AWMGS
All Wales Medical Genomics Service

Severe Infantile Epilepsy 116 Gene Panel

Background

This panel of 116 genes is designed to assist in the diagnosis of genetic forms of severe infantile epilepsy. Epileptic encephalopathies are characterized by recurrent intractable seizures and persistent abnormality of cortical function which results in impaired cognitive, sensory and motor development. In the majority of patients, the epilepsy is caused by structural brain malformations, acquired brain insults or inborn errors of metabolism. However, a proportion of cases have a genetic cause. Identification of a causative variant provides information on prognosis, avoids unnecessary investigations, informs treatment and is useful for genetic counselling.

Genes

For a full list of genes included in this panel please see below.

Recommended Clinical Referral Criteria

For testing criteria, please refer to the NHS England Early Onset or Syndromic Epilepsy (Test R59) at the following link: https://www.england.nhs.uk/wp-content/uploads/2018/08/rare-and-inherited-disease-eligibility-criteria-march-19.pdf

Genomic analysis

Diagnostic screening by sequence analysis **Next Generation Sequencing (NGS):** Target genes are enriched using an Illumina TruSight One assay and sequenced on an Illumina HiSeq. This assay aims to cover the coding sequence and 5bp of flanking intron to a minimum vertical depth of 20X. Where this is not achieved (i.e. % horizontal coverage is less than 100%) due to design or patient-specific gaps then Sanger sequencing is available for some of the genes on request. The selection of gaps to be filled may be guided by the patient's phenotype or by interaction with the referring clinician
Family follow-up: Testing for known familial pathogenic variants in any of the genes in the panel

Full Gene List

ABAT	COL4A2	HCN1	NHLRC1	SLC9A6
ADSL	CPA6	HLCS	NRXN1	SMS
ALDH7A1	CSTB	HNRNPU	**PCDH19**	SPTAN1
ALG13	CTSD	IQSEC2	PIGA	SRPX2
ARHGEF9	DIAPH1	ITPA	PLCB1	ST3GAL3
ARID1B	DNM1	KCNA1	PNKP	**STXBP1**
ARX	DPYD	KCNJ10	PNPO	SUOX
ATP1A2	DYRK1A	KCNMA1	POLG	SYNGAP1
ATP1A3	EFHC1	KCNQ2	PPT1	TBC1D24
ATRX	EHMT1	KCNQ3	PRICKLE1	TBL1XR1
BTD	EPM2A	KCTD7	PRODH	TCF4*
CACNA1A	**FOXG1***	KIAA1279	PRRT2	TPP1
CACNA1H	GABRA1	KIAA2022	RANBP2	TRPM6
CASK	GABRB3	LGI1	SCARB2	TSC1
CDKL5*	GABRG2	MAGI2	SCN1A	UBE2A
CHD2	GAMT	MBD5	SCN1B	UBE3A
CHRNA2	GLRA1	**MECP2***	SCN2A	WDR45
CHRNA4	GLYCTK	**MEF2C***	SCN8A	WDR45B
CHRNB2	GOSR2	MFF	SCN9A	WWOX
CLN3	GPHN	MFSD8	SLC16A2	ZEB2
CLN6	GRIN1	MOCS1	SLC25A22	
CLN8	GRIN2A	MOCS2	SLC2A1	
CNTNAP2	GRIN2B	MOGS	SLC6A1	
COL4A1	GSS	NEDD4L	SLC6A8	

For cases where NGS panel analysis has not identified a genetic cause of the patient's condition, bi-directional sequence analysis of the entire coding regions of those genes in the table above marked in **BOLD** text and MLPA for those marked with an asterisk (*) are available as second line tests for patients referred through the specialty of Clinical. This testing strategy is available by arrangement only. Please contact the laboratory to discuss your requirements.

Test (price available on request)	TAT (Calendar days)
Severe infantile epilepsy panel screen	84
Testing for known familial variants in panel genes	42
Testing for known familial (likely) pathogenic variants in panel genes during the prenatal period (please contact the laboratory in advance to arrange this)	3

Contact Details
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http://www.wales.nhs.uk/AWMGS/
Accredited to ISO 15189:2012 (8988)

Sample Requirements
Blood – 5ml in EDTA (1ml neonates/infants);
Please contact lab prior to sending a prenatal sample.
Please label samples with three identifiers and date of collection
All samples must be accompanied by request form
Consent for testing & DNA storage is assumed when request for test received

Links
Orphanet - http://www.orpha.net/
EDDNAL - http://www.eddnal.com/
OMIM - http://www.omim.org/
Gene Testing Registry - http://www.ncbi.nlm.nih.gov/gtr/

Support
http://www.epilepsy.org.uk/
http://www.cafamily.org.uk/medical-information/conditions/w/west-syndrome/
http://youngepilepsy.org.uk/