Frequent *SLC35A2* brain mosaicism in mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy (MOGHE)

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SUPPLEMENTARY FILES

Supplemental data Full list of genes included in the panel

PIK3CA (NM_006218), *PIK3R2* (NM_005027), *PIK3R1* (NM_181523), *PTEN* (NM_000314), *AKT1* (NM_005163), *AKT2* (NM_001626), *AKT3* (NM_005465), *GSK3B* (NM_002093), *GSK3A* (NM_019884), *MTOR* (NM_004958), *TSC1* (NM_000368), *TSC2* (NM_000548), *TBC1D7* (NM_016495), *DEPDC5* (NM_001242896), *NPRL2* (NM_006545), *NPRL3* (NM_001077350), WDR24 (NM_032259), MIOS (NM_019005), SEC13 (NM_183352), *WDR59* (NM_030581), *SEH1L* (NM_001013437), *RHEB* (NM_005614), *RHEBL1* (NM_144593), *RRAGA* (NM_006570), *RRAGB* (NM_016656), *RRAGC* (NM_022157), *RRAGD* (NM_021244), *BMT2* (NM_152556), *DEPTOR* (NM_022783.3), *RPTOR* (NM_020761), *MLST8* (NM_001199173.1), *AKT1S1* (NM_032375), *RICTOR* (NM_001285439.1), *PRR5* (NM_001198721), *PRR5L* (NM_024841), *MAPKAP1* (NM_001006617), *PDPK1* (NM_002613), *RPS6KB1* (NM_003161.3), *RPS6KB2* (NM_003952), *SESN1* (NM_014454), *SESN2* (NM_031459), *SESN3* (NM_144665.3), *CASTOR1* (NM_001037666), *CASTOR2* (NM_001145064), *FLCN* (NM_144997), *KPTN* (NM_007059), *SZT2* (NM_015284.3), *ITFG2* (NM_018463), *C12ORF66* (NM_001300940), DDIT4 (NM_019058), *LAMTOR1* (NM_017907), *LAMTOR2* (NM_014017), *LAMTOR3* (NM_021970), *LAMTOR4* (NM_001008395.3), *LAMTOR5* (NM_006402), *SLC38A9* (NM_173514), *SLC35A2* (NM_005660.2), *KRT1* (NM_006121), *KRT10* (NM_000421), *SRY* (NM_003140).

Supplementary Table 1 Neuropathological reassessment of multicentric cohort of 43 MCD cases

Patient ID	Initial histology	Histology reclassified	Genetic findings	Previous report
FR-1	mMCD2, blurred grey-white matter border*	MOGHE	SLC35A2:p.Tyr267*	Baldassari *et al.* 2019
FR-2	mMCD2, blurred grey-white matter border, increased oligodendrocytes density*	MOGHE	SLC35A2:p.Ser212Leu*fs**9	Baldassari *et al.* 2019
FR-3	mMCD2, blurred grey-white matter border*	MOGHE	SLC35A2:p.Leu296del	Baldassari *et al.* 2019
FR-4	mMCD2, blurred grey-white matter border, increased oligodendrocytes density, white matter pallor*	MOGHE	SLC35A2:p.Pro269Thr*fs**25	Baldassari *et al.* 2019
FR-5	FCD unclassified	MOGHE	SLC35A2:p.Leu307_Val310del	unpublished
FR-6	Not conclusive (fragmented tissue)	Not conclusive (fragmented tissue)	SLC35A2: p.His96Pro*fs**7	unpublished
FR-7	mMCD2	mMCD	Panel-negative	Baldassari *et al.* 2019
FR-8	mMCD2	mMCD	Panel-negative	Baldassari *et al.* 2019
FR-9	mMCD2	mMCD	Panel-negative	Baldassari *et al.* 2019
FR-10	mMCD2	MCD with gliosis and possible sEEG-induced infarction	Panel-negative	Baldassari *et al.* 2019
FR-11	FCD1b	MCD with possible sEEG-induced infarction	Panel-negative	Baldassari *et al.* 2019
FR-12	FCD1	FCD3d with L4 necrosis	Panel-negative	Baldassari *et al.* 2019

