *TMEM106B* rs3173615 and *ATXN2* CAG repeats).

Sample	TMEM106B rs1990622	TMEM106B rs3173615	ATXN2 CAG repeats
9548	AA	CC	22/22
9686	AG	CG	22/22

Note: Intermediate *ATXN2* alleles (27–33 CAG-repeats) were reported as modifiers in *C9orf72* carriers, rendering susceptibility to ALS ⁷. The homozygosity for the minor allele (G) of rs3173615 in *TMEM106B* was reported to protect against developing FTD in *C9orf72* patients ⁸. The major allele (A) of rs1990622 (conferring risk for developing FTL) was associated to later age of onset and age of death in *C9orf72* patients ⁹. These results were not able to explain the phenotype difference between 9548 and 9686.

Table e-2. The CpG methylation status in the 5' region close to the *C9orf72* repeats in the tissues of 9686. M represents methylated site; U represents unmethylated site.

CpG site	Frontal cortex	Motor cortex	Occipital cortex	Hippocampus	Thalamus	Brain stem	Temporal cortex	Cerebellum	Heart	Liver	Kidney	Lung	Tongue	Testicles	Epididymis	Cervical spinal cord	Thoracic spinal cord	Lumbar spinal cord
1	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
2	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
3	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
4	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
5	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
6	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
7	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
8	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
9	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
10	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
11	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
12	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
13	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
14	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
15	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
16	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
17	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
18	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
19	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
20	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
21	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
22	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
23	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
24	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
25	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
26	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U

Table e-3. The CpG methylation status in the 3' region close to the *C9orf72* repeats in the tissues of 9686. M represents methylated site; U represents unmethylated site.

CpG site	Frontal cortex	Motor cortex	Occipital cortex	Hippocampus	Thalamus	Brain stem	Temporal cortex	Cerebellum	Heart	Liver	Kidney	Lung	Tongue	Testicles	Epididymis	Cervical spinal cord	Thoracic spinal cord	Lumbar spinal cord
1	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
2	U	U	U	U	U	M	U	U	U	U	U	U	U	U	U	U	U	U
3	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
4	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
5	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
6	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
7	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
8	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
9	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	M	U
10	U	U	U	M	U	U	U	U	M	U	M	U	U	U	U	M	U	U
11	U	U	M	M	U	U	U	U	U	M	U	U	U	U	U	U	U	U
12	U	U	M	U	U	U	U	U	U	M	U	M	U	U	U	M	M	U
13	U	U	U	U	U	U	U	U	U	M	U	U	U	U	U	U	U	U
14	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	M
15	U	U	U	U	U	M	U	U	U	U	U	U	U	U	U	U	U	U
16	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
17	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
18	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
19	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	M	M
20	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
21	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
22	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U

Table e-4. *C9orf72* repeat size in multiple tissues of small expansion carriers according to previous studies. NA represents not available.

Studies ⁹	Sample ID	Pheno-type	Age of onset, years	Duration, years	Blood	Frontal cortex	Temporal cortex	Cerebellum	Spinal cord	Occipital	Parietal lobe	Spleen	Heart	Muscle	Kidney	Dura Mater	Cauda Equina	RNA foci	DPR	TDP43	
Van Blitterswijk et al. 2013 ¹⁰	P20	MND-FTD	NA	NA	small	large(smear)	Large (smear)	large (dominant)	small/large(smear)	small/large(smear)	small/large	small/medium	Small	small/medium							
Fratia et al. 2015 ¹¹	61776	ALS	57	6	small (90)	small/large		large (dominant)	small/large							small	small	SF and ASF: FC, HC, CBL, HC	HC, CBL	SC	
Gijssels et al. 2016 ¹²	DR439.1	FTLD	54	15	small (56)	small(weak)/large(smear)	small(weak)/large(smear)	large (dominant)												FC, HC, CBL	HC, FC
Nordin et al. 2015 ¹³	P9	ALS	63	2	small (61)	small(weak)/large		large (dominant)	small/large		small/large	small/large	small	small	small						
Nordin et al. 2015 ¹³	P11	MND	75	5	small (92)	small(weak)/large		large (dominant)	small(weak)/large					small							

Only those studies that had both CNS and non-CNS tissues were included.

Reference:

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