FR-13	FCD1a	FCD1a	Panel-negative	Baldassari *et al.* 2019
FR-14	FCD1a	Likely mMCD	Panel-negative	Baldassari *et al.* 2019
FR-15	mMCD2	mMCD	Panel-negative	unpublished
FR-16	FCD1b	HS type I and mMCD	Panel-negative	Baldassari *et al.* 2019
FR-17	mMCD2	mMCD	Panel-negative	Baldassari *et al.* 2019
FR-18	FCD1a	No HS, temporal cortex	Panel-negative	Baldassari *et al.* 2019
FR-19	FCD1	Ulegyria or HET	Panel-negative	Baldassari *et al.* 2019
FR-20	mMCD2	Infarction	Panel-negative	Baldassari *et al.* 2019
NL-1	mMCD2	MOGHE	SLC35A2:p.Gln129*	unpublished
NL-2	mMCD2	MOGHE	SLC35A2:p.Gln185*	unpublished
NL-3	FCD2a	FCD 2a	DEPDC5:p.Thr1385*fs*	unpublished
NL-4	FCD2a	FCD 2a	DEPDC5:p.Ala1386*fs*	unpublished
NL-5	FCD2a	FCD 2a	DEPDC5:p.Asn1353*fs*	unpublished
NL-6	FCD2a	FCD 2a	DEPDC5:p.Gly756*fs*	unpublished
KR-1	mMCD	MOGHE	SLC35A2:p.Asn235His	Sim *et al.* 2018
KR-2	Gliosis	MOGHE	*SLC35A2*:c.275-1G>T	Sim *et al.* 2018
KR-3	No abnormality	MOGHE	SLC35A2:p.Gln185*	Sim *et al.* 2018
KR-4	mMCD	MOGHE	SLC35A2:p.Glu254*	Sim *et al.* 2018
KR-5	mMCD	MOGHE	SLC35A2:p.Gln197*	Sim *et al.* 2018
KR-6	mMCD	MOGHE	SLC35A2:p.Gln168*	Sim *et al.* 2018
KR-7	Gliosis	MOGHE	SLC35A2:p.Leu120Pro	Sim *et al.* 2019
KR-8	Gliosis	MOGHE	SLC35A2:p.Gly281Asp	Sim *et al.* 2019
KR-9	Gliosis	MOGHE	SLC35A2:p.Leu224Pro	Sim *et al.* 2019
KR-10	mMCD	MOGHE	SLC35A2:p.Leu120His*fs**7	unpublished

KR-11	FCD2a	FCD2a	DEPDC5:p.Gln372*	Sim *et al.* 2019
KR-12	FCD2b	FCD2a	DEPDC5:p.Phe1399*fs* DEPDC5:p.Thr1508*fs*	Sim *et al.* 2019
KR-13	FCD2a	FCD2a	DEPDC5:p.Trp1213*	Sim *et al.* 2019
KR-14	FCD2a	FCD2a	DEPDC5:p.Arg1268*	Sim *et al.* 2019
KR-15	mMCD	FCD2a	*DEPDC5*:c.3021+1G>A	Sim *et al.* 2019
KR-16	FCD2a	FCD2a	DEPDC5:p.Arg1136*	Sim *et al.* 2019
KR-17	No abnormality	Inconclusive	DEPDC5:c.1324+1G>A	Sim *et al.* 2019

GM: grey matter; WM: white matter; mMCD: mild Malformations of Cortical Development; FCD: Focal Cortical Dysplasia; sEEG: stereo EEG; HS: Hippocampal Sclerosis; HET: Heterotopia.

Supplementary Table 2 Clinical comparisons between SLC35A2-mutated and panel-negative MOGHE cases

	MOGHE *SLC35A2*-mutated cases (n=26)	**MOGHE without variant identified (n=11)**	**p-value**
Age at epilepsy onset (years, mean)	1.3 [0.25-7]	2.1 [0.25-6.25]	0.13
Duration of epilepsy before surgery (years, mean)	4.4 [1-16.7]	6.9 [0.33-21.8]	0.29
Infantile spasms (%)	77% (n=20/26)	36% (n=4/11)	**0.01**
Tonic seizures (%)	66% (n=12/18)	90% (n=10/11)	0.13
Myoclonic seizures (%)	31% (n=8/26)	45% (n=5/11)	0.39
Autistic features (%)	31% (n=8/24)	27% (n=3/11)	0.72
Developmental delay (including mild, moderate and severe) (%)	92% (n=24/26)	90% (n=10/11)	0.88
Good post-operative outcome (Engel I-II, %)	77% (n=20/26)	80% (n=8/10)	0.84
Poor post-operative outcome (Engel III-IV, %)	23% (n=6/26)	20% (n=2/10)	0.84
Multiple surgeries (%)	15% (n=4/26)	9% (n=1/11)	0.6

MOGHE *SLC35A2*-mutated cohort (n=26) was obtained associating German *SLC35A2*-MOGHE cases identified in this study (n=9) together with multicentric histologically reassessed *SLC35A2*-MOGHE cases (n=5 from France, n=10 from Republic of Korean and n=2 from the Netherlands). MOGHE patients without variant identified (n=11) correspond to panel-negative German MOGHE cases. All percentages are presented based on each available patient's characteristics. Statistical analysis were performed using Chi-2 test for percentages comparisons and Wilcoxon test for mean comparisons.